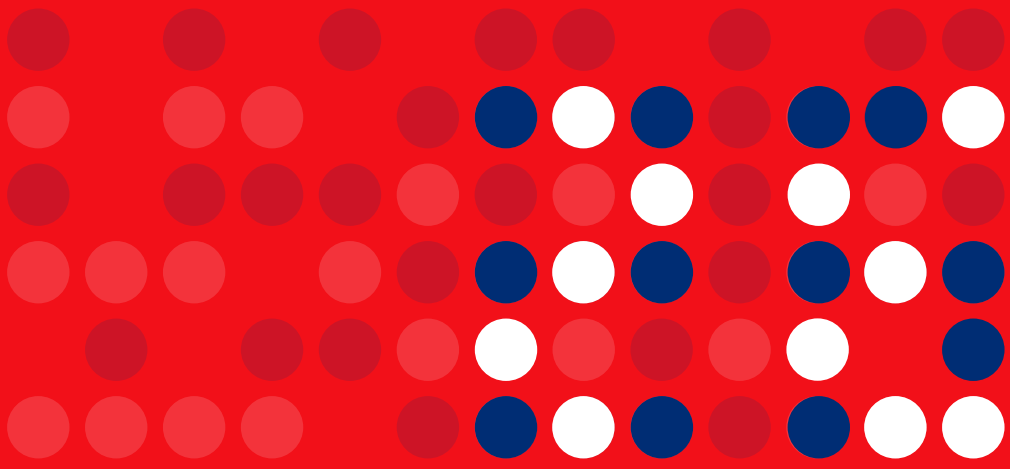
Human Immunodeficiency Virus (HIV)
Infection in the Netherlands

hiv Monitoring

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Chapter 6: Morbidity and mortality



6. Morbidity and mortality

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Summary

AIDS, mortality and causes of death

AIDS-related deaths have fallen dramatically since ART became available in the Netherlands in 1996, and the deaths from AIDS that still occur are concentrated among people who present late for care with advanced immunodeficiency; the number therefore still falls short of the target of zero AIDS-related deaths by 2027 set in the Netherlands' Updated National Action Plan on STIs, HIV and Sexual Health. Death is now far more often due to a non-AIDS cause: in 2023-2025, non-AIDS malignancies accounted for 27.5% and cardiovascular disease for 10.5% of all deaths, against 9.2% for AIDS. This reflects both the higher risk of non-AIDS morbidity in people with more advanced HIV infection and the continuously increasing age of the population in care. Mortality among people with HIV consequently remains higher than in the general Dutch population, although the excess has diminished: the ratio of observed over age- and sex-standardised expected mortality fell from 8.9 in 1996 to 3.0 in 2010, 2.3 in 2015, and has remained at around 2.0 since 2017, with a ratio of 1.9 in 2025. Several studies have found that mortality in individuals on ART who achieve CD4 cell counts above 500 cells/mm^3 may even drop below general population rates[1,2], but in the total Dutch population of people with HIV the decline in excess mortality has clearly slowed. In all subgroups examined the ratio declined over time yet remained substantially above one in 2025; it was lowest among the native Dutch, men who have sex with men, and those with higher pre-ART nadir CD4 counts.

The crude mortality rate fell from 18.1 per 1,000 person years of follow up (PYFU) in 1996 to 8.9 in 2010 and remained at that level until 2020. It rose to 10.8 per 1,000 PYFU in 2021 during the COVID-19 pandemic – an increase driven mainly by non-AIDS infectious causes of death and proportional to the excess mortality of around 10% observed in the general Dutch population in 2020 and 2021[3] – and had increased further to 11.9 per 1,000 PYFU in 2025. Because the ratio of observed over expected mortality remained stable throughout this period, the recent increase is most plausibly explained by the rising average age of the population in care rather than by a deteriorating prognosis. Two further observations warrant attention: 'sudden death', a category recently introduced for individuals who died suddenly and unexpectedly without a precise cause being established, accounted for 14.3% of deaths in 2023-2025; and the suicide rate among people with HIV, at over 40 per 100,000 person years, remains roughly four times that in the general Dutch population.

Cardiovascular disease, diabetes and chronic kidney disease

The crude incidence of diabetes mellitus remained stable in men but increased slightly in women, and was 4.1 and 6.3 per 1,000 PYFU, respectively, in 2025. The age-standardised incidence declined significantly in men, whereas in women it increased significantly over the observation period. Compared with the general Dutch population in 2024, the prevalence of diabetes was lower in men in nearly all age strata, but higher in women up to the age of 65. Multivariable analysis indicates that the higher age-adjusted incidence in women is largely explained by their higher BMI, which makes the continuing rise in obesity among women with HIV the most plausible driver of this trend. In our cohort, each of the three unboosted oral integrase inhibitors (dolutegravir, bictegravir and raltegravir) was individually associated with incident type 2 diabetes mellitus, whereas no such association was observed with cobicistat-boosted elvitegravir or with long-acting injectable cabotegravir. This association was independent of time-updated BMI, consistent with findings from other cohorts[4,5].

The crude incidence of cardiovascular disease (CVD) remained stable and the age-standardised incidence declined over time in both men and women, while the age- and sex-stratified prevalence of coronary artery disease was comparable to that in the general Dutch population in all age strata. This decline may reflect improved awareness and prevention – including switching away from drugs associated with an increased risk of diabetes mellitus[6] and myocardial infarction[7-11] – better management of traditional risk factors, and an increasing proportion of individuals living with high CD4 cell counts. The risk factors identified for diabetes and CVD (age, hypertension, smoking and obesity) are similar to those reported in other studies[6,12,13], and several of them are more prevalent among people with HIV[14]. Secondary cardiovascular events became significantly less frequent over time in men but more frequent in women; this difference remains unexplained and needs further study.

The crude incidence of chronic kidney disease (CKD) was approximately 10 per 1,000 PYFU in both men and women, and the age-standardised incidence was significantly lower in 2020-2025 than in 2008-2019. The apparent increase in CKD in recent years disappeared, and even reversed, once current use of cobicistat, rilpivirine, dolutegravir and bictegravir was added to the model. This strongly suggests that it reflects drug-induced inhibition of tubular creatinine secretion rather than a true decline in glomerular filtration.

Overweight and obesity

The distribution of BMI has continued to shift upwards in both sexes. Men aged 35 and over were significantly less often overweight or obese than men in the general Dutch population, and the overall proportion of obese men (14.0%) was similar to the national figure (13.7%). In women, by contrast, obesity was about twice as common as in the general female population (34.0% versus 17.7%) and was highest among migrant women from non-Western countries (40.8%); the clinical significance of this continuing increase requires further study. In our cohort, being overweight or obese was independently associated with an increased risk of new-onset diabetes mellitus and CKD, but not with CVD or non-AIDS-defining malignancies. Other studies have reported that weight gain after starting ART is associated with lower mortality in individuals of normal weight, with no clear benefit in those already overweight or obese[15], while also increasing the risk of diabetes and, in those with a normal pre-ART BMI, of cardiovascular disease[16]. Prospective longitudinal monitoring of weight, lipid levels, blood pressure and smoking status remains essential to optimise cardiovascular risk assessment in our ageing population and to evaluate the impact of interventions such as statins and antihypertensive therapy.

