Antiretroviral therapy in a community clinic — early lessons from a pilot project

Linda-Gail Bekker, Catherine Orrell, Larissa Reader, Kwezi Matoti, Karen Cohen, Rob Martell, Fareed Abdullah, Robin Wood

Objectives. To report on operational and clinical problems encountered during the first 6 months of a community-based antiretroviral therapy (ART) programme.

Methods. ART was implemented in a primary care setting utilising an easily replicable service-delivery model based on a medical officer and nurse. Therapeutic counsellors, themselves HIV-infected, provided counselling and adherence support. Drug and monitoring costs were charitably funded and provincial health authorities supplied the medical infrastructure. The HIV Research Unit, University of Cape Town, supplied training and additional clinical support. Local HIV primary care clinics provided patient referrals. Standardised ART regimens were used with strict entry criteria (AIDS or CD4 count < 200 cells / µl).

Results. Demand for the service was high. Referred patients had advanced disease (AIDS 57%, median CD4 count 96 / µl) and high pre-treatment mortality (83 / 100 person-years). Mycobacterial disease was a major contributor to this mortality (40%). Scheduled clinic visit hours were six times higher during recruitment than maintenance. Attributable costs were: drugs 61%, staff 27%, viral load and CD4 cell counts 10% and safety monitoring 2%. Viral load after 16 weeks of therapy was < 400 copies / ml in the first 16 patients.

Conclusions. ART can be successfully implemented within a primary care setting. Drug purchases and staff salaries drive programme costing. The service model is capable of managing 250 - 300 patients on chronic ART, but staffing needs to be increased during recruitment. Attention must be given to the diagnosis of tuberculosis during screening and early ART. Incorporating therapeutic counsellors into the programme increased community involvement and utilised a valuable and previously untapped resource.

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Combination antiretroviral therapy (ART) has substantially improved the prognosis of HIV-infected individuals, resulting in a precipitous drop in AIDS-related mortality in affluent countries.[1-3] In contrast, in the most heavily burdened developing countries of the world, the response to the epidemic has focused on prevention. Prevention strategies have not been successful and the combination of large numbers of HIV-infected individuals compounded by unequal access to medical resources, has resulted in an ever-widening life expectancy gap between wealthy and developing countries.[4] In response to this crisis, the World Health Organisation (WHO) has called for expanded access to ART in resource-poor countries.[5] ART programmes have been successfully incorporated into highly divergent medical environments. Brazil, a middle-income developing country, has incorporated ART into its public health system[6] and a successful ART programme has been implemented in rural Haiti, the poorest country in the Western hemisphere.[7]

HIV Research Unit, University of Cape Town, and Provincial Administration of the Western Cape
Linda-Gail Bekker, MB ChB, FCP(SA), DTM&H, PhD
Robin Wood, BSc, BM, DTM&H, MMed, FCP

HIV Research Unit, University of Cape Town
Catherine Orrell, MB ChB, MSc Med (Clin Pharmacol)
Larissa Reader, MB ChB

HIV Research Unit and Division of Pharmacology, University of Cape Town
Karen Cohen, MB ChB, MCFP(SA)

Community Health Service Organisation, Western Cape Provincial Health Department and Provincial Administration of the Western Cape
Kwezi Matoti, MB ChB, BSc
Rob Martell, MB ChB, BSc, FCP(SA), MBA

Provincial Administration of the Western Cape
Fareed Abdullah, MB ChB, BSc Hons (Epidemiol)

The Usapho Lwethu *Project Team, from left to right: Dr Kwezi Matoti, Poppy, Nomaroma, Mtateleli, Nobafundi, Sr Felicity Cope, Noluvo and Nonsikelelo.*

In South Africa, AIDS is now the major cause of death among young adults.[8] While ART is available to thousands of South Africans in the private medical sector,[9] there is little or no ART access in the public sector, despite demands for such therapy from the HIV-infected community.[10] It has been argued that 'where HIV is the leading cause of death, a basic minimum package that does not include antiretrovirals is not worthy of the name'.[7]

