Mortality and Risk Stratification of HIV Infected Individuals

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For the first decade and a half after the Human Immunodeficiency Virus (HIV) was first identified, the prognosis for most people infected with HIV was quite poor. Life insurance companies responded accordingly and insurance laboratories developed new means to test for the infection. However, it is now clear that people with HIV infection are living longer and that the majority of deaths occurring among those on treatment are now no longer due to AIDS-defining illnesses. This review examines the results of selected studies which analyzed mortality outcomes in those with HIV infection, the many factors which influence those outcomes, and the limitations in the data and in their applicability to an insurance population.

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Determining the long-term mortality implications of HIV infection is a challenging task. In most cases, the prognosis in patients with untreated HIV infection is poor, with an overall mortality rate of more than 90% and an average time from infection to death of 8-10 years. Individual variability ranges though from less than 1 year to long-term non-progression; it is apparent that HIV infection is a rather heterogeneous condition.

However, with the introduction of highly active antiretroviral therapy (ART) in 1996, and the use of increasingly better antiviral regimens, the overall survival with HIV infection has improved markedly over time. Initial mortality studies in the early years of the ART era compared minimally selected groups of HIV infected persons – ie, without regard to treatment or response and including those with IV drug use (IVDU) and AIDS-defining illness (ADI) – to those in the general population. These nonetheless showed improvement with the advent of ART, albeit still with significantly increased crude mortality rates and overall standardized mortality ratios (SMRs). For example in a 1998 analysis, the mortality rate from March 1995 to September 1995 (pre-ART) was 233/1000/year and fell to 41/1000 between September 1997 and March 1998.[1] In a 2004 Swiss study, the overall SMR decreased from 79.3 pre-ART to 15.3 thereafter.[2] Further improvement was demonstrated in a 2007 population-based study showing average estimated life expectancy (LE) for an HIV-positive individual at age 25 increasing from 19.9 years in 2000 to 32.5 years in 2005.[3]

MORTALITY STUDIES IN THE ERA OF ART

Subsequent studies continue to demonstrate improving outcomes over time for those on ART and even better outcomes in selected groups, as summarized in Table 1.

Selected Studies

To a varying degree in these studies, excess mortality was still seen due to AIDS, the presence of comorbid diseases and exposure to co-pathogens (eg, hepatitis C), the side effects of ART, the detrimental impact of non-ART-related lifestyle factors such as smoking and drug abuse, and/or to accelerated aging driven by chronic immune activation. Nonetheless, studies from the most recent years have shown further improvement in mortality outcomes and have longer durations of follow-up. Survival rates in select sub-groups with HIV, and over 5-10 years, have been shown to approach that of the general population. The following are 5 studies worth reviewing.

Study 1

In a Danish population-based cohort of all HIV-infected persons aged 25-65 who started ART between January 1, 1998, and July 1, 2009, (2267 persons) with median age 40, 74% male, and a median 5 years of follow-up, Kaplan-Meier tables were computed of various HIV-infected risk groups. This group was then compared to a general population group without a diagnosis of HIV, who had no known comorbidity or drug or alcohol abuse (Group 0). Those labeled as "Group 1" included HIV-infected patients with a CD4+ count ⩾200 at last measure, no detectable viral load, no AIDs-defining illness (ADI), nor with any comorbidity, drug, or alcohol abuse (including a suspected IV drug use transmission). In this analysis, 58.7% those with HIV met these criteria. The SMR for this group compared to the similarly selected general population was 2.02 for ages 25-45 and 1.14 for ages 45-65. See Figure 1. Crude mortality rate for ages 25-45 was 1.47/1000

compared to 1.27/1000 in the general population, and it was 5.82/1000 at ages 45-65 compared to 4.23/1000.[10]

Though this was a relatively small study group and a more homogeneous population overall, the strength from an insurance perspective was the comparison to a general population group selected to be without comorbidities and likely closer to representing an insurance population than other studies. Their choice of a CD4+ count ⩾200, compared to the usually accepted goal of 350 or 500, raises the question of potentially even lower SMRs at those figures, although this is speculative.