Non-AIDS-defining malignancies

The most common non-AIDS-defining malignancies (NADM) are lung, intestinal, prostate and anal cancer, and haematological malignancies. In men, the age-stratified incidence of NADM (including non-melanoma skin cancer) was significantly higher than the cancer incidence observed in the general Dutch male population; in women it appeared similar to that in the general female population, although the limited follow-up time and number of events restricts the statistical power of that comparison. Despite the increasing average age of the cohort, the crude incidence of NADM remained stable and the age-standardised incidence declined significantly in men, and to a lesser extent in women, which is in line with data from other cohorts, including the Swiss HIV and RESPOND cohorts[17-21]. In addition to older age, risk factors were current or past smoking, a CD4 cell count below 350 cells/mm^3, a low BMI, chronic hepatitis B virus co-infection and a prior AIDS diagnosis; other studies have reported that the effect of immunodeficiency may be stronger for infection-related malignancies[22]. Five-year survival changed little over time and remains poor for lung (22%) and liver (14%) cancer.

Multimorbidity and polypharmacy

The prevalence of non-AIDS multimorbidity continues to increase slowly, driven mainly by the increasing age of the cohort, with women experiencing more comorbidities (driven by a much higher prevalence of obesity) than men in every age group. Multimorbidity is strongly and independently associated with mortality (RR 2.01 per additional comorbidity diagnosed).

Polypharmacy, defined as the concomitant use of five or more medications in addition to ART, is also becoming more prevalent: from 3.4% of adults in active follow up in 2000 to 18.0% in 2025. The main drivers are, again, the increasing age of the population and the accompanying rise in the number of chronic comorbidities per individual. Polypharmacy was likewise strongly and independently associated with an increased risk of death (RR 2.35), independent of demographic and HIV-related parameters, chronic HBV and HCV co-infections, smoking status and the number of comorbidities. The most notable recent change in comedication use is the continued increase in lipid-lowering therapy, used by 7,400 individuals in 2025 compared with 6,209 in 2024 and 5,155 in 2023, following the change in guidance on primary cardiovascular prevention prompted by the REPRIEVE study[9].

Introduction

Since the introduction of combined antiretroviral therapy (ART) in 1996, the life expectancy of people with HIV (PWH) has markedly improved[23]; in a subgroup of recently-diagnosed, effectively-treated individuals, it was shown to be similar to that of the general population in the Netherlands[24]. Whereas the incidence of AIDS-defining infections and malignancies has markedly decreased[25], morbidity and/or mortality associated with non-AIDS-related diseases has increased among PWH during the ART era[26-31]. Examples of these include renal and liver disease, diabetes mellitus, myocardial infarction, stroke, osteoporosis, and non-AIDS-defining malignancies.

Various reports suggest that the risk of non-AIDS-related morbidity may be higher in individuals with HIV treated with ART, than in individuals without HIV of comparable age[32-34]. For example pulmonary hypertension[35], bone disease, and non-traumatic bone fractures[36-38] have each been reported to be more common in PWH. Just as with individuals without HIV, traditional risk factors (such as tobacco use[14], alcohol abuse, and viral hepatitis co-infection[39]) also contribute to the increased risk of certain non-AIDS-related comorbidities in people with HIV.

One of the most prevalent comorbidities is cardiovascular disease (CVD). In addition to traditional risk factors such as smoking, probable additional risk factors with high prevalence among PWH include metabolic abnormalities such as dyslipidaemia; insulin resistance; hypertension; diabetes; and changes in body composition, which may be driven partly by the use of ART, as well as by sustained, residual HIV-associated immune activation and inflammation, despite effective ART[40, 41].

In this chapter, we report on mortality and its causes for adult (18 years and over) PWH using updated stichting hiv monitoring (SHM) data. We look at a total of 33,071 adult individuals ever registered by SHM – which includes 751 individuals who were diagnosed with HIV as children and have since become adults. In addition, we report on the incidence of AIDS and non-AIDS comorbidities, particularly diabetes mellitus, cardiovascular disease, chronic kidney disease (CKD), and non-AIDS malignancies in PWH.

Definitions

AIDS is defined as having experienced any of the United States' Centers for Disease Control (CDC) category C conditions[42]. In contrast to the US approach, a CD4 cell count below 200 cells/mm^3 in the absence of an AIDS-defining condition, does not qualify as AIDS in our analyses.

The following are defined according to criteria established by the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study: diabetes mellitus; CVD (including myocardial infarction, stroke, coronary artery bypass grafting, coronary angioplasty or stenting, and carotid endarterectomy); and non-AIDS-defining malignancies (excluding precancerous stages of anal and cervical cancer, basal cell carcinoma, and squamous cell carcinoma of the skin). In addition, Castleman's disease is also considered a non-AIDS-defining malignancy.

Histological confirmation of malignancies is part of standard clinical practice in the Netherlands. As a result, pathology reports, wherever possible, have been used to establish the presence of any malignancy.

Chronic kidney disease (CKD) is defined as an estimated glomerular filtration rate (eGFR) below 60 ml/min (estimated with the Cockcroft-Gault equation), confirmed after six months or longer. We use this period of time because of the large number of episodes of renal dysfunction that revert shortly after three months, and therefore do not represent true CKD.

Methods

For the analyses of incidence per calendar year and calendar period, we have considered all events after an individual entered care following HIV-1 diagnosis, or after the start of routine collection of data on the condition of interest, whichever was most recent. For instance, data on CKD were analysed from April 2007 onwards, because that was when routinely-collected renal laboratory data became available for analysis.

As the average age of the Dutch HIV population has increased over time, we also estimated the incidence rates for the periods 2000-2009, 2010-2019, and 2020-2025. We standardised these estimates according to the age distribution of the population during the period 2020-2025 (divided into the following age classes: 18-29, 30-39, 40-49, 50-59, 60-69, and 70 years and over), using the indirect method[43]. Indirect standardisation compares the incidence rates in the study and reference period (2020-2025) populations by applying the stratum-specific rates in the reference population to the study population. We investigated risk factors for AIDS, death, and each of the non-AIDS events, as well as a combined non-AIDS endpoint (defined as first occurrence of cardiovascular disease, diabetes mellitus, or non-AIDS-defining malignancy). CKD was not included in this combined endpoint as serum creatinine was not part of routine data collection before 2007.

The baseline for treated and untreated PWH was defined as the date of HIV-1 diagnosis or January 2000, whichever was most recent. Subsequent follow-up time was divided into periods of three months. Poisson regression models were used to estimate the independent association between risk factors and each endpoint. Models were adjusted for:

- the most recent CD4 cell count (lagged by three months);
- body mass index;
- gender;
- region of birth;
- most likely mode of HIV-1 transmission;
- current age;
- having started ART within 12 months of the last negative HIV test;
- known time spent with CD4 cell count below 200 cells/mm^3;
- known time spent with plasma HIV RNA above 1,000 copies/ml while on ART;
- time on ART;
- specific antiretroviral drugs used;
- prior diagnosis of AIDS;
- presence of chronic active hepatitis B and/or C virus infection;
- hypertension, diabetes mellitus, and other chronic comorbidities;
- smoking; and
- calendar period.

