NOT IF, BUT HOW

Munich RE

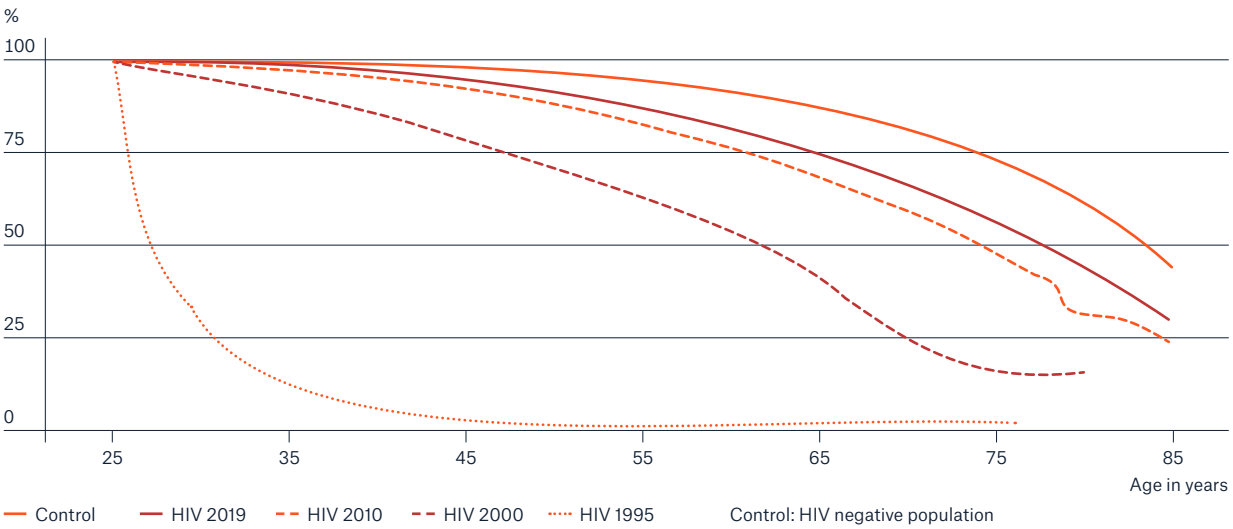
Mira Risk Review

HIV – Destigmatisation of a chronic disease

Treatment of HIV-positive individuals has made huge progress since the mid-1990s (figure 1). In 1995 a patient with HIV aged 25 years old only had an about 10% probability to reach the age of 35, by 2000 this probability had increased to about 90% and from 2020 onwards it is now close to 100%. In addition to medical advances, regulators have questioned whether underwriting guidelines are still appropriate. The „right to be forgotten" is a prominent driver of the need for up-to-date, evidence-based and risk-appropriate underwriting for people living with HIV (PLWH). While in the past the insurance industry's focus was on providing life cover only to PLWH, and clinical medicine focused on ensuring their survival, medical advances have been so impressive that it is no longer a question of survival but of quality of life. Hence, nowadays living benefit covers can be offered to PLWH.

Munich Re in collaboration with the Danish HIV registry conducted a large-scale analysis of not only mortality, but also morbidity in PLWH[1]. The Danish HIV registry is one of the most comprehensive and best maintained HIV registries worldwide. One of the most beneficial features is that its data can be linked to further registries such as the labour market register, the death register and the cancer register, amongst others. This allowed Munich Re to raise targeted questions with end-points relevant for insurance requirements. The result is a straightforward guideline for day-to-day risk assessment. This MIRA Risk Review Paper provides information on the scientific background and facts of the revision.