In this paper we report on the initial medical, ethical and logistic challenges of initiating a community-based ART pilot project in a district where there is an existing network of HIV primary health care (PHC) clinics. The project was called *Usapho Lwethu* (My Family), since treatment was offered to individuals and their partners and children wherever appropriate. An easily replicable service delivery model was chosen based on a team consisting of a medical officer, nurse and therapeutic counsellors. In order to minimise operational complexity, standardised ART regimens were used[11,12] which complied with international[5] and national treatment guidelines.[13] To facilitate expansion of this or similar service delivery models for ART elsewhere in South Africa, there is urgent need to report and share knowledge of the operational challenges that need to be overcome.[10]

Methods

The ART clinic was situated in the Guguletu Community Health Centre in the Nyanga district of Cape Town, which has a population of 325 436 (projected figure from 1996 census data). There are 10 primary care HIV clinics within the district, which served as the patient referral base. Each clinic had trained staff able to provide voluntary testing and counselling services together with prophylaxis and outpatient management of common HIV opportunistic infections. Patients requiring inpatient care were referred to a local 200-bed secondary hospital.

Funding for antiretroviral medication, viral load measurements and CD4 cell counts, sufficient for 150 patients, was provided by UK-based charities. The local Community Health Service Organisation and AIDS Directorate of the Western Cape provided clinic space and medical support services, together with dedicated clinic staff, consisting of a medical officer and nurse. Training, clinical support, protocol development and programme evaluation were provided by the HIV Research Unit of the University of Cape Town.

In August 2002, medical staff of the referring PHC clinics were invited to workshops, where eligibility criteria and patient referral mechanisms were discussed. Referring doctors were requested to select suitable drug-naïve candidates from their regular clinic attendees and to fax contact details and a medical summary to the programme nurse. The medical criteria for ART eligibility were either a prior AIDS diagnosis or a CD4 cell count less than 200 cells / µl.[5]

Branded medications registered with the Medicines Control Council of South Africa were used in standard doses. ART consisted of two schedules, an initial non-nucleoside reverse transcriptase (NNRTI)-based regimen of stavudine (d4T), lamivudine (3TC) and efavirenz (nevirapine was substituted for efavirenz in women of child-bearing potential), with a second protease inhibitor (PI)-based regimen of zidovudine (AZT), didanosine (ddI) and Kaletra. Medication was sourced from a single pharmaceutical supplier with a rapid delivery turnaround time, to minimise on-site drug stocks. Drugs were packaged for each named patient and supplied in 4 x 30 day packs and stored in a secure locked section of the main clinic pharmacy.

During September 2002, the first patients were recruited into the programme, with a schedule of visits as follows: –4 weeks, –2 weeks, treatment initiation, +4 weeks, +8 weeks, +16 weeks and then at 16-week intervals. The early schedule of visits was truncated for women in the latter stages of pregnancy, to maximise therapeutic benefit to mother and baby. At the screening visit (week –4), potential candidates were allocated a therapeutic counsellor, whose responsibility was to provide ongoing counselling support, to reinforce the need for high levels of adherence, to maintain communication between clients and the clinic staff and to visit clients in their homes. The therapeutic counsellors were HIV-infected individuals, many on ART themselves, who had been trained in drug adherence and ART toxicity recognition by a non-governmental organisation, *Sizophila*. The therapeutic counsellor / patient ratio was 1:20. At this initial visit, a treatment readiness assessment questionnaire was completed and 4 weeks of co-trimoxazole were dispensed, with pill counts performed after 14 and 28 days to assess adherence. All patients had a checklist completed, which screened for symptoms and signs of tuberculosis (TB) infection. At the week –2 visit, blood was taken for quantitative viral load and CD4 cell count. These tests were repeated at 16-week intervals thereafter. Drug safety monitoring of liver function test (LFT) and full blood count (FBC) were also performed at weeks –2, +8 and 16-weekly thereafter, with an additional LFT performed at week +2 in those receiving nevirapine to screen for potential hepatotoxicity. The final decision to commence or defer initiation of ART was made at a combined meeting of medical and therapeutic counsellors during the third week (week –1), when information on clinical status, blood tests, treatment-readiness and adherence data were available. Following this meeting, drugs were ordered for those commencing ART. The cohort pre-ART period was defined as the cumulative number of days between the screening visit and the date of either commencement of ART or permanent deferral. The ART exposure period was defined as the cumulative number of days from ART commencement to the censoring date of

