Background

To fully benefit from antiretroviral therapy (ART), HIV infected individuals must be aware of their infection, link to and consistently engage in care, and receive and adhere to HIV treatment. Retention in HIV care is a critical step in this process, it is associated with improved survival, decreased risk of HIV transmission, and reduced risk of HIV transmission to others. Also, retention in care may reduce aggregate healthcare costs by minimizing acute health service utilization.

In the context of HIV management as a chronic disease, evaluating the dynamic nature of retention in care over the longer term is of the utmost importance. Retention is a dynamic process and the treatment intensity must be maintained and not decrease even when a non negligible proportion of patients with HIV may re-engage in care after being lost at different steps of the cascade of care.

Identifying those most at risk for loss to care and the clinical consequences of gaps in care is needed.

Objectives

We therefore studied those lost-to-care (LTC), and those who re-engage care (REC) over a 17-year period in the ICONA cohort.

The aim of this work was to answer the following scientific questions: 1. What were the rates of loss-to-care? 2. What factors predicted lost-to-care and re-engagements? 3. Which is the risk of clinical progression of patients re-engaging in care?

Methods

Study population

HIV-1 infected patients from the ICONA Foundation Study enrolled during the period 1997-2014. Patients were considered lost-to-care (LTC) if they had no clinical visit for at least 12 months; a patient was considered re-engaged in care (REC) if, after being lost-to-care, he/she had a clinical visit. Patients who died or randomized or institutionalized or transferred out of other clinical centers were not considered in this analysis, since we supposed that they were still receiving care.

Statistical Methods

The incidence rate of LTC by study year was calculated as the number of patients LTC divided by PYFU and expressed as rate per 100 PYFU, with 95% confidence intervals (CI).

Since our primary interest was identifying patients with consistent engagement with longitudinal HIV care, we focused our analysis on characterizing patients who were lost-to-care, and contextualizing the factors (psychos, demograph, clinical) that may inform those loss.

Thus, a Poisson regression analysis was used to examine factors associated with clinical and clinical factors associated with the risk of being lost-to-care. Socio-demographic covariates included gender, age, nationality (an immigrant patient was considered a patient born outside Italy), level of education, co-infections status, and clinical covariates included presentation with AIDS or low CD4 level (<350), HIV co-infection, CD4 count, HIV-RNA, ART therapy. The same analysis was also conducted for patients re-engaging in care with respect of the same clinical and demographic covariates but only those were adjusted for calendar year.

For those re-entering the cohort after a gap in care (GIC), CD4-cell count and HIVRNA before and after the gap were evaluated by paired t-test or McNemar’s test.

A Poisson regression analysis was used to investigate the association between having a gap in care and the risk of clinical progression in terms of clinical events after re-engagement in care, by calculation of unadjusted and adjusted relative risks of having a calendar gap-in-care (GIC) was created; for those re-entering care, we assumed that GIC=1 for the first 6 months after the re-engagement in care, and GIC=0 again. Patients who were consistently engaged in care had GIC=0. The clinical events we considered in the analysis were the following: occurrence of AIDS-related opportunistic infections or neoplasms, and AIDS (CDC 1993 classification), serious non-AIDS events, (e.g. malignancies, severe infections, end stage kidney disease, end-stage liver disease, cardiovascular events).

Results

2,728 (21.5%) out of 12,693 patients were lost to care; the incidence rate of LTC ranged from 23.2 in 1997 to 1 per 100 PYFU in 2014 (p<0.001, test for linear trend). Figure 1). The time from the first gap in care, after the retention period, was 3.4 years (IQR: 0.6–4.7) (median=3.2). 480 patients (17.6%) re-engaged in care after a mean gap in care of 2.2 yrs (IQR: 0.7–2.7) (median=1.1).

At last visit before being LTC, median CD4 count were 471 cells /μl (IQR: 298–510); 46% had an HIV viral load >350 and 33% had a viral load <100 copies/ml. In a multivariable Poisson regression model, after adjusting for calendar year, gender, age, nationality, job status, education level, being on ART, current CD4 count, current viral load, current engagement and HIV-HIVco-infection are strongly associated with the risk of being LTC (Table 1). Among patients, use, absence of HIV-HIV co-infection, higher CD4 viral suppression, reduced viral load, older age, a stable working condition and not being HIV cured were associated with a higher risk of being LTC.

ICONA Foundation Study Group

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Figure 1. Lost to Care

In a logistic regression model, after adjusting for calendar year, the only significant predictor of re-engaging care, was a suppressed viral load at last visit before gap (Table 1). For every additional gap in care, median HIV RNA level at last visit before being LTC, while after re-engaging care this value decreased to 444±359 (p<0.018) in patients having had a viral load >350 at 10.7% before to 25% after re-engaging care (p<0.001). An increase was observed in median HIVRNA (4,103 vs before 11,300 copies/ml), also the proportion of patients with 100% suppression of viral load was higher after re-engaged in care (8.8% vs 15.2%, p<0.028).

Clinical events occurred in 170 patients (21%) within 6 months after re-engaging in care, with 55% developed AIDS, 21% a serious non-AIDS event and 48% an HIV hospitalization. In a multivariable analysis adjusted for gender, risk factors, late presentation, HIV-HIV co-infection, current CD4 cells count and calendar year, patients with a gap in care had an increased risk of clinical events (RR=1.36, 95% CI: 2.06-2.71, p<0.01).

Table 1. Risk ratio for lost-to-care and odds ratio Re-engagements from fitting Poisson regression model and logistic regression model, respectively; both models were adjusted for calendar year.

Conclusions

Among patients in ICONA cohort, gaps in care are associated with lower socio-economic status and being born abroad and have become progressively less common over time.

Patients re-engaging care after a gap of at least one year have an increased risk of presenting with a clinical event and viro-immunological deterioration and an increased potential for viral transmission linked to the increase in HIV viral load.

Clinical and cofactors data may contribute to the monitoring of HIV continuum of care at national level. Nonetheless a series of possible limitations must be considered. In particular in our analysis we have assumed that patients were not re-engaged in care during gaps. However we have no information on the possibility that a patients attended clinical centers not belonging to the ICONA cohort, during the gaps and thus we may have overestimated this phenomenon. Further, we might assume that symptomatic patients have a higher probability of re-entering in care, and this may lead to an over estimation of the risk of clinical events associated with gap in care.