Study 2

In the Collaboration of Observational HIV Epidemiologic Research Europe (COHERE) cohort, all-cause mortality in 80,642 individuals from 23 cohorts and 31 European countries starting ART between 1998 and 2008 was compared with the general population. Median duration of follow-up was 3.5 years. The overall mortality rate was 11.5/1000 with an SMR of 4.2 compared to the general population (SMR 8.5 at ages 18-39, 4.2 at ages 40-59, and 1.7 at ages 60 and up), however among 35,316 individuals who were non-IV drug users with CD4+ counts ⩾500, the SMR was 0.9 for men (CI 0.7-1.3) and, after 3 years of ART, was 1.1 in women (CI 0.7-1.7). Even among those with a prior AIDS-defining illness, but with CD4+ count ⩾500, the SMR was 1.2 (0.8-2.0) for ages 40-59.[11]

Study 3

In a well-constructed study designed in part by those in the life insurance industry, the ART Cohort Collaboration (ART-CC) data were used to assess the insurability of HIV positive people treated with ART in Europe. In this study, 34,680 patients were identified who were not infected via IV drug use, were Hepatitis C negative, and who started ART between 1996 and 2008. Data were available to estimate death rates up to 10 years

Table 1. Prognostic Factors Influencing Mortality[4-20]

Study and Year Published	Population	Findings	Comments
ATHENA 2005 (4)	Dutch cohort, 3678 patients starting ART.	Predicted SMR of 5.3 in men age 25 and 1.15 in men age 65.	Results suggested the mortality in some subgroups was approaching that of the general population.
CASCADE Collaboration 2008 (5)	23 cohorts in Europe, Canada and Australia.	Excess mortality rates (per 1000) decreased from 40.8 pre-1996 to 6.1 in 2004-2006.	
Comparative mortality analysis J Insur Med 2008 (6)	Danish Civil Registry cohort, 3990 patients. Data published 2007 *Ann Int Med.*	Annual mortality rate dropped from 119/1000 in 1995-1996, and an overall mortality ratio of 2600%, to 20/1000 in 2000-2005, and a mortality ratio of 570%.	Singer and Milano analysis. Included all patients from HIV clinics including those with advanced disease and those not on ART.
Antiretroviral Therapy Cohort Collaboration (ART-CC) 2008 (7)	43,355 patients from 14 cohort studies, entered over three periods between 1996 and 2005.	Crude mortality rates improved from 16.3 to 9.9/1000 with a commensurate increase in estimated life expectancy at age 35 from 25.0 to 37.3 years.	Stratified by CD4+ cell count, the LE at age 35 for ≥200 at baseline was 37.2 years, compared to 27.0 for a count <100.
ART-CC cohort 2009 (8)	29,935 patients from European and North American cohorts. Mean age 37, mean follow-up 3.75 yrs.	Crude death rate 9.5/1000, overall SMR 3.36.	Data further stratified: SMR was 1.05 to 1.33 for those with CD4+ >350, viral load <500 copies/ml, and no ADI.
Control arms of ESPRIT and SILCAAT trials 2010 (9)	3012 patients (20317 person-years) prospectively followed on ART for nearly a decade, median follow-up of 7 years.	Used Cox regression to identify CD4+ metrics independently predictive of all-cause mortality. Latest CD4+ count was most predictive. Adjusted for CD4+, only the CD4+ slope remained statistically significant.	HIV RNA levels were also an important predictor but it closely correlated with CD4+ count and was not found to be a significant independent factor.
Danish population-based cohort 2011 (10)	All HIV-infected persons aged 25-65 who started ART Jan 1, 1998 to July 1, 2009; 2267 persons.	SMR for those without a detectable viral load, with CD4+ count ≥200 at last measure, and no IVDU or ADI, was 2.02 for ages 25-45 and 1.14 for ages 45-65.	A relatively small group but with excellent data collection. (Study 1)
COHERE cohort 2012 (11)	80,642 individuals from 31 European countries starting ART 1998-2008 and having a CD4+ measurement within 6 months.	Among 35,316 non-IVDU individuals with CD4+ counts ≥500, SMR was 0.9 for men and, after at least 3 years of ART, was 1.1 in women.	Large cohort allowed for extensive data analysis, such as considering those with prolonged maintenance of favorable CD4+ counts. (Study 2)