28 February 2003. Resource utilisation data including scheduled and non-scheduled visits and staff allocated time were prospectively collected in a clinic register. Clinical, laboratory and adherence data were kept in an electronic database.

Results

The number of eligible patients referred and their subsequent status within the programme are outlined in Fig. 1. The mean age of those screened was 34 years (range 7 - 55 years); 78% were female. The population had advanced HIV infection, with 95% having symptomatic disease (WHO clinical stages 3 and 4) and 57% having AIDS (WHO clinical stage 4). The median CD4 count was 96 cells / µl (range 3 - 452 cells / µl), and the median viral load was 4.91 logs (range 2.611 ≥ 500.000).

Eight patients were permanently deferred; 4 because of failure or inability to attend clinic visits, 1 because of advanced debilitating HIV disease and multidrug-resistant pulmonary tuberculosis, 2 because of asymptomatic HIV and CD4 cell counts above entry criteria at screening, and 1 because he denied being HIV-infected. One patient was withdrawn after therapy commenced because of failure to attend clinic visits. Viral load data at 16 weeks were available for the first 16 patients, all of which were < 400 copies / ml. The first child born to a mother on the programme was HIV PCR-negative at 3 months.

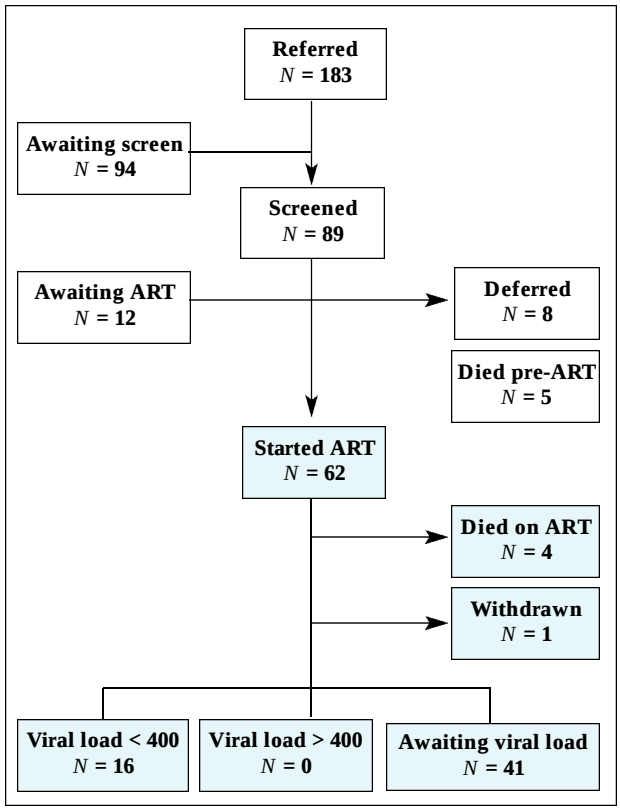

Fig. 1. Numbers of patients referred, screened and started on the antiretroviral therapy (ART) programme, together with their status within the programme and clinical and virological outcomes at week 16. Events occurring on ART are shown in the shaded boxes.

Five deaths occurred between screening and the commencement of ART or treatment deferral. The total pre-ART period for the cohort was 2 186 days, which translated to a pre-treatment crude mortality rate of 83 / 100 patient years. Two of the five patients had active *Mycobacterium tuberculosis* infection. Four deaths occurred on ART, none of which was directly related to ART. The period of ART exposure up to the censoring date totalled 4 271 days.

