Mortality after Hospitalization for Pneumonia among Individuals with HIV, 1995–2008: A Danish Cohort Study

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Abstract

Background: HIV-infected persons are at increased risk of pneumonia, even with highly active antiretroviral treatment (HAART). We examined the impact of pneumonia on mortality and identified prognostic factors for death among HIV-infected.

Methodology/Principal Findings: In a nationwide, population-based cohort of individuals with HIV, we included persons hospitalized with pneumonia from the Danish National Hospital Registry and obtained mortality data from the Danish Civil Registration System. Comparing individuals with and without pneumonia, we used Poisson regression to estimate relative mortality and logistic regression to examine prognostic factors for death following pneumonia. From January 1, 1995, to July 1, 2008, we observed 699 episodes of first hospitalization for pneumonia among 4,352 HIV patients. Ninety-day mortality after pneumonia decreased from 22.4% (95% confidence interval [CI]: 16.5%–28.9%) in 1995–1996 to 8.4% (95% CI: 6.1%–11.6%) in 2000–2008. Mortality remained elevated for more than a year after hospitalization for pneumonia: adjusted mortality rate ratio 5.38 (95% CI: 4.27–6.78), 1.80 (95% CI: 1.36–2.37), and 1.62 (95% CI: 1.32–2.00) for days 0–90, 91–365, and 366+, respectively. The following variables predicted mortality within 90 days following hospitalization for pneumonia (adjusted Odds Ratios): male sex (3.77, 95% CI: 1.37–10.4), Charlson Comorbidity Index score ≥2 (3.86, 95% CI: 2.19–6.78); no current HAART (3.58, 95% CI: 1.83–6.99); history of AIDS (2.46, 95% CI: 1.40–4.32); age per 10 year increase (1.43, 95% CI: 1.11–1.85); and CD4+ cell count ≤200 (2.52, 95% CI: 1.37–4.65).

Conclusions/Significance: The first hospitalization for pneumonia among HIV-infected individuals was associated with elevated risk of death up to more than a year later. Use of HAART decreased the risk, independent of current CD4+ cell count. Prognosis following pneumonia improved over calendar time.

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Introduction

Early in the HIV epidemic it was recognized that morbidity and mortality due to pneumonia were higher in HIV-infected persons than in the general population [1]. In 1993 the United States Centers for Disease Control and Prevention categorized two or more episodes of bacterial pneumonia as an AIDS-defining event [2]. The introduction of highly active antiretroviral therapy (HAART) markedly reduced the incidence of AIDS and death among HIV-infected persons [3,4,5], and improved immune function also led to fewer pneumonia-related hospitalizations [6,7]. However, more than a decade after the widespread introduction of HAART in high-income countries, the risk of pneumonia among HIV-infected persons remains high compared to persons without HIV [7]. A better understanding of modifiable prognostic factors for death after pneumonia could potentially reduce mortality from this illness. In this cohort study we estimated the impact of a first hospitalization for pneumonia on mortality among Danish HIV patients, examined changes over calendar time in mortality following hospitalization for pneumonia, and identified prognostic factors for death following pneumonia.

Methods

Study design and setting

We conducted a nationwide, population-based cohort study among HIV-infected persons in Denmark from 1995 to 2008. Treatment for HIV infection in Denmark is restricted to 8 specialized centers. The Danish health care system provides free, tax-supported medical care for all residents, including antiretroviral treatment of HIV.
The Danish HIV Cohort Study (DHCS)

The DHCS has established a prospective, dynamic, nationwide, population-based cohort of all HIV-infected individuals seen in Danish HIV clinics since 1 January 1995. DHCS has been described in detail elsewhere [8,9]. The study is ongoing, with continuous enrollment of both newly diagnosed patients and immigrants with HIV infection. Study data are updated annually with information on antiretroviral treatment, development of opportunistic infections and other AIDS-defining illnesses, and laboratory data including plasma HIV RNA (viral load (VL)) and CD4+ cell count.

Danish Civil Registration System (CRS)

CRS is a national registry of all Danish residents, which contains information on date of birth, sex, date of migration, and date of death. A 10-digit personal registration number (CPR number), assigned at birth, uniquely identifies each person since 1968. The CRS is updated within a week of a person’s birth, death, or emigration. Use of the CPR number enables Danish HIV clinics to avoid multiple registrations of the same patient and allows tracking of deaths and persons lost to follow-up due to emigration.