Table 1. Continued

| Study and Year Published	Population	Findings	Comments
Australian HIV Observation Database (AHOD) 2012 (12)	2,675 HIV-positive participants who started ART followed up to 15 years (15,936 total pt-yrs).	SMR by CD4+ count alone was 1.5, 2.1, and 8.6, for >500, 350-499, and <350 respectively, but after controlling for age, IVDU, prior ADI, viral load, Hep B or C ever, rates for CD4+ >350 were not significantly different from the general population.	There was no evidence of increasing mortality over time compared to the general population. However, lost to follow-up rate was high at 40/1000.
CRL dataset J Insur Med. 2012 (13)	12,353 positive for HIV among 14.1 million applicants age 20-79 tested 1991-2009, assessed through the Social Security Master Death file through 2010	Overall Hazard Ratio by age group in those HIV-positive by serum sample was 14.8 for ages 20-39, 6.5 ages 40-59, and 3.2 ages 60-79.	Data were analyzed using Cox regression with HIV status, age, smoking, and gender as covariates. No other underwriting information was included.
Collaborative analysis of the ART-CC cohort 2013 (14)	34,680 patients were identified who were not infected via IVDU, were Hep C negative, and started ART 1996 to 2008, and followed for 174,906 person-years.	Sub-groups at older ages and longer ART duration had more favorable mortality ratios. E.g., the MR compared to insured lives was 165% for those age 40-49 who started ART after 2000, had no ADI, had 6 month CD4+ counts >350 and HIV RNA <10,000, and were on ART for 7+ years.	Involved insurance medicine input; Widmer, et al. (Study 3)
Continuous antiretroviral therapy arms of the SMART and ESPRIT trials 2013 (15)	Prospective cohort of 3280 individuals age 20-70 (12,357 person-years of follow-up). 53% from N. America. Excluded those with IVDU.	SMR compared to general population was 1.0 (CI 0.69-1.30) for those with CD4+ counts >500 and viral suppression at last follow-up. It was 1.77 (CI 1.17-2.55) for those with CD4+ counts of 350-499.	Had excellent ascertainment of vital status (a limitation of many studies). Overall mortality 5.0/1000 person-years. Only 3.2% of deaths were felt to be due to AIDS.
NA-ACCORD cohort 2013 (16)	22,937 participants from the North American AIDS Cohort Collaboration on Research and Design age 20 and up, on ART, and with a CD4+ count within 6 months on ART.	Projected weighted life-expectancy at age 20 was calculated to be 42.7 yrs for the overall group, 57.3 yrs selected only by MSM transmission, and 54.6 yrs by CD4+ count >350 only, compared to 59.7 yrs in Canada and 57.0 yrs in the U.S. general population.	The overall unweighted mortality rate was reported as 19.8/1000; 12.5/1000 in MSM transmission, and 11.3/1000 in CD4+ >350 group (which appears possibly counter to the projected LEs).

