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**LABORATORY TESTING**

# Suitability of HIV-Infected Subjects for Insurance

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**Objectives.—**To ascertain the suitability of HIV-positive individuals for insurance coverage based on international data and practices.

**Background.—**During the first decade of HIV epidemic, diagnosis of HIV-infection carried a poor prognosis. Since the introduction of Highly Active Anti-Retroviral Therapy (HAART or ART), HIV infection is more like other chronic diseases with infected individuals often living 20 or more years after the diagnosis of HIV infection

**Methods.—**Review of peer-reviewed publications was undertaken to assess the risk of death in the HIV-infected population as a whole as well as subsets with favorable outcomes and those with additional comorbidities, such as co-infection with hepatitis viruses and drug use.

**Results.—**Review of literature revealed that in well-educated, non-drug using individuals, negative for hepatitis B and C infection, who had CD 4 counts above 500/cmm, viral loads below 500 particles/mL, and were compliant with treatment, the mortality rate was similar to that of general population.

**Conclusions.—**The risk of death, in at least a subset of HIV-positive subjects, is low enough that insurance providers should consider stratifying HIV-infected individuals according to mortality risk and offering insurance rates comparable to people with other diseases with similar mortality risks.

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## INTRODUCTION

HIV infection became known in 1981 and since then about 1.8 million people have acquired the infection in the United States and about 650,000 died from the disease. It is estimated that at this time there are about 1.1 million HIV-infected people in the United States, or a prevalence rate of about 0.3%. For the last decade, the rate of new infections has stayed at about 50,000/year.[1,2]

Globally, about 75 million have been infected with HIV, and about 36 million have died due to the infection. Currently, worldwide about 35 million people are living with HIV infection and 1.6 million died of the disease in 2012; there were about 2.3 million new infections in 2012 or more than 6,300 new HIV infections per day.[3,4]

At the beginning of this epidemic, infection was more common in intravenous drug users and men who have sex with men (MSM). Drug abuse and MSM continue to be high-risk activities; however, unprotected heterosexual activity with multiple partners is also an

important risk factor for both men and women.[5,6] Mortality rates due to HIV have dropped markedly since the introduction of Highly Active Anti-Retroviral Therapy (HAART or ART) to the extent that patients with uncomplicated HIV infection, CD4 counts >500/cmm at diagnosis or soon after initiation of treatment, suppression of viral load with treatment, and good compliance with treatment, have near normal life span.[7-10] However, there is marked variability in mortality rates among different subpopulations as evidenced by data showing that the mortality rate for HIV infected people varied from about 2 per 100,000 among the most-educated white men, compared to a rate of 53 per 100,000 in the least-educated black men.[2,10]

Co-infection with hepatitis viruses B and/or C is common and a significant predictor of poor response to treatment and higher mortality. Substance abuse, including smoking, and non-compliance with treatment portend a higher mortality rate.[9-11] One of the large laboratories performing testing for insurance candidates did not see an improvement in mortality rates for persons, who tested positive, in their client population, over the period 1991 to 2009.[12] European investigators have reported marked improvement in survival from 2005 to 2010.[8,13] Similar observations of improved survival have been documented in the United States.[10] Samji et al reported that a 20-year-old HIV-positive adult on ART in the United States or Canada is expected to live into their early 70s; however, a gap persists between the life span of HIV-positive vs HIV-negative individuals.[14]

Progress in treatment and outcomes showing improved survival and prevention of transmission of mother-to-child infection have resulted in a societal change in perception of HIV infection. The changing attitudes to HIV infection are reflected in the legislation pending in the US congress that would allow use of organs from HIV-positive donors for transplantation, albeit into HIV-positive recipients only.[15,16]

## METHODS

We reviewed the literature for information on survival rates of HIV-positive individuals with the intention of identifying subgroups with favorable survival rates. Consultation with colleagues in The Netherlands and Switzerland was initiated because of the availability of insurance for HIV-infected subjects in these countries, and because of support for the same in the literature.[17,18]

