

PROMOTING ADHERENCE TO ANTIRETROVIRAL THERAPY THROUGH A DIRECTLY ADMINISTERED ANTIRETROVIRAL THERAPY (DAART) STRATEGY IN MOMBASA, KENYA

A principal concern of antiretroviral therapy (ART) programs is the ability of patients to maintain a high level of adherence to the medication regimen. Based on formative research conducted on HIV-infected clients and health workers in Mombasa, Kenya, and lessons learned from directly observed therapy (DOT) strategies to encourage adherence to treatment for tuberculosis, a DAART strategy was developed to promote adherence to ART. This study examines whether the DAART intervention is more effective in fostering adherence than standard follow-up strategies among people living with HIV/AIDS in Mombasa.

Methodology

Researchers from the Horizons Program and the International Centre for Reproductive Health, in collaboration with Coast Province General Hospital, Mkomani Bomu Clinic, and Port Reitz District Hospital, conducted a randomized, controlled two-arm study. Ethical approval for the study was obtained from the Ethical Review Board at Kenyatta National Hospital and the Institutional Review Board of Population Council.

A total of 234 HIV-infected, treatment-naïve patients who initiated highly active antiretroviral therapy (HAART) were enrolled in the study between September 2003 and November 2004; 116 patients were randomized to the DAART arm and 118 to the non-DAART arm. All patients received a first-line non-nucleoside reverse transcriptase inhibitor (NNRTI) containing the treatment regimen (d4T, 3TC, and EFV or NVP). They also received standard adherence counseling consisting of three preparatory sessions before the initiation of HAART as well as ongoing adherence counseling support at routine monthly clinic visits. The DAART patients were observed taking their medication twice weekly at specially designated health facilities for 24 weeks, followed by routine monthly follow-up for another 24 weeks. Non-DAART patients received standard monthly follow-up for the entire 48 weeks. A team of community health workers (CHWs) traced DAART clients who did not show up for observed treatment or pick up their medications; these CHWs also traced DAART and non-DAART clients who did not keep the monthly follow-up clinic appointments.

As reported in this summary, adherence was assessed using monthly clinic-based pill counts, which measured adherence over a one-month period. Adherence is calculated by dividing the number of pills actually taken by the number of pills the client was required to take over the reporting period times 100.



Measures of adherence used for this study are:

- Mean adherence over 24 and 48 weeks.
- Proportion of clients able to achieve a total adherence > 95 percent over 24, 48, and 96 weeks.
- Proportion of clients able to consistently achieve adherence > 95 percent over 24, 48, and 96 weeks.

Patients who did not complete at least 30 days in the study were excluded from the analysis. Zero adherence for a relevant reporting period was awarded to (a) patients who did not visit the clinic and were known not to have collected medications from the pharmacy; (b) patients who were incapacitated, hospitalized, or sick and were known not to have taken their medications; and (c) patients who had dropped out of the program or had left the area; these patients were subsequently dropped from the analysis. Patients who did not bring back bottles or those who missed pill counts but may have taken pills were not included in the analysis on adherence for that relevant reporting period.

Patients who came back with fewer pills than they should have had (e.g., because they dropped them, took extra because of vomiting, etc.), thus implying that adherence was greater than 100 percent, were given an adherence value equal to 100 percent less than the excess percent adherence for that period (e.g., a 102 percent adherence was given a value of 98 percent). More than three-fourths of patients who fell into this category exceeded 100 percent adherence by one to five pills.

Other health outcomes assessed in the study include CD4 cell counts, body weight, depression (Beck Depression Inventory I), and quality of life (HR-QOL 21).

This summary presents the results from baseline to 24 weeks of follow-up, which was the end of the DAART intervention.

Recruitment and Retention

A total of 234 patients were eligible for adherence monitoring; 22 DAART patients and 19 non-DAART patients were lost to follow-up (17.5 percent) since enrollment. The majority of these losses were because of patient deaths (14 DAART and 10 non-DAART patients); 10 patients left Mombasa, five were transferred to other hospitals, one patient was incapacitated, and one was arrested. Four clients were dropped from the study: one DAART and two non-DAART patients stopped treatment and one resumed work and discontinued DAART.

As of 24 weeks, 91 DAART patients and 97 non-DAART patients were being followed in the study. Sociodemographic characteristics were similar across the two groups. Almost two thirds (64%) of patients were female and half of them were currently married; the median age was 37 years (range: 20–58 years).