The Danish National Hospital Registry (NHR)

NHR contains information on all patients discharged from Danish hospitals since 1977. Records for each hospitalization include CPR number, hospital department, inpatient and outpatient discharge diagnoses, and dates of admission and discharge. Diagnoses are coded by the treating physician according to the International Classification of Diseases, 8th revision (ICD-8) until the end of 1993 and 10th revision (ICD-10) thereafter.

Identification of pneumonia

We identified the first hospitalization for pneumonia following HIV diagnosis. We used the NHR to identify all hospital stays with a discharge diagnosis of pneumonia using ICD-8 codes 471.x (influenza with pneumonia), 480.x-486.x (pneumonia), 073.x (ornithosis) and ICD-10 codes J11.0 (influenza with pneumonia), J12.x-J18.x (pneumonia), A481.x (ornithosis), or A709.x (legionellosis). Thus, both community-acquired and hospital-acquired pneumonias were included. The pneumonia diagnoses recorded in the NHR were validated in a previous report [7].

Study population

Our study population consisted of persons in DHCS who were at least 16 years old on the date of HIV diagnosis and who had no recorded hospitalization for pneumonia before entering DHCS. Study subjects were followed from their registration in DHCS to death, loss to follow-up or 1 July 2008, whichever came first.

Definitions

HAART was defined as either a 3-drug regimen that included a non-nucleoside reverse transcriptase inhibitor, a protease inhibitor, and/or abacavir; or a 2-drug regimen with a combination of a non-nucleoside reverse transcriptase inhibitor and a boosted protease inhibitor.

CD4+ cell counts and viral load (VL) were estimated between measurements by carrying forward the value from the most recent measurement. Nadir CD4+ cell count was defined as the lowest CD4+ cell count ever measured for a given patient.

Comorbidity was assessed with the Charlson Comorbidity Index (CCI). The index, which includes 19 major disease categories, has been adapted and validated for use with hospital discharge data in ICD databases for predicting short- and long-term mortality [10]. A CCI score was computed for each patient based on all available preceding NHR discharge diagnoses. A previous AIDS diagnosis (conferring 6 CCI points) was not included in our computations [11].

Hepatitis C co-infection was defined as patients having at least 1 positive result on a hepatitis C virus (HCV)-antibody test or a positive result on HCV RNA test.

The endpoint, defined a priori, was all-cause mortality following the hospital admission date for pneumonia. Causes of death, extracted from patient files and available in the DHCS database, were divided into HIV-related causes (AIDS-defining illnesses and bacterial infections, corresponding to ICD-10 codes A02, A07.2–07.3, A15–19, A31, A81.2, B00, B20–23, B37–39, B45, B58, C46, C53, C83.4, C83.9, F02.4, and J13–17 [pneumonia]), serious non-AIDS causes (cardiovascular disease [i.e. myocardial infarction or stroke], end stage renal and liver disease, COPD, and non-AIDS-defining malignancies), unnatural causes (i.e. drug overdose, suicide, accident) and other/unknown causes.

Statistical analyses

We first computed 30-day and 90-day cumulative mortality following the first hospitalization for pneumonia and constructed Kaplan-Meier survival curves, stratified into 3 calendar periods: 1995–1996 (‘‘pre-HAART era’’), 1997–1999 (‘‘early HAART era’’), and 2000–2008 (‘‘late HAART era’’).

We then assessed the effect of a first hospitalization for pneumonia on mortality. We compared the mortality rate in persons who had no previous history of pneumonia (reference group) with that of persons with a first hospitalization for pneumonia within the last 0–90 days, within the last 91–365 days, and more than 365 days ago. Poisson regression analysis was used to adjust for potential confounders. The following time-dependent variables were forced into the model based on their presumed association with pneumonia and/or effect on mortality: CCI score (0–1/2+), age (10-year intervals), and CD4+ cell count (continuous). Other variables were examined and included in the final model if they changed the effect measure by 10% or more. Constant variables were sex (male/female), hepatitis C coinfection (yes/no), injection drug use (IDU) as presumed mode of HIV infection (yes/no), and race (Caucasian/non-Caucasian). Time-dependent variables were history of AIDS (yes/no), current HAART (yes/no), years since entering the DHCS, and calendar time period (1995–96 vs. 1997–2008). Causes of death were tabulated for all four time periods.