Mortality

Mortality was investigated in all 33,071 adult PWH ever registered in the SHM database. The mortality rate was 18.1 (95% confidence interval [CI] 13.5-23.9) per 1,000 person years of follow up (PYFU) in 1996 and declined to 8.9 (95% CI 7.4-10.6) per 1,000 PYFU in 2010. It remained stable at that 2010 level up to 2020, but the observed mortality rate was noticeably higher in 2021 during the COVID-19 pandemic with 10.8 (9.4-12.2). In 2025 the observed crude mortality rate had increased to 11.9 (10.5-13.4) per 1,000 PYFU (*Figure 6.1A*). Despite the overall improvement over time, the mortality rate in adult PWH remained well above the age-matched and gender-matched mortality observed in the general population in the Netherlands, which was 6.1 per 1,000 PYFU in 2025. The ratio of the observed mortality among PWH compared to the age/sex-adjusted mortality observed in the general population, decreased from 8.9 in 1996, to 6.5 in 2000, to 5.8 in 2005, to 3.0 in 2010, to 2.3 in 2015 and has remained constant at around 2.0 since 2017. In 2025 the ratio was 1.9.

We repeated the analysis of mortality for various subgroups of interest (*Figure 6.1C*). The analyses were stratified based on region of origin (native Dutch, migrants with Western background, and migrants with non-Western background), HIV acquisition category (men who have sex with men, other men who acquired HIV heterosexually, and women) and pre-ART nadir CD4 count (0-199, 200-499, and 500 and more cells/mm^3). The "Ratio in 2025" mentioned in the top right corner of each panel is the ratio of the observed crude mortality rate over the age/sex-adjusted expected mortality in 2025. In all investigated subgroups, the ratio of the observed over expected mortality declined over time but at the end of follow-up in 2025 remained substantially higher than one. The native Dutch, MSM, and those with higher pre-ART nadir CD4 counts had the lowest excess mortality.

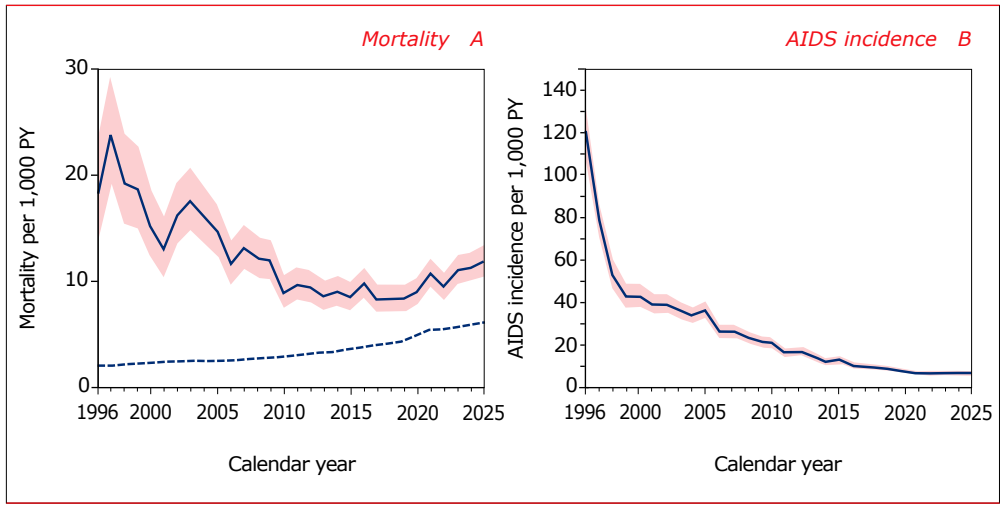
Underlying causes of death

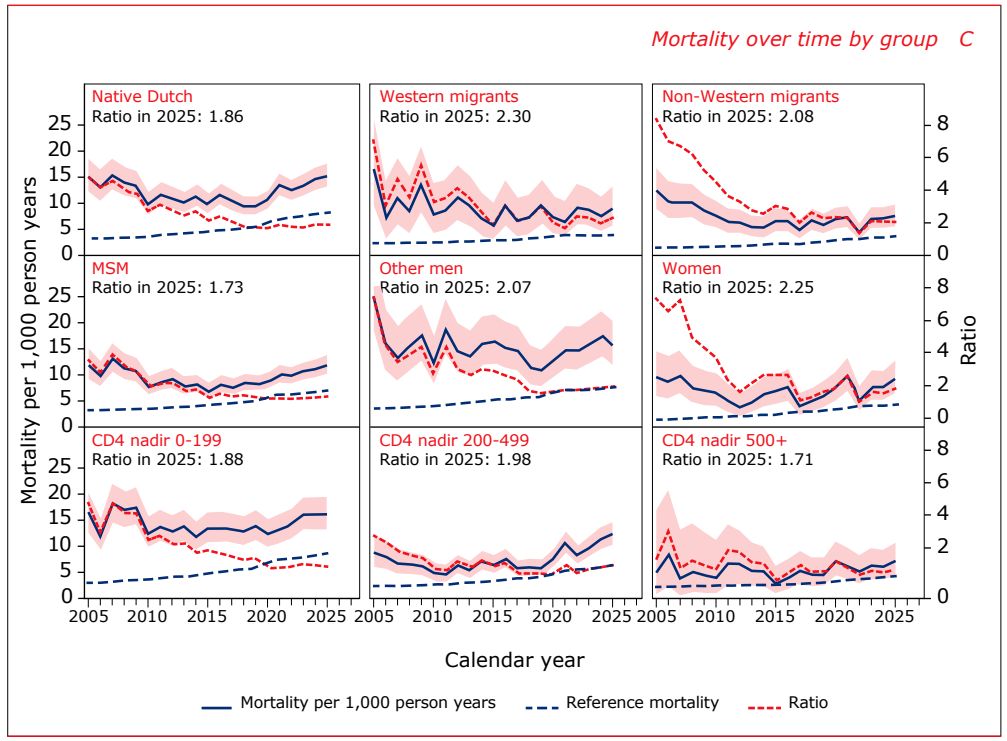
Observed underlying causes of death are presented in *Figure 6.1D* (with exact numbers and percentages presented in *Appendix Table 6.1*). Although the AIDS-related death rate has decreased significantly since the advent of ART, the continued occurrence of deaths due to AIDS is driven largely by the persistent high proportion of newly diagnosed people with HIV who present late for care with advanced immune deficiency. As such, the rate falls short of the aim of zero AIDS-related deaths by 2027, as stated in the Netherlands' Updated National Action Plan on STIs, HIV and Sexual Health, 2023-2027[44]. *Table 6.1* shows the characteristics of adults with HIV who died of AIDS, compared to those who died of non-AIDS causes during the last 10 years, the period 2016-2025. Individuals who died of AIDS were more frequently female, non-MSM males and/or migrants, more recently diagnosed with HIV, had been on ART for a shorter period of time, and had much lower CD4 cell counts at diagnosis (60.3% had advanced HIV at diagnosis with a CD4 cell count below 200 cells/mm^3). In 47.7% of cases, they did not have controlled viremia, and 29.2% of this group was not receiving any ART at the time of death, either because ART had not yet been started or had been discontinued (*Table 6.1*).