Table 1. Continued

Study and Year Published	Population	Findings	Comments
UK-CHIC Study 2014 (17)	21,388 HIV+ individuals receiving care in the UK 2000 to 2012.	After 5 years on ART, expected age at death of 35 year-old men varied from 54 to 80 for those with CD4+ counts <200 and no viral suppression versus CD4+ >350 and viral load suppressed.	Article specifically states that their study supports "that patients successfully treated with ART should be eligible for life insurance." (Study 4)
Multicenter AIDS Cohort (MACS) and Women's Interagency HIV Study (WIHS) 2014 (18)	U.S. population cohorts. Compared mortality rates between the HIV-negative members and the HIV-positive members on ART. Median follow-up 10.2 years.	Median life expectancy of HIV+ group starting ART when their CD4+ counts were >350 was 72, compared to 69 if counts were 201-350, 66 if 200 or less, and compared to 75 in the HIV-uninfected group.	In these socially matched groups, rates of non-AIDS deaths were the same in those starting ART with CD4+ counts ≥350 and those who were HIV-negative.
Data collection on Adverse events of anti-HIV Drugs (D:A:D) study 2014 (19)	11 cohort studies from 212 clinics in Europe, USA, and Australia. 49,731 individuals under active follow-up until 2/1/11 or death, recruited during three waves: 12/99-4/01, 12/03-5/04, and 1/10-12/10.	Major aim was to identify emerging toxicities of ART by looking for changes in mortality rates from specific causes. There were decreases in deaths due to AIDS, liver disease, and CV disease over time, but not for non-AIDS cancer. Adjusted all-cause mortality decreased by 28% over time including a 65% decrease in CV deaths.	Adjusted for age, sex, ethnic origin, mode of HIV acquisition, Hepatitis B and C status, BMI, smoking status, diabetes, HTN, HIV RNA viral load, and CD4+ count.
ART-CC Cohort Subgroup of those with data on smoking status 2015 (20)	17,995 individuals from multiple European and North American cohorts, on ART for at least one year.	MR for smokers vs non-smokers with HIV was 1.94. Estimated life expectancy of virally suppressed, never smokers was 43.5 years, compared with 44.4 years for 35 year-old men in the background (French) population.	Analysis found that the mortality risk from HIV infection was similar to, or less than, that of smoking. (Study 5)

after starting ART and 174,906 person-years of follow-up were registered. In this group, 70% were male, 65% aged 30-49, and 52% with heterosexual transmission, with the majority coming from France or the Netherlands. Relative mortality compared to an insured population in each country, using Poisson models, was estimated. Expected numbers of death were calculated based on "standard" insured lives insurance tables in France, Netherlands, and UK, or on adjustments to population mortality tables in Italy, Spain, and Switzerland, as commonly used in those countries by pricing actuaries.

The overall mortality was 7.1/1000/year. As seen in most other studies, CD4+ count and
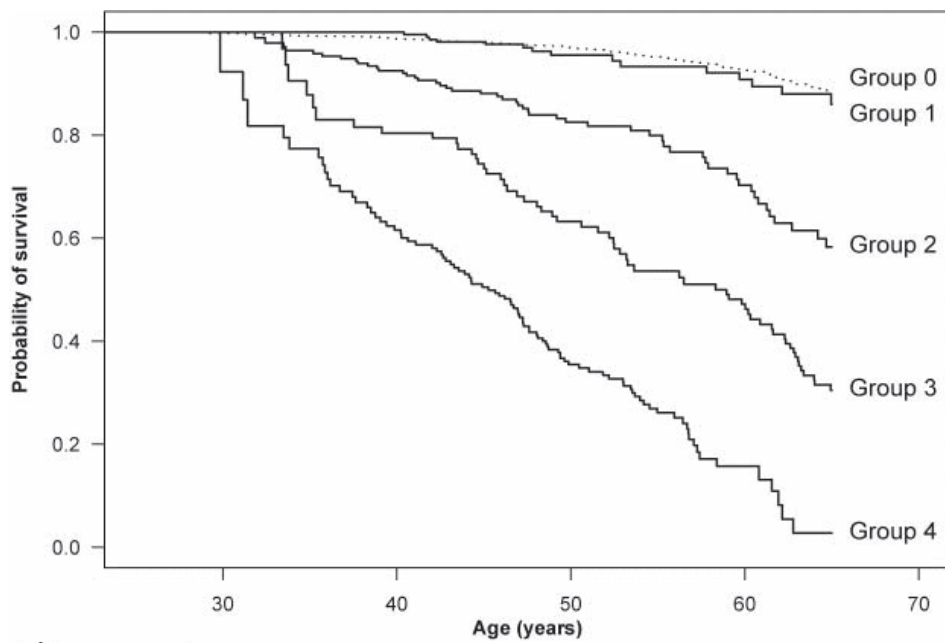
Time was calculated from 1 year after start of HAART.
Group 0: Population comparison cohort (dotted line, N = 9,068).
Group 1: HIV-infected patients without HIV risk factors, comorbidity or alcohol/drug abuse (N = 871).
Group 2: HIV-infected patients with HIV risk factors, but no comorbidity or alcohol/drug abuse (N = 704).
Group 3: HIV-infected patients with comorbidity, but no alcohol/drug abuse (N = 379).
Group 4: HIV infected patients with alcohol/drug abuse (N = 313), detectable viral load (>49 copies/ml), and/or CD4+ below 200 cells/ul and/or AIDS-defining disease as of the index date.
Obel N, et al. doi:10.1371/journal.pone.0022698.g001.