Finally, we used logistic regression to identify prognostic factors for 30-day and 90-day mortality following hospitalization for pneumonia. In the unadjusted analyses we included all the variables listed above as of the time of admission, as well as log-transformed HIV RNA (continuous). In the adjusted analyses of 30-day and 90-day mortality we included all variables from the unadjusted analyses in the models, except: nadir CD4+ cell count because this variable and history of AIDS are interdependent (adjustment for nadir CD4+ cell count thus could cancel out the effect of previous AIDS); IDU as mode of HIV exposure which is interdependent with hepatitis C status; and HIV RNA which is interdependent with use of HAART.

We used Stata software, version 9.2 (StataCorp, College Station, TX, USA) for statistical analyses. The study was approved by the Danish Data Protection Agency. In Denmark, a national board
The Danish Data protection Agency approved the studies. Informed consent was waived. Informed consent was not required by Danish law in order to conduct cohort studies.

Results

DHCS study population

Between 1 January 1995 and 1 July 2008, 699 episodes of an initial hospitalization for pneumonia were observed among 4,352 persons who were at least 16 years old and had no recorded hospitalization for pneumonia before entering the DHCS cohort. Characteristics of persons in our study population at the time of the initial hospitalization for pneumonia are shown in Table 1. Less than half (43.3%) received HAART and the median CD4+ cell count was 281 cells/µl.

Impact of hospitalization for pneumonia on survival among HIV patients

Overall 30-day risk of death after first hospitalization for pneumonia was 6.4% (95% CI: 4.8%–8.5%) (see Figure 1). It was 7.9% (95% CI: 4.6%–13.5%) in 1995–1996, 7.6% (95% CI: 4.1%–13.6%) in 1997–1999, and 5.5% (95% CI: 3.7%–8.2%) in 2000–2008. Overall 90-day risk of death was 12.0% (95% CI: 9.8%–14.7%), decreasing from 22.4% (95% CI: 16.5%–28.9%) in 1995–1996 to 11.4% (95% CI: 7.0%–18.1%) in 1997–1999, and to 8.4% (95% CI: 6.1%–11.6%) in 2000–2008.

The effect of first-time hospitalization for pneumonia on mortality among all HIV-infected persons is shown in Table 2. Adjusting for use of HAART, history of AIDS, years since entering the DHCS, CCI score, age, and current CD4+ cell count, the relative mortality during the first 90 days after an initial hospitalization for pneumonia, compared to those with no previous hospitalization for this indication, was 5.38 (adjusted mortality rate ratio [MRRadj], 95% CI: 4.27–6.78). Mortality was also elevated for days 91–365 (MRRadj = 1.62, 95% CI: 1.32–2.00) and days 366+ (MRRadj = 1.62, 95% CI: 1.32–2.00). Causes of death for persons in all four time strata are presented in Table 3. Among those who died within days 0–90, days 91–365, and after 365 days, 61.9%, 53.7%, and 28.8%, respectively, had an HIV-related cause of death.

Prognostic factors for short-term mortality following hospitalization for pneumonia

In the adjusted logistic regression analysis, the following variables were associated with increased 30-day mortality after a first hospitalization for pneumonia (Table 4): CCI score ≥2 (ORadj = 4.07, 95% CI: 2.03–8.17), male sex (ORadj = 3.86, 95% CI: 1.05–14.2), no current HAART (ORadj = 3.19, 95% CI: 1.42–7.16), history of AIDS (ORadj = 2.78, 95% CI: 1.34–5.78), latest CD4+ cell count ≤200 cells/µl (ORadj = 2.72, 95% CI: 1.28–5.78) and age (ORadj = 1.53 per 10 year increase, 95% CI: 1.11–2.12).

Variables associated with increased 90-day mortality were (Table 5): CCI score ≥2 (ORadj = 3.86, 95% CI: 2.19–6.78), male sex (ORadj = 3.77, 95% CI: 1.37–10.4), no current HAART (ORadj = 3.56, 95% CI: 1.83–6.99), previous AIDS (ORadj = 2.46, 95% CI: 1.40–4.32), CD4+ cell count ≤200 (ORadj = 2.52, 95% CI: 1.37–4.65) and age (ORadj = 1.43 per 10 year increase, 95% CI: 1.11–1.85). Among patients on HAART neither the duration of HAART use or HIV RNA (<50 vs. ≥50 copies/mL) were protective (data not shown).