Among individuals who died of advanced HIV / AIDS but who did not classify as late or advanced presenters (i.e. they had a CD4 cell count above 350 cells/mm^3 at diagnosis), the cause of death was relatively more likely to be an AIDS-related haematological malignancy, which are also known to occur in people on suppressive ART with high CD4 cell counts. The proportion and absolute number of deaths due to non-AIDS-defining conditions have increased significantly over time (*Figure 6.1D*), primarily as a consequence of the ever increasing size and increasing average age of the population of people with HIV in the Netherlands. In recent years, the category 'Sudden death' has been introduced for individuals

who died suddenly and unexpectedly within a precise cause being known. People with HIV who were born in the Netherlands, MSM and men in general are overrepresented among those who died of non-AIDS causes, because people in these three (overlapping) categories have a higher average age compared to migrants, HIV transmission categories other than MSM, and women. Independent risk factors for death and for being diagnosed with an AIDS-defining condition are listed in *Appendix Table 6.2*.

Figure 6.1A–D: *(A) Annual mortality and (B) incidence of AIDS in 33,071 PWH in the Netherlands after entry into HIV care from 1996 onwards. (C) Annual mortality in various subgroups of interest after entry into HIV care from 2000 onwards. Solid lines represent the incidence, while the shaded areas are the 95% confidence intervals. The dashed line is the mortality rate for age-matched and sex-matched individuals from the general population in the Netherlands. The "ratio" is the ratio of observed over age/sex-standardized mortality in the Netherlands in 2025. (D) Relative changes in causes of death in different calendar periods since the introduction of combination antiretroviral therapy (ART) in the Netherlands. The numbers at the top of each bar represent the total number of deaths and the total number of individuals that were at risk during that calendar period. Mortality attributed to 'alcohol use' refers to deaths due to complications of alcohol-related liver cirrhosis.*





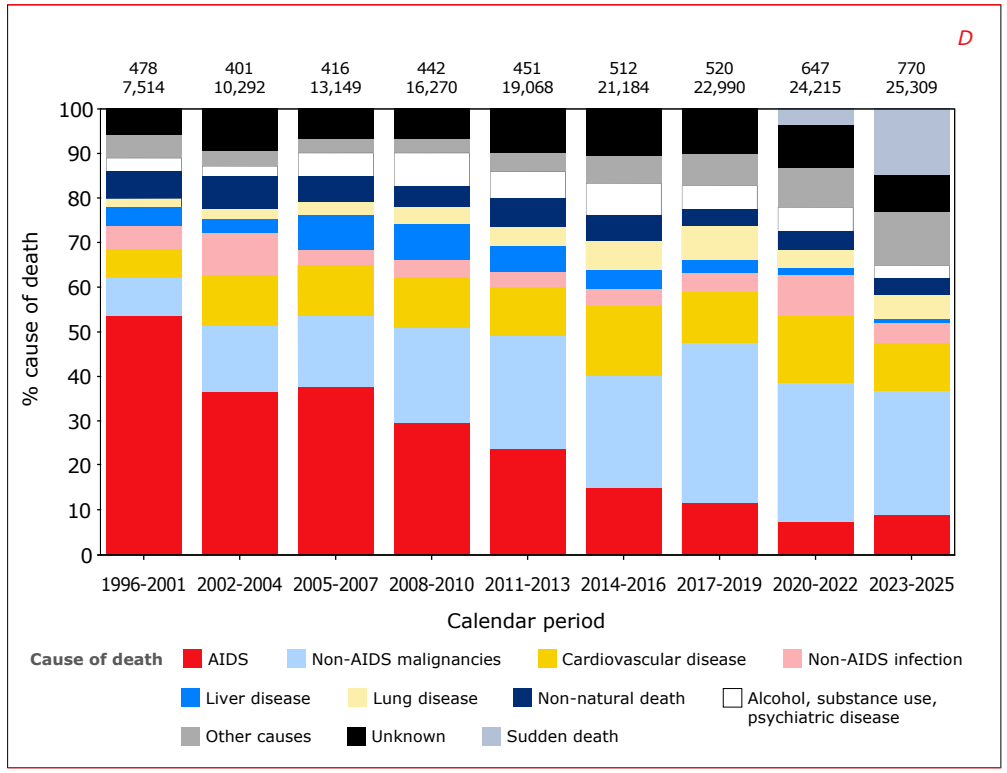


Table 6.1: Characteristics of adults with HIV who died of AIDS compared to adults with HIV who died of non-AIDS causes in the period 2016-2025.

	Died of AIDS	Died of non-AIDS causes	p-value
Number of subjects	209 (9.9%)	1,909 (90.1%)	
Age	56.7 (46.4-67)	62.5 (54.7-70.9)	<.001
Transmission category			<.001
MSM	89 (42.6%)	1,127 (59.0%)	
Other men	71 (34.0%)	403 (21.1%)	
Women	32 (15.3%)	208 (10.9%)	
Transgender	3 (1.4%)	13 (0.7%)	
IDU	7 (3.3%)	121 (6.3%)	
Blood contact	2 (1.0%)	35 (1.8%)	
Pediatric	5 (2.4%)	2 (0.1%)	
Region of origin			<.001
Native Dutch	121 (57.9%)	1,352 (70.8%)	
Western migrants	21 (10.0%)	180 (9.4%)	
non-Western migrants	64 (30.6%)	372 (19.5%)	
Unknown origin	3 (1.4%)	5 (0.3%)	
Years since HIV diagnosis	8.7 (1.03-18.5)	17.4 (10.4-24.3)	<.001
Years since start ART	5.04 (0.46-14.1)	15 (8.69-21)	<.001
CD4 at HIV diagnosis	137 (41-336)	304 (130-530)	<.001
Late HIV diagnosis (CD4<350 at entry in care)	160 (77.3%)	1,051 (55.1%)	<.001
Advanced HIV diagnosis (CD4<200 at entry in care)	126 (60.3%)	660 (34.6%)	<.001
CD4 nadir	60 (20-130)	161 (60-277)	<.001
Last CD4 measured before death	150 (55-344)	530 (336-750)	<.001
Viral load undetectable at date of death	104 (52.3%)	1678 (88.2%)	<.001
Not on ART at date of death*	61 (29.2%)	192 (10.1%)	<.001

**These interruptions likely reflect two different situations: prolonged disengagement from care, which is plausibly more relevant to the AIDS-related deaths, and intentional withdrawal of ART as part of palliative care near the end of life. See also sections "Treatment interruptions" and "Loss of viral suppression" in Chapter 4 Antiretroviral therapy in the Netherlands.*

***Legend:** ART = combination antiretroviral therapy. Data shown are n (%) for categorical variables and median (interquartile ranges) for continuous variables. CD4 cell counts are expressed as cells/mm³, IDU = intravenous drug use.*

Risk factors associated with mortality

We used Poisson regression analysis to examine factors associated with mortality in individuals from the moment they started ART. After correction for all variables listed in *Appendix Table 6.2*, including time-updated age and time-updated lagged CD4 cell counts, we found that, in general, risk of death was higher in (heterosexual) men compared to women, and this risk increased as individuals grew older. It also increased if they:

- belonged to the HIV transmission risk group of people who use/used injecting drugs (PWID);
- had a prior AIDS diagnosis;
- were co-infected with the hepatitis B virus (HBV) or hepatitis C virus (HCV);
- were underweight;
- were current or past smokers;
- had spent more time with an HIV RNA level above 1,000 copies/ml while on ART; or
- had a current CD4 cell count less than 750 cells/mm³, with the risk of death progressively increasing in lower CD4 strata.