Figure 1: Probability of survival



Source: The Danish HIV Cohort Study

Understanding the condition

For many years, the life insurance sector viewed people diagnosed with HIV as uninsurable. This was due to the fact that the virus caused the immunodeficiency syndrome AIDS in almost all sufferers, a disease that resulted in death within a few years. In the mid-1990s, this dire prognosis began to change. Researchers succeeded in developing drugs for antiretroviral therapy (ART), using them in combination and improving survival prospects significantly. Today, this therapy is so successful that the mortality rate has declined dramatically and is still falling steadily. Thanks to this medical breakthrough, those diagnosed with HIV are now no longer uninsurable, and are not only eligible for life insurance, but also for living benefits such as disability cover and even critical illness cover. As early as 2008, Munich Re introduced rating guidelines for insuring HIV patients under certain medical circumstances – demonstrable control of viral load and stable CD4 count, above all. At that time, however, only restricted contract periods were possible given the limited observation periods covered by experience studies. In most established insurance markets only very few applications for life insurance were recorded in which an HIV infection was disclosed by the applicant him- or herself or was identified by screening tests routinely undertaken as part of the medical risk assessment. Hence, there is only very limited data from insurance portfolios available, when it comes to life insurance and virtually none, when it comes to living benefits. The question of "who is insurable for which product" could not be answered. That is: It couldn't be answered up to now. Our cooperation with the Danish HIV registry was able to answer the open questions in a way tailored to the insurance industry.

Until today HIV-infected individuals often do not apply for covers such as income protection or critical illness as they expect to immediately be declined for such covers. This was indeed the case and publicly available information actually states that private disability cover won't be granted for PLWH. Given the most recent research findings and corresponding terms of acceptance, however, it is now time to change this stance. HIV infection is a chronic condition which can be underwritten as a substandard risk similar to other chronic conditions, e.g. viral hepatitis or diabetes mellitus[2]. It needs to lose the stigma of an almost always fatal disease with accordingly massive associated morbidity. The often irrational and emotional reaction to HIV, which still roots in the fear from HIV in the 1980s needs to give way to a more rational approach. A rational approach, that, luckily, the medical community showed from the beginning. Otherwise the advances in the treatment of HIV would never have been possible.

Transformation into underwriting guidelines

Additionally, to having risk adequate ratings, the analysis needed to identify which criteria are relevant for risk assessment, i.e. CD4 count, age, comorbidities etc. From an insurance perspective it obviously is also important to know whether the relevant prognostic criteria can be easily collected as part of the application process, to avoid unnecessary delays when issuing the policy. To establish these parameters, significant long-term data was required to make sure evidence-based assessment rules can be derived using medical, statistical and actuarial methods. The Danish HIV registry could provide the majority of data needed. This data was then augmented with data from published HIV studies.

Significantly better prognosis for HIV patients over time. Our analysis:

Mortality

Although overall survival has improved for the majority of PLWH, it does not reach the life expectancy of the general population if we look at the average survival of PLWH. Especially PLWH who had AIDS in the past demonstrate an up to 5-fold excess mortality in the first years after initiation of ART, and do not reach normal levels even after several years of treatment. This increased mortality risk in PLWH with AIDS history is also present even if CD4 count has recovered while being on ART. In contrast, if PLWH did not experience an AIDS-defining event, do have normal CD4 levels and a supressed viral load, then their hazard ratio remains relatively low and, importantly, stable after a few months from initiation of ART. Importantly, long-term relative risk for extra mortality compared to the general population is higher in younger PLWH vs. older PLWH, which is reflected in our ratings.

Furthermore, we retain differentiated ratings on extra mortality according to current CD4 status as indicated by large study collaborations[3, 4]. This enables standard or relatively low ratings for very-low or low-risk PLWH. In fact, in most countries with access to contemporary ART therapy, these very low and low-risk PLWH represent the largest fraction of the PLWH population. Nevertheless, it is highly relevant to rate also concurrent comorbidities.

Morbidity

For disability, we identified an elevated risk across all age groups compared to the general population, but in particular a higher relative risk in the younger age groups. This was not only true for disability pension in the Danish welfare system but also sickness absence of different durations. Again, current CD4 status differentiates low-risk from high-risk applicants in different age groups. Importantly, our analysis leads today to the first evidence-based, risk-adequate disability ratings, which are applicable to PLWH with ART adherence, normal CD4 level and supressed viral load in the absence of AIDS-defining events, intravenous drug use and Hepatitis C.