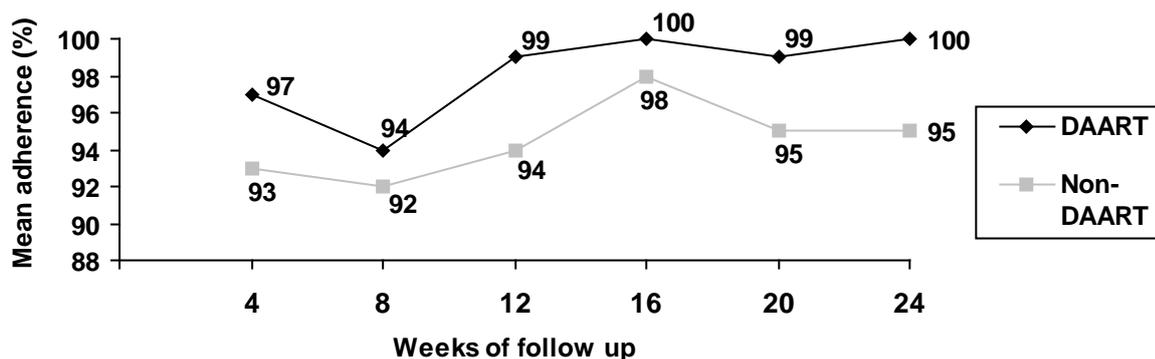
There were no significant differences with regard to age, sex, and CD4 counts between patients lost to follow-up and patients continuing in the study. There were also no changes in treatment regimens among the study respondents during the analysis period.

Key Findings

Data from pill counts indicate higher adherence levels in the DAART group than the non-DAART group.

Data from pill counts show that mean adherence over 24 weeks was significantly higher in the DAART group compared to the non-DAART group (96 percent vs. 90 percent; $p = 0.042$). Figure 1 shows the monthly mean adherence for the two groups for progressive reporting periods over 24 weeks.

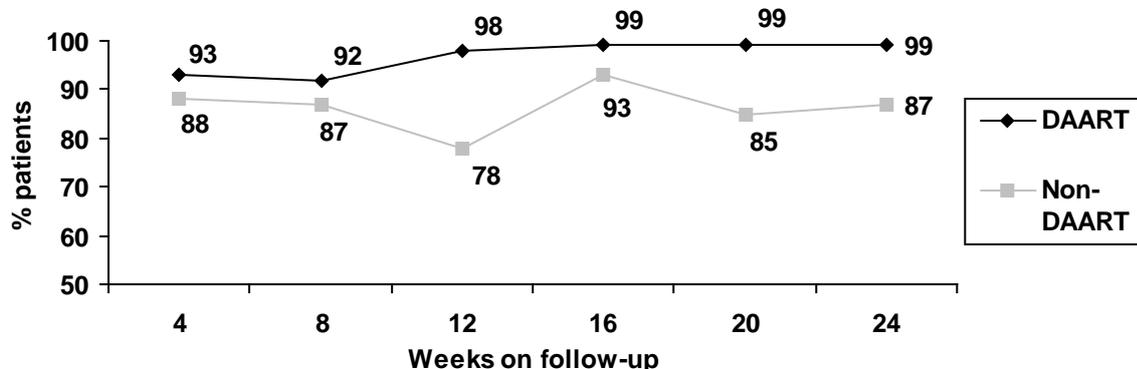
Figure 1 Mean adherence based on pill counts



DAART: Week 4 (n = 104), Week 8 (n = 99), Week 12 (n = 93), Week 16 (n = 90), Week 20 (n = 93), Week 24 (n = 88).
 Non-DAART: Week 4 (n = 93), Week 8 (n = 82), Week 12 (n = 80), Week 16 (n = 80), Week 20 (n = 88), Week 24 (n = 93).

Data from pill counts also show that a greater proportion of DAART clients achieved a total adherence > 95 percent over 24 weeks than non-DAART clients (92 percent vs. 80 percent; p = .012). Figure 2 shows the proportion of patients who were able to achieve > 95 percent adherence for progressive reporting periods over 24 weeks. A significantly higher proportion of DAART patients (n = 91) were also able to consistently achieve > 95 percent adherence over 24 weeks compared to non-DAART patients (n = 98) (DAART: 67 percent vs. non-DAART: 27 percent; p < .001).