Discussion

This study found that short-term mortality after a first hospitalization for pneumonia among HIV-infected individuals decreased from the pre-HAART to the late-HAART era. Despite this decrease over time, an episode of hospitalization due to pneumonia remains associated with an increased mortality among HIV patients. Prognostic factors were male sex, age, pre-existing comorbidity, low CD4 cell count, older age, and absence of HAART treatment. Several studies have shown that persons on HAART have a reduced

### Table 1. Baseline characteristics of HIV–infected individuals at time of first admission for pneumonia.

| Variable | Numbers (N = 699) |
|----------|-------------------|
| Median age, years (interquartile range) | 42.2 (35.2–50.1) |
| Sex, n (%) | |
| Female | 146 (20.9) |
| Male | 553 (79.1) |
| Race, n (%) | |
| Caucasian | 588 (84.2) |
| Black | 73 (10.5) |
| Asian | 12 (1.7) |
| Inuit | 10 (1.4) |
| Other | 15 (2.2) |
| Mode of HIV exposure, n (%) | |
| MSM | 299 (42.8) |
| Heterosexual | 204 (29.2) |
| IV drug use | 147 (21.0) |
| Other | 28 (4.0) |
| Unknown | 21 (3.0) |
| Years since entering DHCS, (interquartile range) | 3.30 (1.18–7.01) |
| On HAART, n (%) | |
| Yes | 403 (57.7) |
| No | 296 (43.3) |
| Median current CD4+ cell countb, cells/µl (interquartile range) | 281 (117–462) |
| Median days since last CD+ cell count measurement, (interquartile range) | 47 (17–87) |
| Nadir CD4+ cell count, cells/µl (interquartile range) | 139 (48–240) |
| Median HIV RNAc, log(copies/ml), (interquartile range) | |
| On HAART | 1.6 (1.3–4.1) |
| HAART-naive | 4.6 (4.0–5.0) |
| Median days since last HIV RNA measurement, (interquartile range) | 48 (19–85) |
| Charlson Comorbidity Index score, n (%) | |
| 0–1 | 532 (76.1) |
| ≥2 | 167 (23.9) |

*DHCS: Danish HIV Cohort Study.

aLast measurement before date of pneumonia.

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risk of pneumonia compared to those not on HAART [6,7,12]. However, our study is the first to show that HAART use also affects prognosis in the presence of a pneumonia-related hospitalization.

The strengths of our study include use of a population-based, nationwide cohort with nearly complete inclusion and minor loss to follow-up; access to complete hospitalization data and vital statistics; and availability of electronically collected longitudinal data on viral load and CD4+ cell counts. The quality of the data minimized selection and information biases. Because we considered only the first hospitalization for pneumonia, our estimates were not biased by multiple pneumonia episodes occurring in highly susceptible individuals.

![Figure 1. Mortality after first hospitalization for pneumonia among persons with HIV by time period.](doi:10.1371/journal.pone.0007022.g001)

**Table 2.** Short- and long-term impact of pneumonia on mortality among all HIV–infected individuals.

| No of deaths | Follow-up | MR<sup>b</sup> | Crude MRR ratio | Adjusted<sup>c</sup> MRR |
|--------------|-----------|----------------|-----------------|--------------------------|
| At any time after first hospitalization for pneumonia | 263 | 3,131 | 0.23 (0.20–0.26) | 3.56 (3.09–4.10) | 2.79 (2.40–3.26) |
| Day 0–90 after admission | 84 | 159 | 1.44 (1.17–1.79) | 20.5 (16.3–25.7) | 5.38 (4.27–6.78) |
| Day 91–365 after admission | 54 | 420 | 0.35 (0.27–0.46) | 4.98 (3.77–6.57) | 1.80 (1.36–2.37) |
| Day 366+ after admission | 125 | 2,552 | 0.13 (0.11–0.16) | 1.90 (1.57–2.30) | 1.62 (1.32–2.00) |
| No previous pneumonia | 691 | 26,775 | 0.07 (0.07–0.08) | 1 (ref) | 1 (ref) |

<sup>a</sup>In years.  
<sup>b</sup>Per 1000 days.  
<sup>c</sup>Adjusted for use of HAART, history of AIDS, years since entering the DHCS, Charlson Comorbidity Index score, age, and current CD4+ cell count.  
<sup>d</sup>Adjusted MRR for use of HAART, history of AIDS, years since entering the DHCS, Charlson Comorbidity Index score, age, and current CD4+ cell count.

