ENROLMENT EXPERIENCE AND THE MEASUREMENT OF SURVIVAL IN A PRIVATE SECTOR HIV/AIDS DISEASE MANAGEMENT PROGRAMME

M S Hislop, *MSc*
L D Regensberg, *MB ChB, MRCP*
Aid for AIDS Pty (Ltd), PO Box 38597, Howard Place, 7450

Aid for AIDS (AfA) is a disease management programme (DMP) available to beneficiaries and employees of contracted medical funds and companies in Africa who are living with HIV or AIDS. The programme has been running since mid-1998 and as a result a considerable amount of outcome data have been acquired. A report on the experience obtained during the first 4 years of the programme was published in 2003.[1] The purpose of this article is to elaborate on some of the challenges alluded to in the first article, including late enrolment and the measurement of survival, especially in patients with advanced disease.

LATE ENROLMENT FOR DISEASE MANAGEMENT

The majority of AfA beneficiaries belong to one of several large open medical aid schemes. The rate at which HIV-positive scheme beneficiaries would enrol, and the stage of disease at which they would do so, was an issue of great interest at inception of the programme. Contracted medical schemes in particular were very keen to see 'all' of their HIV-positive beneficiaries enrolled as quickly as possible. The difficulty in defining this point is that calculation of exactly what the rate of enrolment is going to be is very complex.

Within individual medical schemes this rate may be dependent on:

- the HIV prevalence and incidence (new infections)
- the disease stage distribution
- the turnover of beneficiaries (joining and leaving the scheme), and
- the likelihood of beneficiaries discovering their HIV status.

In addition to the latter, beneficiaries must also be aware that their scheme offers a DMP, and must be willing to disclose their HIV status. Because these variables can change with time, it is no easy matter to predict with certainty how quickly all HIV-positive beneficiaries within a medical scheme are going to enrol for disease management.

Now, almost 6 years later, it is interesting to review some of the enrolment experience. The general trend has been a steady monthly increase in uptake in the 4 years between 1998 and 2001. Thereafter, enrolment has become more constant from month to month. An area of concern reported previously[1] was the high proportion of patients who enrolled when already in late-stage disease, especially with a CD4 count < 50 cells/µl.

In the early days, it was hypothesised that this trend would reverse over time:

- as stigmatisation around HIV/AIDS decreased
- as the relatively smaller pool of late-stage individuals were enrolled (estimated to be 7% in stage 4 (AIDS) in 2002[2]), and
- as more medical scheme beneficiaries became aware of their DMP and the benefits of antiretroviral therapy (ART).

Unfortunately this has not been the case. In fact, the opposite trend has occurred over the past few years (Fig. 1), despite AfA providing on-going education and awareness programmes for members and frequent communication with doctors. The reasons for this surprising trend are not clear. The reality of this situation is that medical schemes have to fund unnecessary hospitalisation costs for beneficiaries who leave enrolment on AfA far too late. Length of hospital stay in the year prior to AfA registration is over three times higher for patients with a CD4 count < 50 cells/µl than it is for those with an entry CD4 count between 200 and 350 cells/µl.

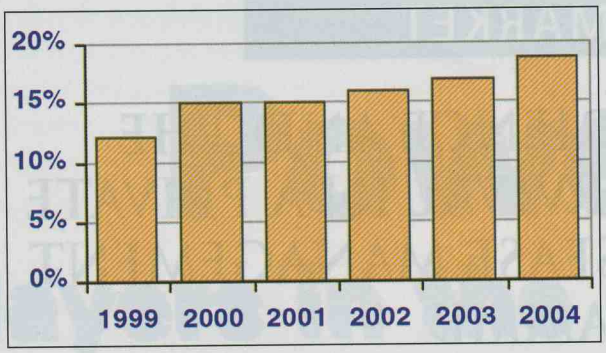

Fig. 1. Percentage of beneficiaries from selected open medical schemes registering on Aid for AIDS with a CD4 count < 50 cells/µl.

Preliminary data from corporate clients suggest that late enrolment among unfunded employees may be less of a problem than with medical scheme members.

SURVIVAL EXPERIENCE

To date over 33 000 HIV-positive medical scheme beneficiaries or employees have enrolled on the AfA programme, with 22 000 having been eligible for ART. Table I shows application status by CD4 band, at the time of ART commencement, for beneficiaries of open medical schemes. In effect this table provides a crude measure of absolute survival. Also evident in the 'left scheme' percentage is the significant amount of membership 'churn' that occurs in open medical schemes. In total, 18% of AfA beneficiaries have left their medical scheme for unspecified reasons over the past 6 years.

TABLE I. APPLICATION STATUS BY CD4 BAND AT ART COMMENCEMENT FOR BENEFICIARIES OF SELECTED OPEN MEDICAL SCHEMES

Application status	CD4 band (cells/µl)			Total
	200 - 349	50 - 199	< 50	
Current	79%	74%	59%	72%
Deceased	4%	9%	22%	11%
Left scheme	17%	17%	19%	18%

The large size of the 'left scheme' group presents a challenge for statistical survival analysis. Individuals who leave a study are termed 'censored' in these analyses. Ideally, the pattern of censoring should be independent of the survival times, otherwise survival estimates may be too high. To illustrate, non-adherent patients with CD4 counts less than 50 cells/µl have a greater chance of leaving the scheme due to death than adherent patients with entry CD4 counts > 200/µl.