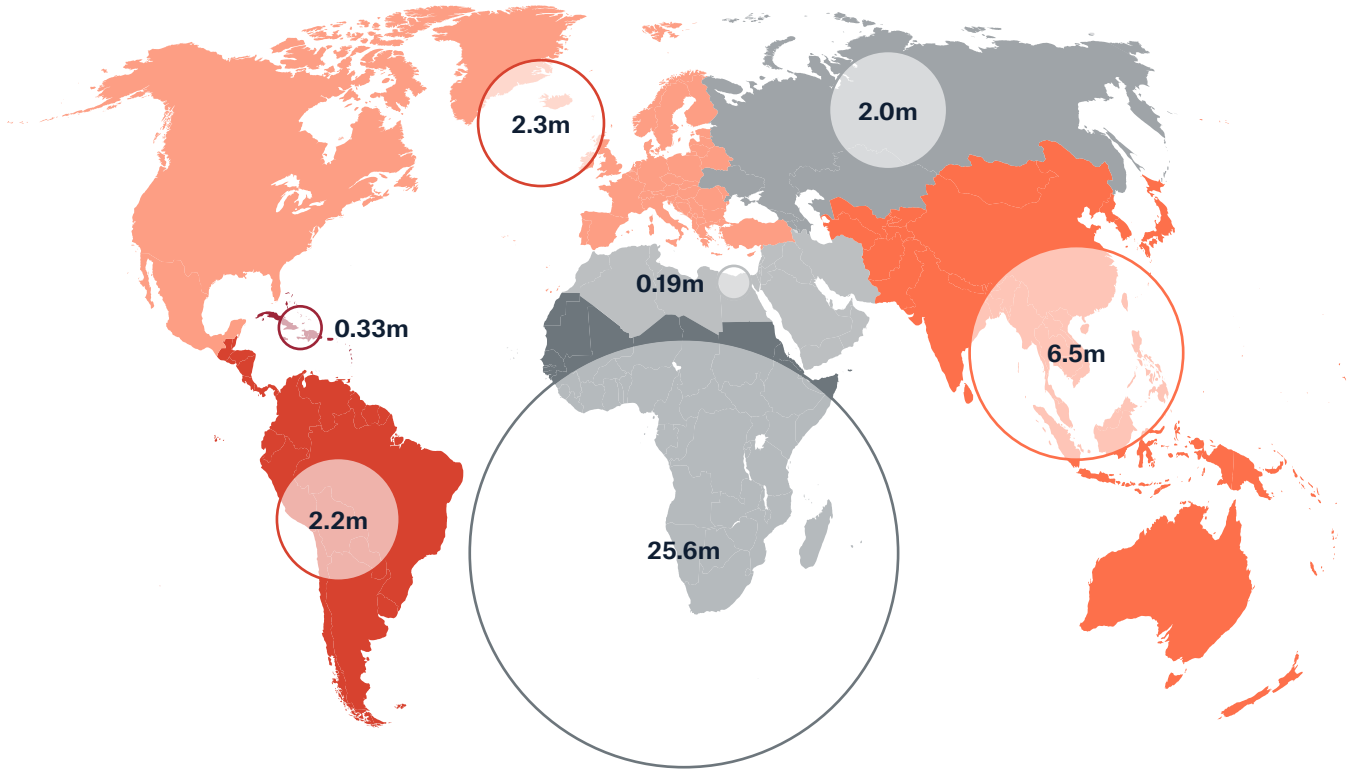
For Critical Illness cover, we were able to analyse the most important triggers for this insurance product, namely ischaemic heart disease, cancer, stroke, bypass surgery, aortic surgery, terminal kidney failure (dialysis). In addition, we looked at depression risk, as it is known that mental disorders are more common in PLWH[5]. Notably, the risk for all major triggers (ischemic heart disease, cancer, stroke, dialysis) was increased and ranged between 1.2-fold and 3-fold compared to the general population. This increased risk was age-dependent, with higher relative excess risks in younger PLWH compared to age-matched individuals from the general population. In total, our ratings account for the additional risk, but can be differentiated with current CD4 levels to low-risk and high-risk cases. Additionally, it is well-known that PLWH have a very high risk for HIV-associated cancers, which comprise AIDS-defining cancers but also human papillomavirus (HPV) or Epstein-Barr virus (EBV)-associated cancers, ranging from 1.6-fold for oral cavity/pharyngeal cancer to almost 500-fold for Kaposi's sarcoma[6]. For this excessive risk, we recommend applying an exclusion clause for critical illness cover. Importantly, other cancers like breast cancer or prostate cancer are not excluded.