The proportional costs of drugs, staffing, quantitative viral load with CD4 cell counts and laboratory safety monitoring are shown in Fig. 2. Programme costs were dominated by drug procurement and personnel costs. Of the personnel costs, the medical officer contributed 39.3%, the nurse 16%, *Sizophila* counsellors 15.7% and specialist medical support and training 29%.

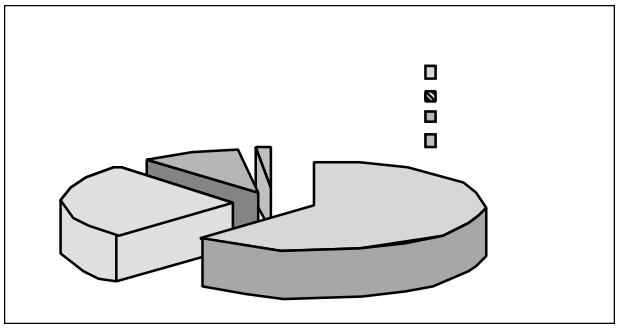

Fig. 2. The first 6 months'financial costs of the programme introducing ART to an HIV primary care service. The attributable proportion of costs for the following components are shown: drug acquisition; staffing — medical, nursing and counsellors; monitoring of CD4 and viral load; and laboratory safety monitoring.

Patient referrals reached 150 after 8 weeks of the programme. Initiation of the 150 patients onto ART was scheduled over 9 months, with a mean of 15 patients starting therapy per month. In the first 6 months there were 421 scheduled and 20 unscheduled visits. Duration of scheduled visits varied between 15 minutes for a week-8 visit and 45 minutes for a treatment-initiation visit. The number of scheduled clinic hours per week was not evenly distributed and the projected weekly scheduled visit hours required for the programme are shown in Fig. 3.

Discussion

This ART pilot project is a unique collaboration between funding organisations from a developed country, local and

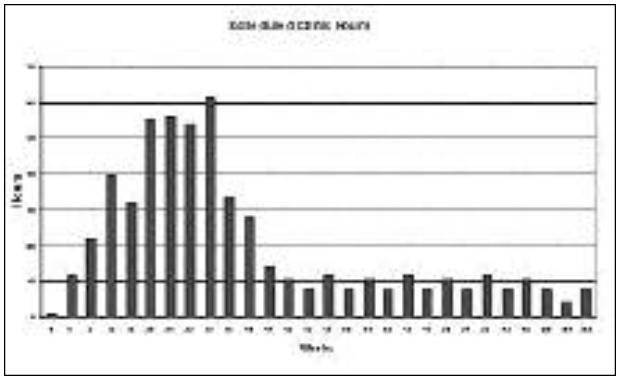

Fig. 3. Number of hours of scheduled visits per week required for 150 patients initiating HAART over a 9-month period. There is an initial staffing requirement, which peaks at approximately six times the long-term staffing needs.

regional public sector health authorities and a local academic institution. The programme was designed to identify the attributable resources needed when adding an ART programme to an existing primary care HIV service using an easily reproducible service model.

Public debate around treatment access, together with the large numbers of HIV-infected individuals with advanced disease, has created a backlog of demand for access to ART. The programme was initially limited by funding sources to treatment of 150 individuals. Recruitment to the programme was completed by 8 weeks, confirming a high demand for ART in our patient population. Many patients are desperate to access therapy and perceive that they may not survive a delay of several weeks. The clinic nurse highlighted this therapeutic urgency when she reported her distress at 'watching patients' faces, informed of the waiting time before they access antiretroviral therapy'.