## RESULTS

Subpopulations of HIV-infected individuals with favorable outcomes were identified by literature review; HIV-infected individuals with the most favorable outcomes include individuals with the following characteristics: (a) highly educated, (b) non-drug user subjects, (c) non-smokers, (d) without co-infection with hepatitis viruses, (e) CD 4 counts >500/cmm at the start of treatment or with initiation of treatment, (f) viral suppression with HAART/ART to viral load of <500 particles/ml for 6 years since initiation of treatment, (g) consistent compliance with treatment and (h) lack of AIDS defining conditions or events. This subgroup has near normal life span as compared to the general population.[18-23] In some selected locations up to 50% of the HIV-infected subjects may be suitable for insurance.[18]

Risk factors associated with increased likelihood of death included injection drug use, lower CD4 count, failure of viral load suppression with treatment, smoking, diabetes, low body mass index, HBV and/or HCV co-infection, AIDS events and the interruption of treatment. A low CD4 count at any time during the illness, despite recovery on treatment pointed to a less favorable prognosis. The occurrence of CDC-B events in early stages of the disease is associated with a worse prognosis, even in non-drug using patients.[22-27]

Analysis of a cohort of 29,935 individuals, treated with anti-retroviral therapy and followed for 4 years revealed that men infected through sex with men or heterosexual contact had a standardized mortality ratio (SMR) of

<2.0. In this cohort, men who acquired HIV through sex with men, were free of AIDS at the start of treatment, had a CD4 count >350/cmm and a viral load of <500 copies/mL at 6 months after starting treatment, the increase in mortality was estimated at 5% or an SMR of 1.05. Mortality was increased >70 times (SMR 73.7) in persons who acquired HIV through injection drug use.[28]

Lewden et al reported that in 5402 person-years with CD 4 count >500/cmm, mortality reached the same level as for general population after sixth year of treatment (SMR 0.5, 95% confidence interval 0.1-1.6).[29]

In cohort of 39,272 HIV-positive, persons treated in 1996-2006, of the 792 deaths, 50.5% were due to non-HIV/AIDS causes, such as non-AIDS malignancies, non-AIDS infections, violence, liver disease, and cardiovascular disease.[23]

Lohse et al estimated that the remaining life span of a 25-year-old infected with HIV was about 39 years, the same as for a person of similar age with diabetes. The remaining life span of a non-infected 25-year-old was estimated to be 51 years. They also observed that the highest mortality was observed in the first year after the initiation of treatment.[7]

In brief, studies in both Europe and United States have documented that in selected HIV-infected applicants the mortality is similar to that of the general population.[10,18,21,29-32]

## DISCUSSION

Given the relatively low prevalence of HIV in the US, insurance companies should consider re-evaluating the need for testing applicants with low face value policies. (Specimens received at Heritage Laboratories had a positivity rate of 0.042%.) Some European companies have stopped HIV testing for policies with a face value of less than 300,000 Euros (about$420,000).) It is understandable that this would run the risk of inviting people with HIV infection who are not applying for insurance at this time, ie, negative selection. Dutch companies are not testing applicants for insurance with a face value lower than 300,000 Euros, after determining that this testing strategy was cost effective.[17]

The insurance industry should reconsider offering coverage to HIV-infected applicants given that patients with controlled hypertension, mild chronic obstructive airway disease (COPD), well controlled asthma in non-smoker without hospitalization, renal failure with estimated glomerular filtration rate (eGFR) greater than 60, well controlled type 2 diabetes mellitus not requiring insulin treatment and without vascular or renal or ophthalmic complications, are generally offered non-preferred rating. Additional points are assessed for complicating factors and a similar strategy could be used for HIV-infected applicants. It needs to be kept in mind in 50% of the deaths in AIDS-infected subjects the cause of death is not related to HIV-infection.[23,29] As stated earlier, despite effective treatments, HIV infected individuals tend to have shorter life span than non-infected persons.