Facts and background

It is estimated that 35 million people are infected with HIV worldwide, with the majority found in Sub-Saharan Africa. However, there are also large numbers of people living with HIV in Europe, North America and other parts of the world (figure 2).

Human immunodeficiency virus (HIV) is a pathogen that causes an infection which eventually results in acquired immune deficiency syndrome (AIDS). It is transmitted through bodily fluids, e.g. via transfer of blood products, unprotected sex, intravenous drug use, mother-to-child transmission. Risk groups differ geographically; in Sub-Saharan Africa transmission of HIV via heterosexual contact is most frequent, in Europe and the US MSM (men who have sex with men) and IDU (injecting drug users) are important and common risk groups.

Figure 2: Number of people living with HIV infection



North America and Western and Central Europe	2.3m (1.9m–2.6m)
Caribbean	330,000 (290,000–380,000)
Latin America	2.2m (2.0m–2.5m)
Middle East and North Africa	190,000 (160,000–220,000)
Sub-Saharan Africa	25.6m (21.6m–32m)
Eastern Europe and Central Asia	2.0m (1.8m–2.1m)
Asia and the Pacific	6.5m (5.3m–7.8m)

Total: 39.1m (32.9m–47.6m)

Source: HIV/AIDS, J.U.N.P.o., UNAIDS DATA 2023

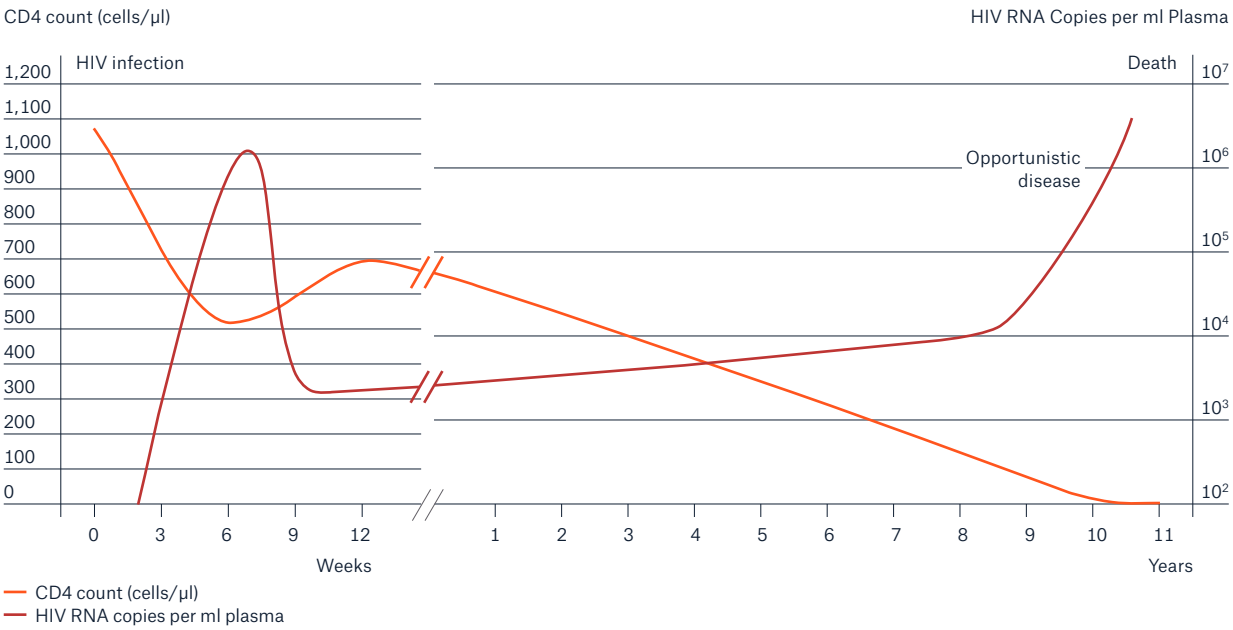
Pathophysiology

HIV is a RNA retrovirus that docks onto a certain type of white blood cells, termed CD4 cells (also T-helper or T4 cells), which are responsible for the immune defence system, and destroys them. This harms the immune response of the infected individual, allowing opportunistic infections as well as cancers to develop. Uninfected individuals usually have CD4 counts > 500 cells/µl. With decreasing CD4 counts the probability of developing AIDS-defining diseases increases. Over the years, treatment recommendations changed and now promote immediate initiation of ART due to clear improvements in morbidity and mortality in treated patients, reduction of the toxic side effects of medication and improved adherence to current, simplified regimens. In addition, immunologic recovery and CD4 counts seem to be worse in patients who start treatment late and at low CD4 counts. Observational mortality studies and clinical trials have consistently demonstrated substantial improvements in survival and mortality since the introduction of ART.