In individuals who had initiated early ART (i.e. within 12 months of their last negative HIV test, or within 12 months of a diagnosed acute HIV infection [Fiebig stages I-V]), the risk of death was significantly lower compared to individuals who did not initiate ART early (relative risk 0.75, 95% CI 0.58-0.97, p=0.027). Although a lower mortality risk was observed in individuals of non-Dutch origin, this is likely due to a larger proportion of migrants becoming lost to care (*Appendix Table 6.3*). In native Dutch individuals the risk of becoming lost to care was not linked to their CD4 cell count. In contrast, people from all other non-Dutch groups were far more likely to become lost to care if they had very low CD4 cell counts. One explanation could be that those born overseas often return to their families in their country of origin when they experience a severe deterioration in health. As a result, it is likely that mortality rates in these groups have been considerably underestimated.

Suicide and euthanasia

Individuals who had a psychiatric disease as the recorded underlying cause of death, and for whom the immediate cause of death was recorded as suicide, have been re-classified as 'suicide' for the current analysis (*Appendix Table 6.1*). The number of recorded suicides among people with HIV in the Netherlands in the period 2011 to 2025 was stable at around ten recorded cases per calendar year, which is a much higher rate than the known rates of suicide in the general Dutch population. The latter has been stable in the last 10 years; at between 10.4-11.2 instances per 100,000 individuals per year, compared to more than 40 instances per 100,000 person years in the population with HIV[45, 46].

For patients with a serious somatic condition, who opted for euthanasia in the terminal disease stage, the underlying somatic condition was recorded as the cause of death. In the entire follow-up period from 1996 to 2025, a total of 206 instances of euthanasia were recorded; 14% of cases occurred in patients who died of AIDS, 46% in patients who died of non-AIDS-defining malignancies, and the remaining 40% in patients who died of other diseases. Our definition of euthanasia does not include the use of standard practice palliative care, like palliative sedation in the terminal phase of the underlying disease.

AIDS-defining events

In the group of 33,071 adult PWH ever registered in the SHM database, the incidence of first AIDS-defining events decreased sharply from 121.3 (95% CI 108.7-134.9) in 1996 to 6.4 (5.4-7.6) cases per 1,000 PYFU in 2025 (*Figure 6.1B*). *Appendix Table 6.4* gives an overview of the first AIDS-defining events occurring between 1996 and 2025. The most common first AIDS-defining events between 2020 and 2025 (n=835) were:

- *Pneumocystis jirovecii pneumonia (20% of all events);*
- *esophageal candidiasis (18%);*
- *recurrent bacterial pneumonia (13%);*
- *tuberculosis (9%, of which pulmonary 5% and extrapulmonary 4%);*
- *Kaposi's sarcoma (8%);*
- *AIDS-defining lymphoma (7%);*
- *AIDS-related wasting (5%);*
- *cytomegalovirus-associated end organ disease (4%);*
- *herpes simplex virus chronic ulcer (4%);*
- *AIDS dementia complex / HIV encephalopathy (3%); and*
- *toxoplasmosis of the brain (2%).*

Risk factors for AIDS-defining events are shown in *Appendix Table 6.2*.

In the present analyses, we concentrate on the first occurrence of any AIDS-defining event after the start of ART. The results of these analyses show that individuals were more likely to experience their first AIDS-defining event if:

- they were older;
- were born in a non-Western country;
- had a current CD4 cell count below 500 cells/mm^3 (although the likelihood was even higher if their CD4 cell count was below 200 or 50 cells/mm^3);
- had more than 1,000 HIV RNA copies/ml for a longer period of time while on ART; or
- were co-infected with HCV.

Because the main findings of the analysis of AIDS events after the start of ART were heavily influenced by events occurring shortly after the start of ART and/or while HIV-1 RNA was still detectable, we also analysed the incidence of CDC-B (moderately symptomatic HIV disease) and AIDS-defining events in individuals who had started ART at least one year before and had undetectable viraemia or transient low-level viraemia (i.e. 'blips'; below 200 copies/ml) at the moment the HIV-related event was diagnosed. In other words, we focused on those individuals with an optimal virological response to ART. Events were classified into CD4 strata based on the current or previously measured CD4 cell count, whichever was the lowest. Use of opportunistic infection prophylaxis was not accounted for in this analysis. Only 'definitive' or 'probable' diagnoses were considered; 'possible' events or events with incomplete ascertainment were excluded. Cervical dysplasia was excluded from this analysis.

Between 1 January 2000 and 31 December 2025, 28,415 individuals contributed a total of 315.1 thousand PYFU, during which 4,030 CDC-B and/or CDC-C (AIDS-defining events) were diagnosed. This resulted in an incidence rate of 12.8 events per 1,000 PYFU (2,212 CDC-B events, 7.0 events/1,000 PYFU; 1,818 CDC-C/AIDS events, 5.8 events/1,000 PYFU) (Table 6.2). As expected, the incidence rates were highest in the CD4 strata below 200 cells/mm^3. Although the incidence rates declined sharply in the higher CD4 strata, the incidence rates of AIDS-defining illnesses in the 200-349 and 350-499 cells/mm^3 strata remained substantial, with 10.0 and 5.0 AIDS-defining illnesses/1,000 PYFU, respectively. The incidence rates of AIDS-defining illnesses in the CD4 strata of 500-749 and over 750 cells/mm^3 were 2.8 (95% CI 2.5-3.2) and 1.8 (1.5-2.0) events/1,000 PYFU, respectively. Note that the incidence in the over 750 cells/mm^3 stratum is statistically significantly lower compared to the 500-749 cells/mm^3 stratum. In these highest CD4 strata, the main AIDS-defining events that still occurred were:

- recurrent bacterial pneumonia;
- Kaposi's sarcoma;
- oesophageal candidiasis;
- non-Hodgkin's lymphoma;
- tuberculosis (pulmonary and extrapulmonary); and
- chronic genital Herpes simplex virus (HSV) ulcers

Appendix Table 6.6 shows the type and number of HIV-related diagnoses by CD4 strata. We repeated the Poisson regression for risk factors for AIDS, limited to individuals on ART with undetectable viral load and a current CD4 count of at least 500 cells/mm^3. We found that the main risk factor for incident AIDS-defining conditions in this subgroup was higher age: compared to those aged

30-39 years old, the IRR was significantly increased in those aged 60-69 (RR 1.57, 95%CI 1.15-2.15), over 70 years old (RR 1.90, 95%CI 1.28-2.81). Of note, the nadir pre-ART CD4 count was not statistically significantly associated with incident AIDS-defining conditions in this analysis (IRR 1.02, 95%CI 0.75-1.38).
In the period 2020-2025, Kaposi's sarcoma occurred not much less frequently in people with suppressed viremia (n=41, 40.6%) compared to people not on ART or with poorly controlled viremia (n=60, 59.4%).