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**Table 3.** Causes of death among HIV patients with and without pneumonia.

| No of deaths | HIV-related<sup>a</sup> | Serious non-AIDS conditions<sup>b</sup> | Unnatural<sup>c</sup> | Other/unknown | No of deaths |
|--------------|-------------------------|---------------------------------|----------------|----------------|--------------|
| Day 0–90 after pneumonia, n (%) | 52 (61.9) | 15 (17.9) | 2 (2.4) | 15 (17.9) | 84 (100) |
| Day 91–365 after pneumonia, n (%) | 29 (53.7) | 7 (13.0) | 3 (5.6) | 15 (27.8) | 54 (100) |
| Day 366+ after pneumonia, n (%) | 36 (28.8) | 36 (28.8) | 5 (4.0) | 48 (38.4) | 125 (100) |
| No previous pneumonia, n (%) | 296 (42.8) | 145 (21.0) | 42 (6.1) | 208 (30.1) | 691 (100) |

<sup>a</sup>AIDS-defining illnesses and bacterial infections.  
<sup>b</sup>Cardiovascular disease (i.e. myocardial infarction or stroke), end stage renal and liver disease, COPD, and non-AIDS-defining malignancies.  
<sup>c</sup>I.e. drug overdose, suicide, and accident.  
<sup>d</sup>Adjusted MRR for use of HAART, history of AIDS, years since entering the DHCS, Charlson Comorbidity Index score, age, and current CD4+ cell count.

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Our study had a number of limitations. First, previous studies have found identifiable bacterial pathogens in 24%–38% of HIV-infected patients with pneumonia [13,14]. As data on specific pathogens were not available, we do not know the percentage of pneumonia cases in our study population caused by bacteria and how this may have affected prognosis. Second, causes of death registered in DHCS were based on information extracted from medical records. Thus the exact cause of death may be uncertain or, in some cases, multifactorial. For this reason we chose to group causes of death into broader categories to determine whether HIV was the key factor. We were unable to adjust for use of opportunistic infection prophylaxis, smoking status, and/or pneumococcal vaccination status since these data were not available in DHCS database. Our results are restricted to inpatients. Finally, despite our efforts to control for potential confounders, it is possible that the observed protective effect of HAART was due to confounding by indication (i.e., patients on HAART had an a priori reduced risk of death for example due to a healthier lifestyle compared to HAART-naive patients).

The incidence rates of pneumonia in HIV-infected individuals decreased from 51 hospitalizations per 1000 person-years during 1995–1996 to 20 hospitalizations per 1000 person-years during 2005–2007 [7]. In our study population, 30-day mortality did not change over calendar time and was comparable to the mortality risk of 6%–8% following pneumonia found in other studies of HIV-infected persons [6,13], and consistent with the finding that most pneumonia-related deaths occur within 30 days of hospital admission [15]. Contrary to studies on invasive pneumococcal disease [16], we found a decline in 90-day mortality from the pre-HAART era to the HAART era. We even may have underestimated the decline in mortality over calendar time because the median age in our cohort increased from 1995 to 2008. Therefore, while the acute course of pneumonia has change little over time, the reduction in 90-day mortality may be due to reduced risk of death from sequelae following the initial episode of pneumonia [17], perhaps stemming from a general improvement in immune function after introduction of HAART.

In a study of non-HIV infected individuals aged 40–64 hospitalized for the first time with pneumonia, 30-day mortality was 7.8%, and 90-day mortality was 11.6% [18]. These estimates are comparable to what we found in HIV-infected individuals.
Further, the overall impact on risk of death following a first hospitalization pneumonia was similar to the increased risk recently reported for “mild” AIDS-defining events (i.e., pulmonary and extrapulmonary tuberculosis, *Pneumocystis jiroveci* (carinii) pneumonia and esophageal candidiasis) [19].

Others have found a four to five-fold increased risk of death (follow-up ≤51 months) among HIV-infected persons with pneumonia, compared to those without pneumonia [6,13], which is in accordance with our findings. Contrary to other studies [20], however, we found that the increased risk of death persisted beyond one year. Although unmeasured confounding factors cannot be ruled out as a contributory cause of the increased long term risk of death, pneumonia could also be viewed as a marker of immune system frailty that may not be reflected by the CD4+ cell count.

We found that HAART use improved the prognosis after a pneumonia-related hospitalization pneumonia was similar to the increased risk recently reported for “mild” AIDS-defining events (i.e., pulmonary and extrapulmonary tuberculosis, *Pneumocystis jiroveci* (carinii) pneumonia and esophageal candidiasis) [19].