In a managed care setting it is difficult to follow up and ascertain the reason for leaving in all patients. On the whole, the majority of AfA beneficiaries enrol early, and are adherent to ART. In this large group the probability of bias, and the risk of significantly over-reporting survival, is small. In contrast, survival analyses for late-stage non-adherent patients have a higher probability of over-stating survival. To address these limitations in the latter sub-group, we can evaluate two different scenarios:

- a 'normal' one, where censoring is assumed to be independent of the survival times (best case), and
- a far more conservative scenario, where 'left date' is assumed to coincide with date deceased (worst case).

In order to benchmark the outcomes, it is interesting to compare survival results from the AfA cohort with those from another setting, such as the British Columbia Centre for Excellence in HIV/AIDS (BC).[3] Although it is risky to compare results from two such different settings, several useful observations can be made by attempting to control some of the key determinants as closely as possible. Inclusion criteria for the AfA cohort included the following:

- no ART prior to commencing full (ongoing) ART
- adult (age > 18), and
- a beneficiary of an open medical scheme.

Survival analysis was done using the Kaplan Meier method by means of the Statistica package (StatSoft). To provide overall context, Fig. 2 shows the total 36-month survival by CD4 stage grouping for the AfA cohort compared with that from the BC study.

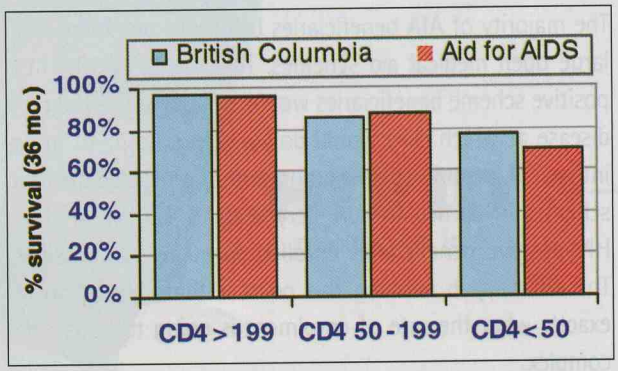

Fig. 2. Comparative 36-month survival by CD4 count at ART commencement in patients from British Columbia (N = 1 416)[3] compared with selected open medical schemes contracted to Aid for AIDS (N = 11 115).

Analysis of a subgroup with a high probability of death shortly after leaving (for unspecified reasons) shows how true survival can be estimated by evaluating the 'best' and 'worst' case scenario. In this instance, the subgroup is defined as late stage (CD4 count < 50 cells/µl) and non-adherent. In the BC data, patients were defined as non-adherent if they received antiretroviral medications < 75% of the time during the *first year of follow-up.*

The (arbitrary) AfA non-adherence measure is 'less' stringent, with non-adherence defined as < 80% of ART scripts claimed over the *entire period* of ART authorisation. Fig. 3 shows the results of the 'best' and 'worst' case scenarios for the AfA cohort compared with the BC cohort.

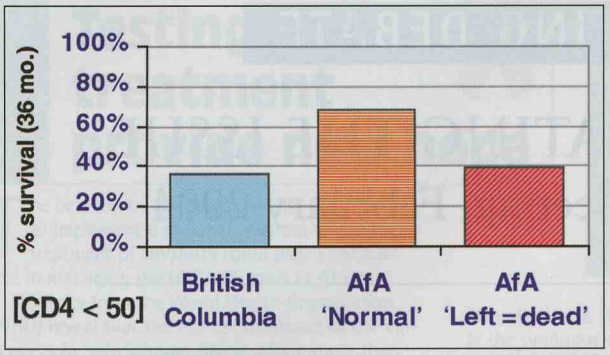

Fig. 3. Comparative 36-month survival for patients with a CD4 count < 50 cells/µl *at ART commencement and* poor adherence to ART *in the British Columbia cohort (left), 'normal' survival analysis where AfA patients who left the scheme are 'censored' (middle), and modified survival analysis where patients are assumed to have died at the time they 'left the scheme' (right).*

The 'true' 36-month survival rate for non-adherent AfA patients entering with CD4 counts < 50 cells/µl is likely to be somewhere between the two extremes of 39% and 68%. Given that survival for the BC cohort was 36% with more stringent adherence criteria, the 'true' survival for the AfA cohort is likely to be in the region of 45 - 60%.

CONCLUSIONS

Late enrolment continues to be a problem, and making education and awareness programmes available has not had the expected impact. Early information suggests that it may be more of a problem with medical scheme beneficiaries than with uninsured employees of companies that provide ART to their workforce. The reason for this is probably related to a greater opportunity for structured education programmes within individual companies, as opposed to open medical schemes, which frequently involve a large number of different pay points. AfA has embarked on a campaign to make doctors aware of the need to offer voluntary counselling and testing to all of their patients with the hope of making more people aware of their HIV status and the need to register as early as possible.

The ultimate goal of providing ART is to delay progression to AIDS and improve survival outcomes. Survival analysis is therefore a useful tool for monitoring and evaluation, but needs to be carefully interpreted in the medical scheme environment, where large numbers of patients leave for unspecified reasons. Allowing for this, survival outcomes within AfA compare favourably with those reported from developed countries.

REFERENCES

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3. Wood E, Hogg RS, Yip B, Harrigan PR, O'Shaughnessy MV, Montaner JSG. Is there a baseline CD4 cell count that precludes a survival response to modern antiretroviral therapy? *AIDS* 2003; **17:** 711-720.