***Table 6.2:** CDC-B and CDC-C/AIDS events occurring between 2000 and 2025 in individuals on ART, while having an undetectable viral load.*

CD4 category (cells/mm³)	CDC events (n)	CDC B events (n)	CDC C events (n)	PYFU follow-up (x1,000)	Incidence rate CDC events (/1,000 PY) (95%CI)	Incidence rate CDC-B events (/1,000 PY) (95%CI)	Incidence rate CDC-C events (/1,000 PY) (95%CI)
0-50	452	191	261	1.1	420 (382-460)	177 (153-204)	242 (214-274)
50-199	870	449	421	11.8	73.5 (68.7-78.5)	37.9 (34.5-41.6)	35.6 (32.2-39.1)
200-349	764	413	351	35.2	21.7 (20.2-23.3)	11.7 (10.6-12.9)	9.98 (8.96-11.1)
350-499	705	398	307	61.2	11.5 (10.7-12.4)	6.51 (5.88-7.18)	5.02 (4.47-5.61)
500-749	775	465	310	109.7	7.07 (6.58-7.58)	4.24 (3.86-4.64)	2.83 (2.52-3.16)
750+	464	296	168	96.1	4.83 (4.40-5.29)	3.08 (2.74-3.45)	1.75 (1.49-2.03)
Total	4,030	2,212	1,818	315.1	12.8 (12.4-13.2)	7.02 (6.73-7.32)	5.77 (5.51-6.04)

***Legend:** CDC = Centers for Disease Control and Prevention Classification System for HIV Infection; CDC-B = moderately symptomatic HIV disease; CDC-C = AIDS-defining events; ART = combination antiretroviral therapy; PYFU = person years of follow up.*

Mycobacterial disease: tuberculosis (TB) and non-tuberculous mycobacteria (NTM)

Between 1 January 1996 and 31 December 2025 a cumulative total of 1,252 cases of active TB were diagnosed in 1,036 individuals, of which 731 (58.4%) were pulmonary cases and 521 (41.6%) were extrapulmonary/disseminated cases. During that same period, 609 cases of NTM disease were diagnosed in 536 individuals: 117 pulmonary and 492 extrapulmonary/disseminated cases. *Figures 6.2A&B* and *Appendix Table 6.4* describe the incidence over calendar time of active TB and NTM disease.

Geographical region of origin

Migrants who originated from non-Western regions (72.2% of cases, 34.1% of the population) were strongly overrepresented among the active TB cases, while those who were born in the Netherlands (14.5% of cases, 50.0% of the population) were strongly underrepresented. Migrants originating from Western regions (which includes countries from Eastern Europe) represented 12.5% of cases and 15.3% of the population. Region of origin was not strongly associated with the incidence of NTM disease. Table 6.3 describes some key characteristics of the individuals diagnosed with either active TB or NTM disease. In case individuals had multiple diagnoses, the date of the first event was used.

Disease-related mortality rates

4.8% of the individuals diagnosed with pulmonary TB and 4.4% of the individuals diagnosed with extrapulmonary/disseminated TB died within 365 days of the diagnosis, with the reported cause of death being 'AIDS' or 'infection'. The disease-related mortality rates within 365 days of diagnosis were 5.1% for pulmonary and 17.1% for extrapulmonary/disseminated NTM disease.

Latent tuberculosis infection (LTBI): screening and preventive treatment (TPT)

The current national guidelines recommend performing screening for LTBI in all individuals newly diagnosed with HIV who are at increased risk for TB (migrants from high-endemic regions or individuals who have been in close contact with cases of tuberculosis). The recommended method for LTBI screening is the interferon gamma release assay (IGRA) in combination with a tuberculin skin test (Mantoux test). TPT in individuals in whom LTBI has been diagnosed considerably lowers their risk of developing active TB.

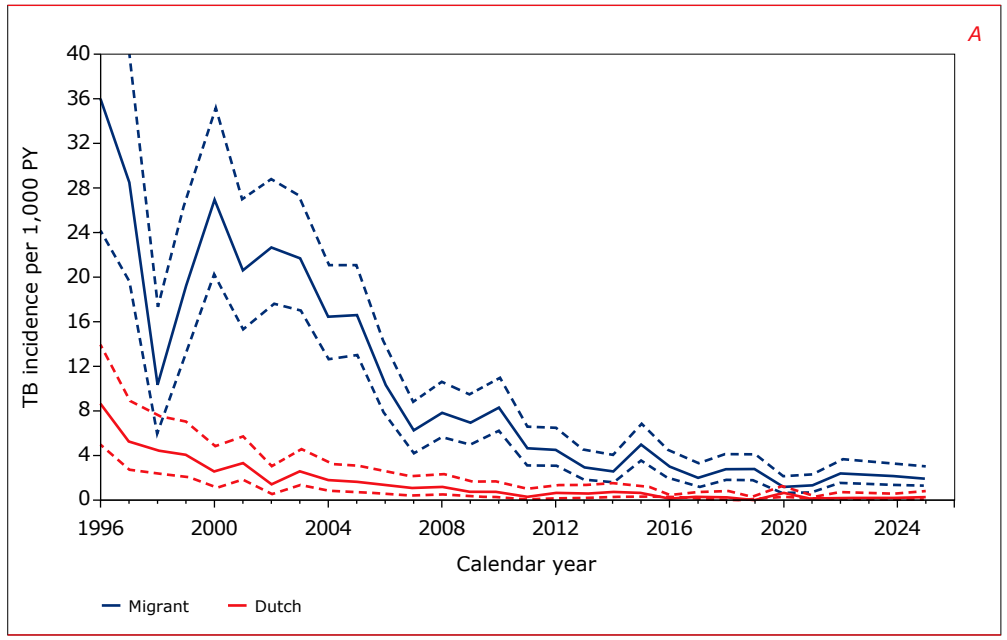
SHM has been collecting data on LTBI screening and TPT since 2018. IGRA testing during an episode in which active TB was diagnosed was excluded from this dataset. A limitation of our analysis of LTBI screening is that we do not have data on whether, at the time of IGRA testing, the individual had complaints that may have been caused by TB, which then prompted the treating physician to perform IGRA testing. In 23.2% of cases a chest X-ray or CT scan was taken, indicating that in some of these instances the individual might also have had pulmonary symptoms at the moment of IGRA testing.