Natural course of HIV infection in the absence of antiretroviral medication

If no therapy is applied, the natural disease course typically looks like the following: Around one month after infection, patients may experience flu-like symptoms which are classified as acute/primary HIV infection or acute seroconversion syndrome. During this time, virus replication in the blood is at its highest, causing very high viral load levels. Consequently, CD4 counts start to decline due to the destruction of T-helper cells. Seroconversion develops within four weeks in almost 100% of infected individuals, at which time the viral load stabilises[8]. In the years that follow, infected individuals are usually free of symptoms. However, without antiretroviral therapy, CD4 cell counts steadily decline. Higher age and high viral load lead to a faster decline of CD4 cells[9]. AIDS develops on average ten years after infection. Without antiretroviral therapy, patients with AIDS survive an average of three years (figure 3)[10].

Figure 3: Natural course of HIV infection (without ART)



Recovery of the immune system with increasing CD4 counts during antiretroviral therapy

Antiretroviral therapy inhibits viral replication and leads to recovery of the immune system with increasing CD4 counts. The first antiviral drugs were introduced in 1987. From 1996 onwards, the combination of three different drugs from at least two different HIV treatment classes became standard. In 2016 four active ingredients in a single tablet became standard. This treatment, which became known as HAART/cART for Highly Active/combined Antiretroviral Therapy, is referred to in this paper simply as ART. Many new drugs have been developed since the advent of ART, and the therapy has proved to be very effective, causing a marked decrease in mortality and morbidity. More than 90% of patients achieve viral suppression within a year of starting ART.

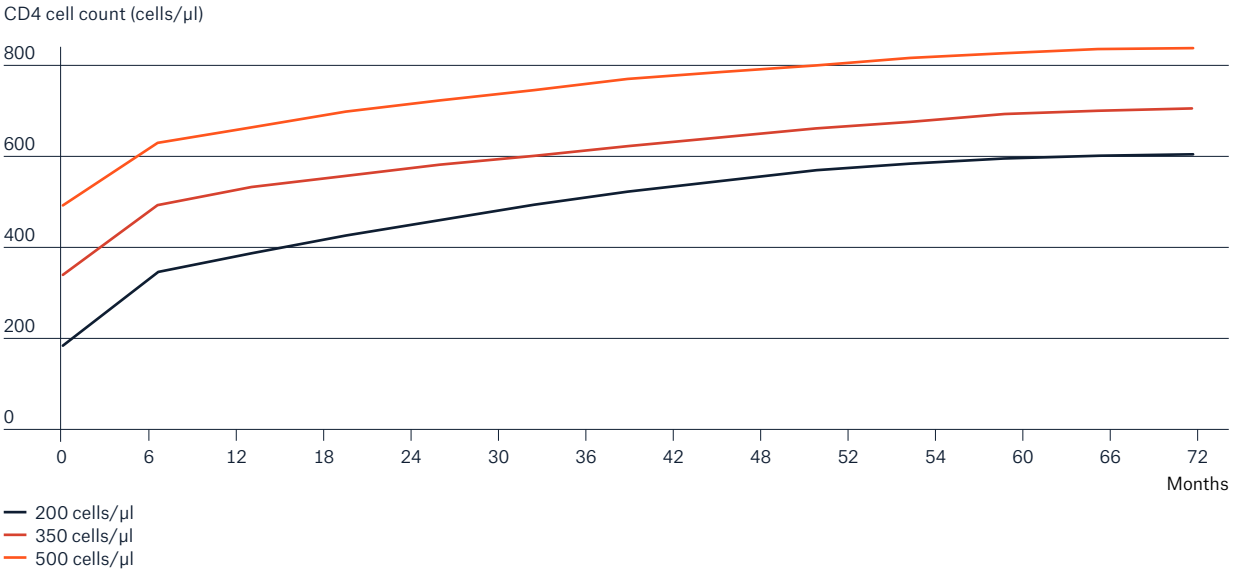
Depending on the activity of the HIV pathogen, CD4 counts increase with time spent on ART. This increase is faster during the first year on ART and stabilises after three to five years of ART[11, 12] (figure 4).