Figure 2 Proportion of patients achieving > 95% adherence



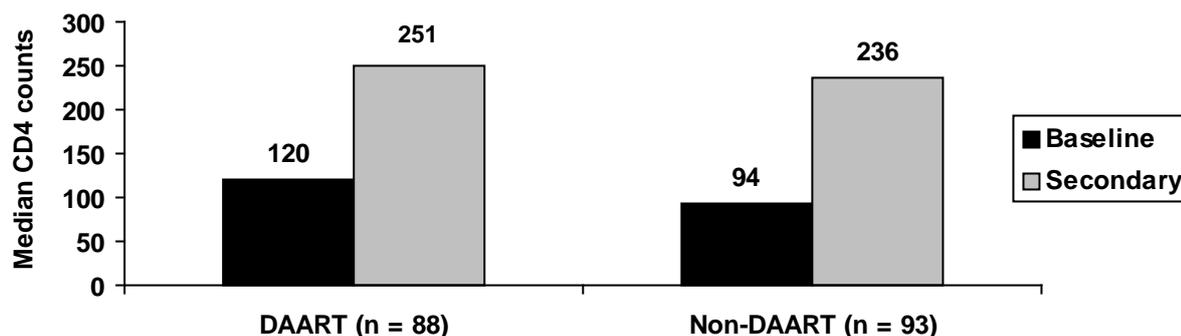
DAART: Week 4 (n = 104), Week 8 (n = 99), Week 12 (n = 93), Week 16 (n = 90), Week 20 (n = 93), Week 24 (n = 88).
 Non-DAART: Week 4 (n = 93), Week 8 (n = 82), Week 12 (n = 80), Week 16 (n = 80), Week 20 (n=88), Week 24 (n=93).

Both groups demonstrated improvement in immune status.

HIV disease is characterized by a progressive decline in immunity. CD4 counts, a measure of immunological function, are expected to rise with HAART.

At baseline, there were no significant differences in median CD4 counts between groups (DAART (n = 113): 106 cells/mm³ vs. non-DAART (n = 117): 96 cells/mm³; p = .225). In both groups, significant improvements in median CD4 counts among patients with baseline and secondary measurements were observed over 24 weeks (Figure 3). Change in CD4 cell counts was calculated for each patient and median change was calculated for the group. The DAART group had a slightly higher median change in CD4 counts compared to the non-DAART group, but the difference was not statistically significant (DAART (n = 88): 153 cells/mm³ vs. non-DAART (n = 93): 141 cells/mm³; p = .422).

Figure 3 Median CD4 counts

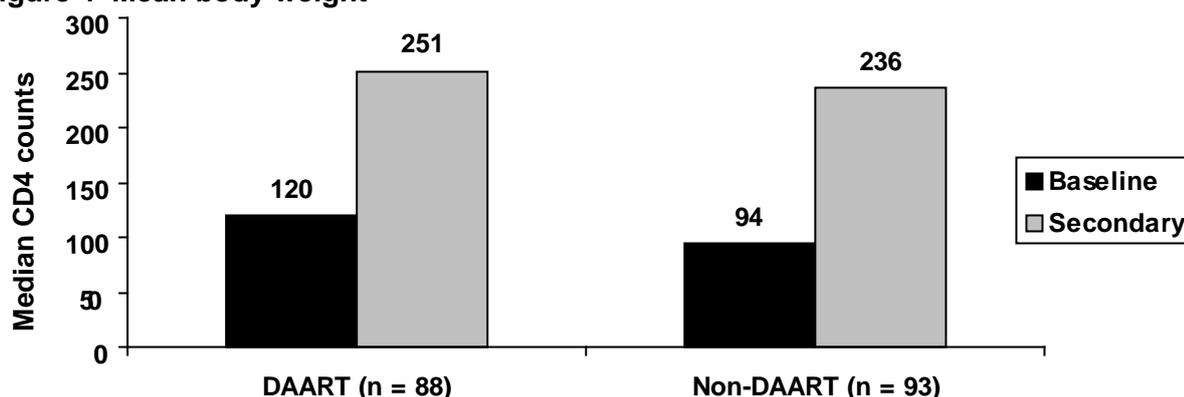


*Clients with both measurements. DAART: $p < .001$; Non-DAART: $p < .001$.

Improvements in body weight were observed in both groups.

Weight loss is a common feature of advanced HIV disease and body weight is expected to rise with effective HAART. Similarly significant improvements in body weight were observed in both groups; there were no statistically significant differences between groups at baseline or at 24 weeks (Figure 4).