In conclusion, a first hospitalization for pneumonia in HIV-infected individuals predicted an increased risk of death beyond one year. Among those hospitalized with pneumonia, use of HAART was associated with a reduced risk of death, independent of the CD4+ cell count which is interdependent to AIDS and HIV RNA which is interdependent to use of HAART.

### Table 5. Prognostics factors for 90-day mortality after first hospitalization for pneumonia among HIV–infected individuals.

| 90 day mortality | n | Deaths | Mortality (%) | OR (95% CI) | p | OR(adj) (95% CI) | Coefficient (SE) | p |
|------------------|---|--------|---------------|-------------|---|-----------------|------------------|---|
| Intercept        |   |        |               |             |---|                 |                  |   |
| Age (per 10 year increase) | 699 | 84 | 12.0 | 1.36 (1.11–1.66) | 0.003 | 1.43 (1.11–1.85) | 0.36 (0.13) | 0.007 |
| CD4+ cell count < 200 cells/µl | No | 411 | 28 | 6.8 | 1 (ref) | 1 (ref) | 0 (ref) | |
|                    | Yes | 241 | 49 | 20.3 | 3.49 (2.13–5.73) | <0.001 | 2.52 (1.37–4.65) | 0.93 (0.31) | 0.003 |
| Charlson Comorbidity index | missing data | 47 | 7 | 14.9 | 2.39 (0.98–5.83) | 0.055 | 1.91 (0.67–5.43) | 0.65 (0.53) | 0.223 |
| 0–1               | 532 | 44 | 8.2 | 1 (ref) | 1 (ref) | 0 (ref) | |
| ≥2                | 167 | 40 | 24.0 | 3.49 (2.18–5.59) | <0.001 | 3.86 (2.19–6.78) | 1.35 (0.29) | <0.001 |
| History of AIDS   | No | 236 | 35 | 7.6 | 1 (ref) | 1 (ref) | 0 (ref) | |
|                    | Yes | 463 | 49 | 20.8 | 3.20 (2.01–5.11) | <0.001 | 2.46 (1.40–4.32) | 0.90 (0.29) | 0.002 |
| On HAART          | Yes | 347 | 25 | 7.1 | 1 (ref) | 1 (ref) | 0 (ref) | |
|                  | No  | 352 | 59 | 16.8 | 2.59 (1.58–4.25) | <0.001 | 3.58 (1.83–6.99) | 1.27 (0.34) | <0.001 |
| Sex               | Male | 533 | 79 | 14.3 | 4.40 (1.79–10.9) | 0.001 | 3.77 (1.37–10.4) | 1.33 (0.52) | 0.010 |
|                  | Female | 146 | 5 | 3.4 | 1 (ref) | 1 (ref) | 0 (ref) | |
| Mode of HIV exposure | Non-IDU | 552 | 66 | 12.0 | 1 (ref) | 1 (ref) | 0 (ref) | |
|                  | Yes | 191 | 21 | 11.0 | 0.87 (0.52–1.47) | 0.610 | 1.13 (0.61–2.11) | 0.12 (0.32) | 0.701 |
| HIV RNA (per log10 increase in copies/ml) |
| On HAART         | 403 | 39 | 9.2 | 2.27 (0.43–12.1) | 0.337 | ... | ... | ... |
| HAART-naïve      | 296 | 45 | 14.9 | 0.24 (0.03–2.18) | 0.206 | ... | ... | ... |

*This logistic regression model was adjusted for all variables in the table except: IDU as mode of HIV exposure which is interdependent to hepatitis C status, Nadir CD4+ cell count which is interdependent to AIDS and HIV RNA which is interdependent to use of HAART.

*Last measurement before date of pneumonia. adj = Adjusted; OR = Odds Ratio; CI = Confidence Interval.

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of CD4 cell counts. While the former finding may indicate that acquisition of pneumonia is a marker of frailty, the latter may indicate that this frailty can be partly offset by use of HAART. These findings support the need for additional research to assess the role of HAART in reducing morbidity and mortality associated with non-AIDS-defining infections. Promotion of early HAART initiation may not only lead to reduced mortality after pneumonia, it may also reduce the risk of acquiring pneumonia severe enough to require hospitalization [6,7]. Finally, it is reassuring that the prognosis following pneumonia has improved over calendar time.

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Author Contributions

Conceived and designed the experiments: OSS NL HS NO. Performed the experiments: OSS. Analyzed the data: OSS NL HS. Contributed reagents/materials/analysis tools: OSS JG GK L CP GP NO. Wrote the paper: OSS NL JG GK L CP GP HS NO.