Since 1 January 2018, SHM has recorded LTBI screening using IGRA with or without an additional tuberculin skin test in 3,338 individuals. In 332 (10.0%) of these individuals LTBI testing was positive, and 120 (36.1%) of those 332 individuals received a course of TPT. TPT consisted of:

- isoniazid plus rifampicin (typically for a duration of 3 months) in 37 individuals;
- isoniazid monotherapy (typically for a duration of 6 to 9 months) in 71 individuals; and
- rifampicin monotherapy (typically for a duration of 4 months) in 5 individuals.

A further 7 individuals received another non-standard TPT. In the 332 individuals who tested positive on LTBI screening, 4 cases of pulmonary and 2 cases of extrapulmonary TB were diagnosed later during follow-up. Five of these 6 cases had received a course of TPT. Of the 212 individuals with positive LTBI screening who did not receive TPT, 26 (12.3%) were known to have been diagnosed with and treated for active TB prior to the LTBI screening.

Figure 6.2A–B: Crude incidence rates of active TB and NTM disease in Dutch and migrants per 1,000 person years of follow up (solid lines) and 95% confidence intervals (dashed lines).



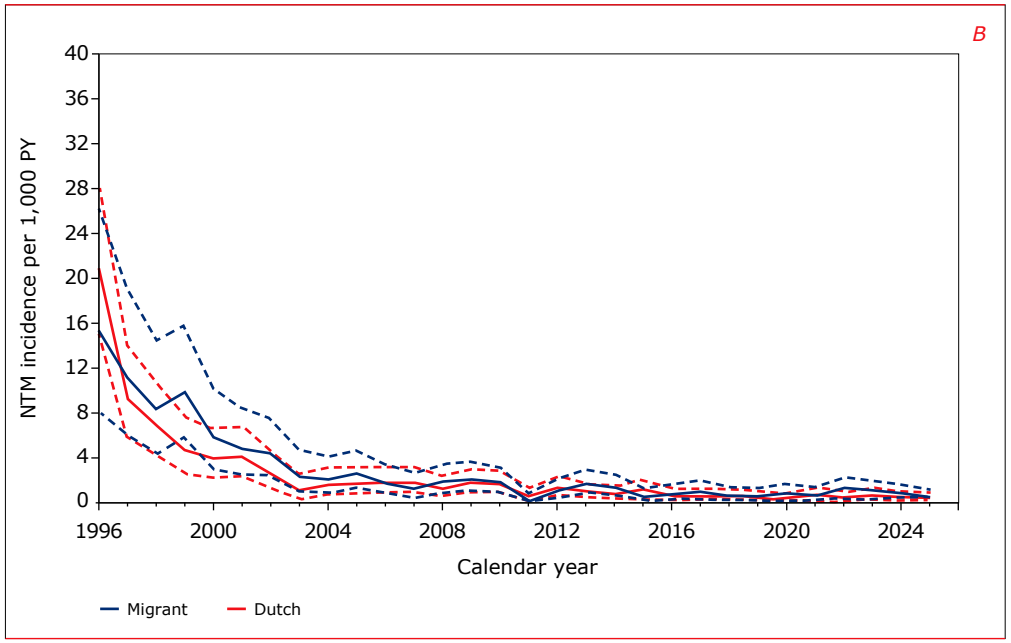


Table 6.3: Characteristics at the time individuals were diagnosed with active TB or NTM disease for the first time.

	Active TB	NTM disease	p-value
Number of subjects	1,036 (65.9%)	536 (34.1%)	
Age	37.1 (30.9–44.8)	40.4 (34.6–48.3)	<.001
Transmission category			<.001
MSM	219 (21.1%)	234 (43.7%)	
Other men	387 (37.4%)	161 (30.0%)	
Women	319 (30.8%)	102 (19.0%)	
Transgender	19 (1.8%)	5 (0.9%)	
IDU	63 (6.1%)	25 (4.7%)	
Blood contact	27 (2.6%)	6 (1.1%)	
Pediatric	2 (0.2%)	3 (0.6%)	
Region of origin			<.001
Native Dutch	182 (17.6%)	295 (55.0%)	
Western migrants	102 (9.8%)	61 (11.4%)	
non-Western migrants	747 (72.1%)	179 (33.4%)	
Unknown origin	5 (0.5%)	1 (0.2%)	
Diagnosed before HIV diagnosis	241 (23.3%)	35 (6.5%)	<.001
Years since HIV diagnosis	0.93 (0.5–4.93)	1.12 (0.57–6.73)	0.011
Years since start ART	0.46 (0–1.37)	0.63 (0.26–1.27)	<.001
CD4 at HIV diagnosis	192 (70–401)	40 (10–200)	<.001
Late stage at HIV diagnosis (CD4<350 at	468 (68.4%)	393 (83.8%)	<.001
Advanced stage at HIV diagnosis (CD4<200	696 (67.2%)	418 (78.0%)	<.001
CD4 nadir	120 (40–250)	20 (10– 50)	<.001
Last CD4 measured before event	200 (88–360)	70 (20–160)	<.001
Undetectable at date of event	191 (18.4%)	133 (24.8%)	0.004
Not on ART at date of event	738 (71.2%)	259 (48.3%)	<.001