Figure 4 Mean body weight



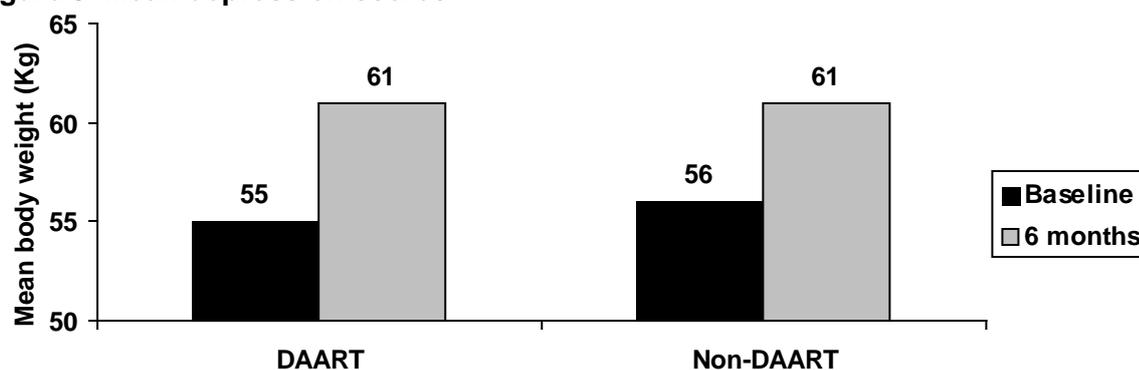
DAART: $p < .001$; non-DAART: $p < .001$ (Paired Samples T Test).

Both groups showed marked improvement in depression and quality of life scores.

Beck Depression Inventory I, a 21-item validated tool, was used to assess depression among study participants. A third of the patients in both groups reported moderate to severe depression at baseline. Although both groups demonstrated significant improvements in depression scores after five months on treatment, there were no differences between groups either at baseline (DAART (n = 108): 15.6 vs. non-DAART (n = 116): 14.5) or at 20 weeks (DAART (n = 89): 9.2 vs. non-DAART (n = 88): 8.9). Figure 5 shows mean depression scores for the two groups. The DAART group had a slightly larger decrease in mean scores compared to the non-DAART group; however, the difference was not statistically significant (mean change DAART (n = 89): 6.58 vs. non-DAART (n = 88): 5.02; $p = .331$).

Quality of life was assessed using the Health Related Quality of Life, a 21-item scale used widely in National Institutes of Health AIDS Clinical Trials Group (NIH-ACTG) studies. As shown in Table 1, the scale includes nine dimensions. The scale was adapted to the Kenyan cultural context and there were no significant differences between the two groups at baseline. Improvements were seen on all dimensions in both groups; DAART patients had significantly greater improvement in the dimensions assessing pain and mental health as reflected by higher scores compared to non-DAART patients.

Figure 5 Mean depression scores*



*Patients who have both baseline and secondary scores. DAART: $p < .01$; non-DAART: $p < .001$.

Table 1 Quality of Life standardized scores

| | DAART | | Non-DAART | |
|-------------------------------|-----------------------|----------------------|-----------------------|----------------------|
| | Baseline (n = 111) | 6 months (n = 94) | Baseline (n = 115) | 6 months (n = 99) |
| Self-rating of current health | 51 | 70 | 51 | 70 |
| General health perception | 31 | 71 | 34 | 65 |
| Physical functioning | 62 | 94 | 60 | 92 |
| Role functioning | 57 | 92 | 62 | 89 |
| Social functioning | 63 | 97 | 69 | 94 |
| Cognitive functioning | 79 | 95 | 81 | 95 |
| Pain | 54 | 92** | 58 | 86** |
| Mental health | 67 | 89** | 68 | 83** |
| Energy and fatigue | 23 | 51 | 26 | 49 |

Note: All increases in DAART and non-DAART groups from baseline to 6 months $p < .01$; only patients with both baseline and 6-month readings.

** Differences between DAART and non-DAART groups $p < .05$

Conclusions

High levels of adherence to HAART were observed for all patients during the first 24 weeks of the regimen. However, patients exposed to the DAART intervention achieved higher mean adherence levels compared to those who received standard follow-up. A higher proportion of DAART patients achieved adherence levels in excess of 95 percent over 24 weeks consistently at each reporting period as compared to those receiving standard follow-up.

Despite greater adherence in the DAART group, there were no significant differences in CD4 counts and weight between the two groups at 24 weeks of follow-up. The following are possible explanations:

- Because of the lag between virological and clinical failure, differences in clinical outcomes may not be evident early in treatment but could become apparent later in the follow-up period at 48 weeks and 96 weeks.

