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Late presentation at entry into HIV care limits the impact of cART.

Colette Smit[1], Tim Hallett[2], Frank de Wolf [1,2], Joep Lange[3], Geoff Garnett[2]

[1] HIV Monitoring Foundation, the Netherlands; [2] Imperial College, London, UK; [3] Academic Medical Centre of the University of Amsterdam, The Netherlands

HIV Monitoring Foundation
Meibergdreef 9
1105 AZ Amsterdam, The Netherlands
Phone/Fax: 31-20-5664172/566 91 89
Email: colette.smit@amc.uva.nl

BACKGROUND:

Comparing different HIV treatment centres is not straight forward.

Indicators of good patient management and successful treatment are influenced by patient characteristics, attributes of the centre and late presentation into care.

Hypotheses:

1. the quality of treatment administered varies between the treatment centres;
2. more frequent patient monitoring in some centres generates better patient survival; or
3. patients entering care earlier in some centres generates better patient survival.

- The observed mortality of HIV-infected patients in different treatment centres in the Netherlands was compared with the predictions of a mathematical model.
- Predictors for late presentation were selected.

METHODS:

Treatment outcomes and patient profile

- In the ATHENA observational cohort, the risk of dying in the first 3 years on cART was estimated for each Dutch treatment centre, using a Cox-Proportional Hazards Model.
- The risk of dying in each centre was compared to that of the total HIV population in the Netherlands.
- 3 centres with widely varying mortality rates were selected for the comparison with the mathematical model.
- Dutch homosexual (MSM) only were included to prevent socio-ethnicity status of the patients interfering with the comparison of the model.

Natural History of HIV infection among Dutch men:

- To describe the natural history the mathematical model includes the:

  decline in CD4 counts after seroconversion

  3 years survival rates on cART, stratified by CD4 counts at time of cART initiation.

Mathematical Model:

represents patients entering care, being monitored for the need to start treatment and treatment outcomes (Hallett et al, PLOSMedicine 2008)

Using the mathematical model we investigated:

(1) whether the chance of individuals surviving on cART varied between treatment centres when patients are stratified by the initial CD4 cell count;

(2) whether the model could reproduce the observed variation in mortality between the three treatment centres when parameterised in this way; and,

(3) the relative influence of these treatment centre parameters on the predicted level of mortality on treatment.

Predictors for late presentation: Were determined for the total HIV population, using a multivariate logistic regression model.

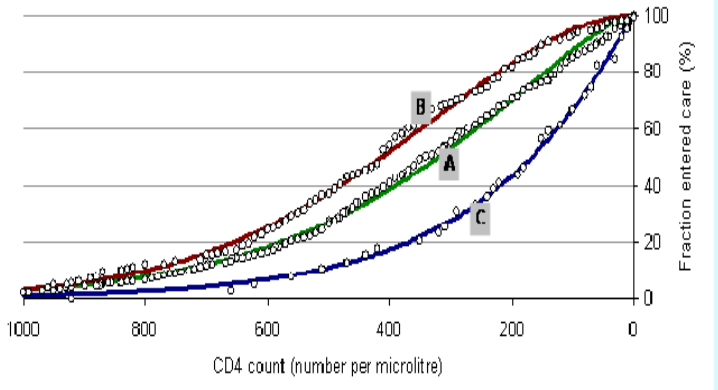

Figure 1 Distribution of CD4 count at presentation in three hospitals. Dots show data and lines show fitted Weibull curves with shape (α) and scale (β) parameters as follows: Hospital A α= 1.43 β=414.46; Hospital B α= 1.83 β= 505.12; Hospital C α= 1.06 β= 236.45.

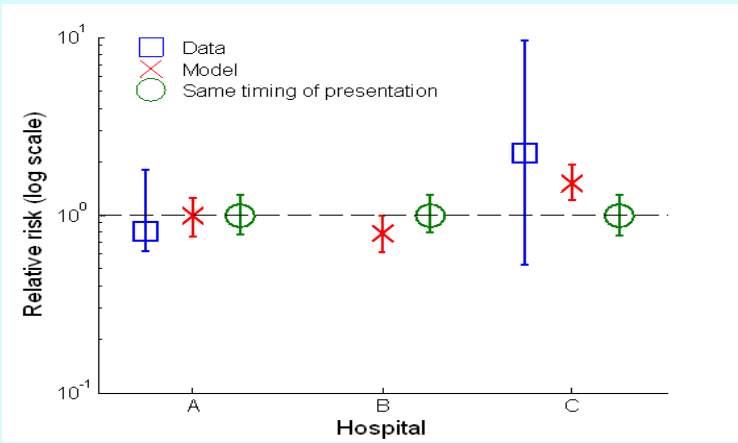

Figure 2: Observed and modeled risk of dying in first three-years of ART relative to national average. Errorbars show 95% confidence interval (data) or inter-quartile range from 500 simulations (model).

RESULTS mathematical model

- At the level of the treatment centre, the fraction of Dutch MSM dying in the first three years of treatment ranged from 0% to 8%.

The risk of dying compared to the national average:

centre A: hazard ratio (HR): 1.08; 95% confidence interval (CI): 0.51-2.29.

centre B: no men died in the first three years of treatment

centre C: HR: 2.22; 95% CI: 0.53-9.53.

- Patients presenting at centre C had much lower CD4 count than patients presenting at centre A or B (figure 1)

- The model captures the large variation in observed mortality when parameterised using the age distribution, frequency of monitoring and the distribution of CD4 cell counts at entry to care observed in each centre (Figure 2, cross)

- When the same national average distribution of CD4 count at entry was used, the variation in predicted mortality between all centres was diminished. (Figure 2, circles).

- Manipulating the age-distribution of patients or the frequency of monitoring did not affect the model predictions.

RESULTS predictors of late presentation into HIV care:

Of all HIV patients entering care, 35% had a CD4 cell count< 200 x 10^6cells/L

		Adjusted Odds Ratio (95%CI)
Gender:	Male **Female**	1 0.68 (0.59-0.79)
Age (per 10 years increase)		1.32 (1.26-1.39)
Exposure category:	MSM **Heterosexual** **IDU** **Other**	1 1.68 (1.45-1.94) 1.52 (1.07-2.15) 2.40 (1.99-2.90)
Region of origin	Netherlands Western **Caribbean/ Latin America** **Sub Saharan Africa** **Other**	1 1.07 (0.85-1.31) 1.56 (1.32-1.84) 2.17 (1.85-2.54) 1.74 (1.43-2.13)
Symptoms at first presentation	No **Yes**	1 3.78 (3.41-4.19)
Calendar Year of HIV diagnosis	<2000 2000-2002 **2003-2007**	1.02 (0.87-1.18) 1 0.65 (0.55-0.74)

CONCLUSIONS:

Patients entering care with low CD4 counts are the main source of variation in the mortality rates between centres.

if patients present with at least 400 CD4 cells/mm3, then the model predicts a reduction of the mortality in the first three years of cART by approximately 20%.

Recruiting HIV-infected individuals to care earlier could lead to substantial improvements in cART outcomes.