Figure. Cumulative survival for HIV-infected patients starting HAART and persons from the general population.

viral load at 6 months were the most strongly prognostic factors. Mortality rate ratios also decreased with age and with ART duration and were higher in those who started ART before 2001. The relative mortality ratio for those ages 20-39, who started ART after 2000, had 6 month CD4+ counts $\geq$350, 6 month HIV RNA <10,000 copies/ml, had no AIDs diagnosis, and were during the first 3 years of ART, compared to insured lives, was 459%. Sub-groups at older ages and longer ART duration had more favorable mortality ratios. For example, with the above features but at age 40-49 the MR was 324% in the first 3 years, 223% during years 4-6, and 165% after 7 or more years on ART. At ages 50-59, these values were 250%, 172%, and 128%, respectively.[14]

As good as these data are for insurance purposes, there are limitations worth noting. As with other studies, data are for only up to 10 years of ART therapy (and the results extrapolated beyond 10 years). There were limited numbers of those age >60. In addition, these European results may not be matched in the United States, especially when considering the importance of maintaining long term treatment compliance. There were no data on smoking and other risks, which are generally found to be overrepresented in HIV positive groups, and this could have skewed the results toward higher MRs.[20,23] Finally, comparison to ultimate tables was used since the population was not tightly selected, but this may not reflect insurance practices – it assumes that the impact of additional underwriting would be the same in the HIV group as in a non-HIV infected group.

Study 4

In the UK Collaborative HIV Cohort (UK-CHIC) Study, data from 21,388 HIV-positive individuals receiving care in the UK between

2000 and 2012 were used to estimate life expectancy according to latest CD4+ count and viral suppression status. Those with suspected IVDU and mother-child transmission were excluded. In this group, 69% were men, of whom 73% were aged 30-49. Abridged life tables were constructed for men and for women from age-specific mortality rates grouped in 5-year age bands – describing the mortality experience that hypothetical cohorts of HIV-positive individuals would have if they were subjected to the mortality in the observed period. After 5 years on ART, the expected age at death of 35 year-old men varied from 54 for those with CD4+ counts <200 and no viral suppression, to 80 for those with CD4+ ≥350 and viral load suppressed. In this analysis, there was no apparent difference in mortality between those with CD4+ cell count 350-499 and those ≥500. Most of the effect of viral suppression on decreasing mortality was mediated through increasing CD4+ counts; there remained, however, an independent effect of detectable viral load on LE as well.

Crude mortality rates were 9.0/1000 person-years for men and 7.9 for women. Mortality rates for those ages 20-44, after 5 years of ART, varied from 2.7/1000 with viral suppression and CD4+ ≥350 to 38.1/1000 for those with unsuppressed HIV and low CD4+ counts.[17]

Study 5

Studies consistently find higher rates of many mortality risk factors in those who are HIV positive, and this may be a confounding factor in the increased mortality risk associated with HIV infection. For example, in one analysis, a simulated cohort of HIV-negative people in the United States with a similar demographic and risk profile to the HIV-infected population had an estimated 8.33 year reduction in life expectancy compared to the population as a whole.[20] Thus, mortality rates among the HIV population may be better than recognized after adjusting for additional factors.

To address specifically the issue of a higher prevalence of tobacco use amongst those infected with HIV, an additional analysis of the ART-CC dataset was recently published. The 17,995 individuals for whom smoking status had been collected were studied, and causes of death and overall mortality were compared with the general French population (selected as best representative of the entire group). Of those individuals, 59.8% where classified as smokers. The proportion of men was 71.3%; 70.6% had a viral load <400 copies/ml, and 56.2% had CD4+ cell counts ≥350.