Initiation of ART was staggered over 9 months, which still resulted in staffing time requirements peaking at approximately six times the level required for subsequent long-term management of these patients. The high clinic time requirement resulted from the combined effects of the recruitment rate, increased frequency of protocol-required visits and increased time per visits during the early weeks of ART initiation. The team of medical officer, nurse and therapeutic counsellors allocated to the clinic would be sufficient to supply 20 hours per week of scheduled clinic visits, enough for a daily clinic of 4 hours' duration. This scheduled clinic time could service 250 - 300 patients on stable ART; however, it is insufficient for the recruitment and initiation phase of the ART programme. In any new programme this increased staffing requirement will coincide with the need for staff training in ART. Our training personnel were able to provide the extra staffing capacity during the recruitment phase. There will be a need for programmes to allocate increased logistical support to ART clinics during the initial 'set-up' phase.

Patients on the programme had a functional status sufficient to be able to attend an outpatient clinic; however, the pre-treatment crude mortality rate was 83/100 patient years. The on-treatment mortality showed significant decline; the mortality rate has not been presented at this stage because the drug exposure period is subject to a major confounder of 'right censoring' and these data will be reported later. TB was a significant contributor to mortality and the exclusion of active TB presents a particular challenge to those initiating ART in high TB-prevalence populations such as South Africa.[14,15]

Present treatment guidelines[5,13] give an upper threshold of 200 CD4 cells/µl for initiating therapy, but there is no lower limit. This introduces the dilemma of whether patients are ever too sick to join a programme. While the sickest patients have much to gain, they utilise programme resources disproportionately and a high death rate can impact negatively on community perceptions of the programme and affect staff morale adversely. The non-medical therapeutic counsellors required specific counselling support around this issue. In an analysis of 12 574 individuals on ART, the CD4 count and clinical stage at the time of initiation of treatment were the dominant prognostic factors.[16] In a cohort with very advanced HIV disease and low CD4 counts such as ours, between 11% and 15% would be predicted to develop further AIDS-related complications during the first year of therapy, with the majority of these events occurring within the first 6 months.[16] Despite this high predicted complication rate, European and North American experience indicates that only 1.5 - 3.1% of advanced patients with 50 - 100 CD4 cells/µl die in the first year of ART.[16] These data support initiation of therapy at low CD4 counts, which can still result in a reasonable prognosis if the initial complications around the time of starting therapy can be managed. Staff of the clinic and referral hospital therefore need a high level of expertise in the recognition and management of medical complications occurring during early ART, particularly if very ill patients are to be entered into a programme.

Drug procurement accounted for 61% of the attributable cost of adding ART to the existing primary care HIV management programme. Although retail costs of ART have declined in South Africa in recent years, they remain a major obstacle to wider implementation in the public sector. In the next few months the programme is expected to access UNAIDS preferential pricing which will reduce the cost of the initial regimen to approximately 50% of current retail pricing. Availability of generic formulations could reduce the cost of our initial schedule by an additional 50%, to approximately R350 per month.[12,17] Medical specialist support contributed 29% of initial staffing costs; however, this component will also decrease as training requirements decline and an increasing

proportion of patients are stabilised on ART. Viral load and CD4 cell measurement contributed 10% of total attributable expenditure. Until recently these high-technology assays were considered to be too expensive for 'low-cost programmes' and the use of low-technology substitutes such as total lymphocyte counts was proposed.[5] The recent marked cost reduction of these assays in South Africa makes low-technology substitution less attractive.

The preliminary viral response data are very encouraging and demonstrate that an ART programme can be initiated successfully within an existing primary care facility. The ART delivery model chosen was well suited for those districts with an existing HIV primary care infrastructure. Expansion to other sites will be dependent not only on funding for antiretrovirals, but also on the allocation of sufficient resources for the development of a training and support infrastructure, particularly during the early recruitment phase of the programme. There are significant ethical issues concerning the selection of patients into an ART programme where resources are very limited. While there is a need for clear, transparent and strictly maintained criteria for ART access,[10] both the inclusion and exclusion of very sick patients was very challenging and stressful for the clinic team. Therapeutic counsellors gave valuable input to the programme from persons in the local community living with HIV and AIDS. The incorporation of HIV-infected individuals as 'treatment buddies' and to give counselling support meant that a previously untapped resource of expertise and talent was utilised.

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