Predictive factors for mortality and morbidity

Apart from age and a suppressed viral load, the immune response of the patient as measured from the CD4 count is recognised as the main prognostic parameter. Mortality increases with decreasing immune status/CD4 counts. Studies investigating the relationship between the CD4 count and mortality measure CD4 at different times, e.g. at onset of ART (= baseline CD4 count), six months after initiation of ART (= 6-month CD4 count), or according to measurements taken within the last six months (= current CD4 count). Baseline CD4 counts have been investigated in early studies and in studies of the timing of treatment initiation, consistently revealing that mortality increases as CD4 counts decrease[13]. Unsuppressed viral load is usually due to non-compliance or in some unfortunate cases, due to non-response to therapy and resistance to the drugs. The latter group is very small and would be identified close to the actual diagnosis as immediate ART initiation is now recommended. Successful ART results in mortality close to that of the general population.

Individuals co-infected with HIV and viral hepatitis B or C have an increased risk of liver cirrhosis, end-stage liver disease and hepatocellular carcinoma[14]. Most studies report an increase in the mortality risk of patients with a dual infection of hepatitis B and HIV by a factor of 1.6 to 1.8 in comparison with HIV patients without hepatitis B. Even higher mortality risks have been reported for co-infection with hepatitis C[15, 16].

Figure 4: CD4 cell count over time (CD4/µl development during cART with suppressed viral load)



Source: Egger S, Petoumenos K et al. Long-term patterns in CD4 response are determined by an interaction between baseline CD4 cell count, viral load, and time: The Asia Pacific HIV Observational Database (APHOD). J Acquir Immune Defic Syndr. 2009 Apr 15; 50 (5): 513-20

Extremely favourable outcomes during the first years of ART are assumed to persist for decades to come. This is supported by continuously improving medication and treatment success. However, the impact of cumulative damage from a persistently low level of inflammation caused by the virus, independent of CD4 counts and accumulated exposure to ART, cannot yet be completely assessed.

Regarding morbidity, quality of life is still not assumed to be equal to that of the non-infected population[17]. As a result of the increased life expectancy of HIV-infected patients and modern ART, non-AIDS related morbidities become more important. HIV infection is seen as a risk factor for cardiovascular, liver and kidney diseases, neurocognitive deficits and malignancies. Higher morbidity is explained by the consequences of immunologic decline, persistent immune activation due to the virus itself and ART side effects. However, recently developed ART medication has fewer side effects than earlier drugs[18].

Conclusion

For PLWH on treatment, mortality and morbidity have steadily improved over time. In addition, PLWH whose viral load is suppressed can be considered non-infectious, which is obviously also a major benefit to society. In general, the well-being of an HIV-infected person depends very much on the quality of and access to medical treatment and on patient compliance, which is why, for example, intravenous drug users or people with certain co-morbidities are excluded from coverage. However, HIV therapy is a medical success story, unrivalled by many so-called breakthrough therapies in other areas of medicine.

Munich Re is pleased to announce not only updated guidelines for life insurance, but also sound and evidence-based guidelines for disability and critical illness covers.

This not only protects us from reputational damage but – more importantly – it also means that we fulfil our social responsibility as a (re)insurance company and treat customers fairly.

HIV can now be seen as a chronic disorder similar to many others. HIV – destigmatised.

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