The adjusted mortality ratio comparing smokers with non-smokers was 1.94, similar to that seen between smokers and non-smokers in insurance populations. Unadjusted all-cause mortality rates were 7.9 per 1000 person-years among smokers and 4.2 among non-smokers. For those with CD4+ counts ≥200 and no AIDS diagnosis, the corresponding rates were 5.4 for smokers and 2.9 for non-smokers.

Abridged life tables were used to estimate life expectancies among men – there were too few deaths among non-smoking women to obtain an adequate analysis. LE at age 35, if CD4+ count was ≥200, was 37.8 in smokers and 43.4 in non-smokers, compared to 44.4 years in the background population. At age 65, the loss of life years associated with smoking was estimated to be 6.6 years, whereas that associated with HIV was 2.9 years. The conclusion was that the risk from smoking appeared to be as great as, or greater than, that of adequately controlled HIV infection.[21] (See Table 2)

INDUSTRY STUDIES FROM INSURANCE LABORATORIES

Insurance lab analysis of HIV risk is complicated by the fact that little additional data is available to stratify the risk, and it is likely that many, if not most, of those found to be HIV-positive at time of insurance examination had yet to seek treatment. A subsequent analysis of the above noted insurance lab data

Table 2. Limitations of Most Clinical HIV Mortality Studies

○ Limited long-term follow up
○ Changes in ART regimens and in compliance over time
○ European results may not be fully applicable to a North American population
○ Most are not population-based and may have some selection bias
○ Incomplete death ascertainment and/or high lost to follow-up numbers in some
○ Lack of access to information on major pre-HIV infection and post-ART HIV risk factors
○ Lack of information on risk factors in general population comparison cohorts – non-HIV mortality risk factors are often found to be higher in the HIV-infected groups

from Clinical Reference Laboratory attempted to further adjust the confounding risk factors by obtaining a *SmartScore* value and assigning those with scores >130 (not including the HIV score component) as being considered to have significant comorbid risks. Excluding that group, and then comparing those who tested HIV-positive to those HIV-negative, the MR for men aged 18-49 was 659% and for men 50-89 was 156%, suggesting that some of the excess risk previously noted is due to comorbid risk factors which can be identified in underwriting (Mike Fulks, unpublished data, November 2013).[13]

Furthermore, an insurance medicine analysis done by ExamOne also looked at the mortality risks associated with a positive HIV result in insurance applicants, analyzed through the Social Security Death Master File and their proprietary *Risk IQ* assessment. They found remarkable improvements in prognosis for HIV infection over time and yet there continued to be a large number of extremely high-risk individuals amongst this group. For example, the HIV positive group was nearly twice as likely to be cotinine positive (19% vs 11%) and 10 times more likely to be cocaine positive (2.1% vs 0.2%). The overall mortality ratio from the most recent study years was 7.4; however, based on the *Risk IQ* analysis, an estimated 80% of the increased risk seen in HIV positive applicants was related to other factors – leading to an MR closer to 2.4, once these factors were taken into account. In particular, an elevated serum globulin and/or a low serum albumin were

especially prominent added risks (Brian Lanzrath, unpublished data, November 2013).

It is useful to note that since these insurance laboratory data are assessing a group that has not undergone any underwriting, it is likely that additional adjustment by whether they were clinically diagnosed and under treatment, and by CD4 count, viral load, and duration and compliance with treatment, would decrease these mortality ratios further.

PROGNOSTIC FACTORS INFLUENCING MORTALITY

Based on these studies, and others, Table 3 lists those factors best identified as mortality risk factors amongst those with HIV infection. In addition to finding CD4+ count, viral load, and AIDS-defining illness history to be significant prognostic factors, an analysis of mortality factors in HIV-infected US veterans also looked at non-HIV biomarkers and identified anemia, thrombocytopenia, renal insufficiency, AST elevation, and a hepatitis history all to be independent mortality risks.[22]

WAYS TO ASSESS THE MORTALITY DATA

When assessing these HIV mortality data from an insurance perspective, as with any condition, there are various options. However, short of data from actual insurance company experience, which is not known to exist for HIV, each of these approaches has important limitations. Considerations include:

Table 3. Probable or Possible Favorable Prognostic Factors for HIV[2-12, 14-18, 21, 22]