We are recommending the following stratification for HIV positive applicants for consideration for insurance coverage:

A. Well educated applicants (Generally considered to be people with a college degree) who acquired HIV infection through sexual contact, including sex between men (MSM) and have the characteristics listed below; have the same mortality risk as other applicants and could be offered life insurance based on other risk factors, as would be the case of applicants in general:

(a) Are not engaged in parenteral substance abuse and/or smoking
(b) Are not co-infected with hepatitis B and/or C viruses
(c) Lack AIDS markers, listed in Figure 2
(d) Had CD 4 counts >500/cmm at presentation or within six months of initiation of treatment
(e) Compliant with treatment
(f) Viral load consistently <500 particles/mL
(g) Maintenance of above characteristics for 6 years

We understand that the mortality of individuals offered insurance coverage is lower than that for the general population and even this, the most favorable; sub-group of HIV-infected individuals may be subject to greater scrutiny than the standard applicant.[28]

B. The other extreme being poorly educated applicants, engaged in parenteral substance abuse, co-infection with hepatitis viruses, presenting with symptoms of AIDS, poor compliance with treatment, poor response to treatment as judged by CD4 counts and viral load assays. It is questionable if such individuals are even applying for life insurance and would likely have other reasons for being declined coverage.[33] This group will not be discussed further.

C. There is likely a significant population that falls in-between these two polar groups and there may be insufficient data to arrive at acceptable rating tables for the group. However, it may still be possible to examine the merits of each case individually.

Other factors in predicting mortality are:

- Risk of death follows a gradient of CD 4 counts, for counts below 500/cmm. There is no added benefit from counts higher than 500/cmm. A CD4 count below 400/cmm at any time during the course of illness portends a poorer outcome and is included as one the items in the proposed data from the attending physician.
- Women may have better outcomes than men, however this has not held up in some countries.
- Smokers have three fold higher risk of death.
- Heavy drinkers experience a 2.2 fold higher rate of all-cause mortality.
- BMI $>$ 35 had 1.5 -2.5 x higher risk of death.
- Low BMI risk/Wasting syndrome is an AIDS marker and hence indicates increased risk to the extent to be denied coverage.

Even for the most favorable group, ie, category A, due to lack of long term follow-up data, insurance providers may offer only a term policy without assurance of renewal at the end of 10-20 year term. Rating factors for other health issues could be applied, as would be the case with any applicant. The observation by Stout et al that mortality in insurance applicants with HIV has not changed over time may in part be due to greater awareness of HIV status in the general population and people discovered to have HIV during insurance testing may have been infected for a longer period and thus have a poorer outcome than people detected and treated early in the course of disease.[12]

### Template for attending physician's summary (APS) for HIV infected persons:

A proposed template for information needed in APS is included as Figure 1.

The rationale for most of the questions is based on the observations noted in the literature, and a brief explanation for the others follows:

a. HIV-infected patients on retroviral therapy, even with controlled viral load and CD 4 counts, often have abnormalities of lipid metabolism, accelerated atherosclerosis with consequent cardio-vascular morbidity and mortality.[34,35]
b. Liver pathology in HIV-infected individuals, even without co-infection with Hepatitis B and C, is noted and may be due to effects of therapy.[25]
c. Drug toxicity and HIV-nephropathy combine to produce renal damage, hence, the recommendation to measure serum creatinine.[36]
d. HIV-infected individuals may have a higher incidence of even non-HIV-related malignancies.[37,38]

## PROPOSED SCHEME FOR INSURANCE COVERAGE

The individuals meeting the criteria listed in category A above are likely to have a mortality comparable to that of the general population. It is understood that the insured population has lower mortality than the general population. It is also understood that

- Date of HIV diagnosis
- Date of likely exposure to HIV
- Date on which HAART was initiated, if on treatment
- Unintended interruptions in treatment
- Was the patient ever on monotherapy
- CD 4 count: Current and prior CD4 counts
- Lowest CD 4 count ever
- Viral Load: HIV viral load current and prior counts
- Highest viral load ever
- HIV type
- Other sexually transmitted diseases
- History of substance abuse
- History of hepatitis
- Is the applicant infected with Hep B
- Is the applicant infected with Hep C
- Smoking status
- Fasting blood lipids
- Liver function tests
- Serum creatinine

Other health issues: eg, diabetes, heart disease, lung disease, liver disease, auto-immune disorders, tuberculosis, non HIV infections, and history of malignancy.
Education: High school, college, post-graduate, professional.
AIDS markers: Check appropriate items in Figure 2 that are present in the applicant.