Factor	Comments
Current CD4+ count >350 cells/ul	Consistently identified as the most significant mortality factor. Some found further improvements for counts >500.
HIV viral suppression - current	Variably defined as viral load <50, <400, or <500 copies/ml
HIV viral load 6 months after ART	Values <400-500 copies/ml
CD4+ count >350 at start of ART	Probably correlates with duration of infection
Flat CD4 count slope over 2 years	Adverse if CD4+ counts are declining, even if still >350
Diagnosis after 2000	After adjusting for duration of ART
Consistent compliance	Interruption of treatment is adverse even if counts remain up
Longer duration of ART	Longer treatment likely associated with better compliance
No AIDS-defining illness	Though does vary by type of ADI
No tobacco use	Smoking-related diseases are a leading causes of death in HIV
No alcohol or substance misuse	
No Hepatitis B or C co-infection	
No anemia, thrombocytopenia, AST elevation, or eGFR decline	
Mode of acquisition not IVDU	
Higher socio-economic class	
Male gender?	The worse outcomes often noted in women may represent confounding factors such as IVDU or socio-economic factors
Increased inflammatory/coagulation markers?	Increased interleukin (IL)-6, sCD14, and D-dimer are associated with increased morbidity and mortality
Older age	Crude mortality rates increase with age but relative mortality ratios decline due to competing mortality causes

1) Comparative Standardized Mortality Ratios – useful to assess relative risks by age and established time periods but the comparative population is not a true insurance population; we cannot assume that the same overall health status breakdown between groups (usually HIV-infected persons and the general population) would lead to the same SMR for an insurance-seeking HIV positive individual compared to an insurance buying population.

2) Crude mortality rates – mortality rates (for example per 1000 person-years) compared to those expected based on insurance tables. These data can be used to determine excess death rates (EDRs), however they generally are not adjusted fully for age, underlying health status, and other risk factors needed to obtain accurate results.

3) HIV specific death rates – looking only at deaths directly attributable to HIV infection can provide an estimate of expected EDRs but that doesn't account for the potential non-AIDS mortality risks, which have been identified. This is also often complicated by reporting bias as to the true underlying cause of death.

4) In addition, any of these approaches is limited by a time bias. With the apparent continually improving outcomes and changes in treatment over time, data from even a few years ago may now be inaccurate.

Nonetheless, the amount of data that have been accumulated from varied sources could provide some very reasonable estimates in much the way data with similar limitations have been used for many other medical conditions, which are routinely insured.

CONCLUSION

It is evident that the life expectancy of individuals infected with HIV has increased

significantly since the introduction of ART. And although the overall mortality rates for HIV-positive individuals as a group remain higher than would be expected, sub-groups with a more favorable prognosis have clearly been identified. A low CD4+ count remains the most consistently identified mortality risk factor. HIV viral levels, the slope of CD4 + count over time, mode of HIV acquisition, absence of ADI or hepatitis infection, and stage at initiation of ART are all probable additional contributing factors (see Table 3). Taking these factors into account identifies a group with 10-year survival approaching that of the general population. For those studies in which the data were available, roughly 1/3 to 1/2 of those on ART have generally favorable profiles. Individuals with HIV also have a greater tendency to exhibit lifestyles and behaviors that place them at increased risk of mortality, particularly from non-AIDS causes, and these factors have often not been fully accounted for in mortality comparisons. Doing so may, therefore, demonstrate further reductions in the identified mortality rates among the HIV infected population.

Of vital significance, however, is the recognition that the results of these studies apply to the follow-up of HIV-infected individuals over approximately 10 years of treatment. With the products available in the North American insurance industry, the prognosis beyond 10 years is also important, yet how these results will hold up across subsequent decades is still to be determined. To best extrapolate the results over a longer time frame, the effects of chronic immune stimulation, premature aging, long-term drug toxicity and tolerance, accessibility of treatment, and other, as yet unseen, risks must be weighed against the possibility of continued advances in treatment, risk factor mitigation, or even potential cures. In other words, one must look upon HIV as a chronic condition and make an educated estimate of the degree of impact that each of these factors will have on the future of HIV.

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