**Figure 1.** *Template for HIV-specific information for Attending Physician's Statement (APS).*

the long-term survival/mortality data on even the best risk group is only about ten years old and extrapolating may be riskier than the insurers may tolerate. It is reasonable to propose that term insurance for 10-20 year-term be offered to the best risk group at the standard rates. In 10 years, we are likely to have additional data on survival/mortality that may allow us to reassess the policy.

Empirical data shows that HIV infection is a major risk factor for death and needs to be considered carefully in any underwriting decision. However, in at least a subgroup of the subjects falling in category C given above, the risk may be comparable to commonly occurring chronic diseases such as diabetes mellitus, hypertension, asthma, coronary artery disease with a history of acute coronary event. Therefore, applicants with HIV infection could be considered for term policies of 10 years, with ratings comparable to other chronic diseases with excess mortality, without undue risk to the underwriting company. It is quite likely that adhering to strict criteria suggested in this report will result in only a very small number of people qualifying for coverage; however, it would be prudent to take a cautious approach while we gather additional information about the insurability of this subset of the population. Using more liberal criteria that may results in unexpected loses to the industry would raise the bar even higher and may delay the availability of coverage even further. A cautious approach is also indicated because the survival data from randomized controlled trials (RTC) is not likely to be directly applicable to the general and insured populations and the results of RTCs are unlikely to be replicated in general practice. However, results in real-life healthcare settings, including less than favorable circumstances, have shown similar improvement in decline in mortality in HIV-infected individuals.[10,30-32]

To answer the question posed by MacKenzie, ''Life insurance for the HIV-positive applicant – are we there yet?''[39] Yes we are, with qualifications. We believe that HIV-positive applicants falling in category A should be evaluated thoroughly to exclude undue risk and be offered term-coverage for 10-20 years. It is likely that by that time we will have additional information to address the issue of continuing coverage and a possible change in policy in favor of HIV-infected applicants.

- Acute necrotizing ulcerative stomatitis, gingivitis, periodontitis
- Angular cheilits
- Bacterial infections, multiple or recurrent, with or without bacteremia
- Candidiasis of mouth, airways or lungs, or esophagus, and extrapulmonary sites
- Carcinoma of uterine cervix
- Coccidiodomycosis
- Cryptococcosis
- Cryptosporidosis with diarrhea for >1 month
- CMV disease, including retinitis
- Encephalopathy - HIV related
- Fungal nail infections
- Herpes simplex, chronic: orolabial, genital, anorectal of >1month
- Herpes simplex, visceral
- Herpes zoster
- Histoplasmosis
- HIV nephropathy
- HIV cardiomyopathy
- Isosporiasis
- Kaposi Sarcoma
- Leishmaniasis
- Lymphoid interstitial pneumonia
- Lymphoma
- Mycobacterium avium complex
- Mycobacterium tuberculosis infection of any site
- Mycobacterium infection of any type
- Nocardiosis
- Papular pruritic eruptions
- Pneumocystis jirovecci infection
- Pneumonia, recurrent
- Progressive multifocal leukoencephalopathy
- Oral hairy leukoplakia
- Recurrent non-typhoid salmonella infection
- Recurrent oral ulceration
- Salmonella septicemia, current or history of
- Seborrhoeic dermatitis
- Stroglyloidosis
- Toxoplasmosis
- Unexplained cytopenia (Hb <8 gm/dL, Neutrophils <500/cmm, Platelets <50,000/cmm)
- Unexplained chronic diarrhea >1month
- Unexplained persistent fever (above 37.6$^{o}$C) for >1 month
- Wasting syndrome: Involuntary weight loss of >10% of baseline

**Figure 2.** *AIDS Markers/Events/AIDS-Defining Conditions.*

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