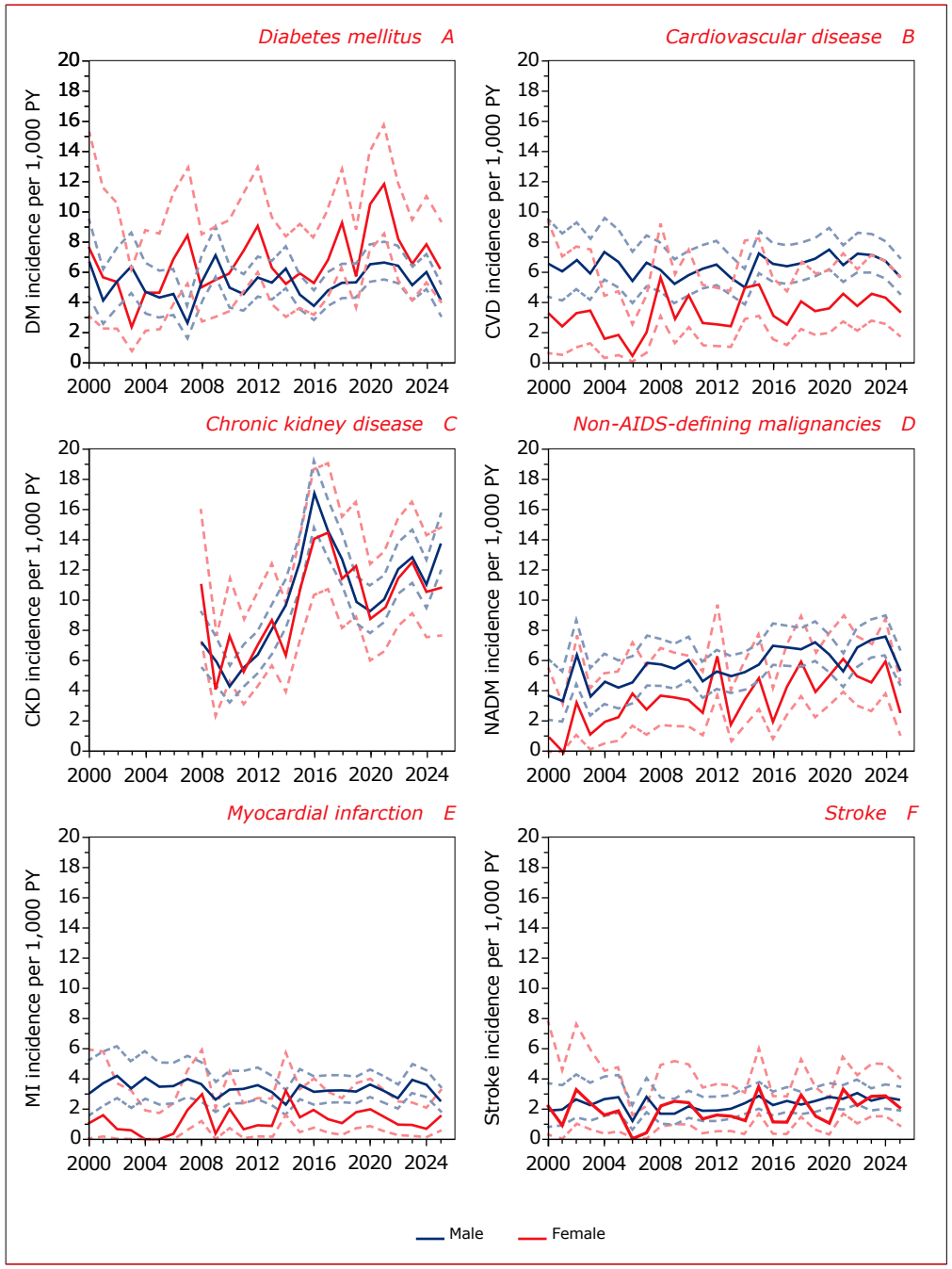
Non-AIDS-defining events

Of the 33,071 adult PWH ever registered with SHM, 32,721 were aged 18 years and over while in follow up in, or after January 2000. For these treated and untreated adults, we report incidence figures and risk factors for:

- diabetes mellitus;
- a composite cardiovascular disease endpoint (and also separately for myocardial infarction and stroke);
- non-AIDS-defining malignancies; and
- Chronic kidney disease (CKD).

We also present the incidence of the first occurrence of diabetes mellitus, cardiovascular disease, or non-AIDS-defining malignancies as a combined non-AIDS disease endpoint (*Figure 6.3A-F*).

Figure 6.3A-F: *Crude incidence rates per 1,000 person years of follow up (solid lines) and 95% confidence intervals (dotted lines) of (A) diabetes mellitus, (B) cardiovascular disease, (C) chronic kidney disease, (D) non-AIDS-defining malignancies, (E) myocardial infarction, (F) stroke, stratified by gender.*



Diabetes mellitus

Of the 32,721 individuals aged 18 years and over, who were in follow up in, or after January 2000, a total of 2,227 (1,704 men and 523 women) were diagnosed with type 2 diabetes from 2000 onwards. The crude incidence of diabetes remained stable over time for men, whereas there was a slight increase in women (*Figure 6.3A*), and in 2025 was 4.1 (95% CI 3.2-5.2) per 1,000 PYFU in men and 6.3 (4.0-9.4) per 1,000 PYFU in women. In men, the age-standardised incidence ratio declined over time and was significantly lower in 2010-2019 and 2020-2025 than in 2000-2009. In women, however, an opposite effect was seen, as the age standardised incidence in significantly increased over the observation period (*Table 6.4*).

Demographic and clinical factors independently associated with an increased risk of new-onset diabetes mellitus were:

- non-Dutch/Western origin;
- older age group;
- a BMI greater than 25 kg/m^2;
- hypertension;
- a latest CD4 cell count below 200 cells/mm^3;
- treatment with NRTI mono or dual treatment prior to the modern combination ART era (in particular zidovudine and didanosine);
- treatment with the integrase inhibitors bictegravir, dolutegravir or raltegravir (but not elvitegravir and cabotegravir) and
- a prior AIDS diagnosis (*Appendix Table 6.5*).

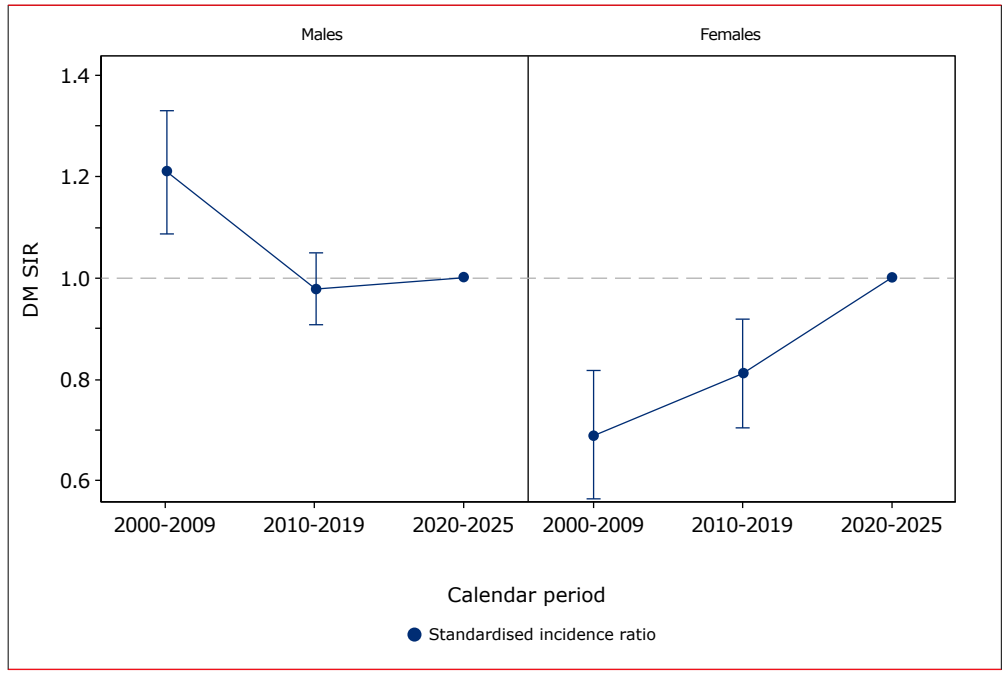
Moreover, the risk of new-onset diabetes in the periods 2000-2009 and 2010-2019 was significantly higher than in the period 2020-2025. Starting ART within 12 months of the last negative HIV test was also associated with a lower risk of new-onset diabetes. Note that multivariate analysis showed that the higher age-adjusted incidence rates of diabetes in women are largely explained by their higher BMI.

We compared the age- and sex-stratified prevalence of diabetes mellitus in the population of people with HIV with that observed in the general Dutch population in 2024, which was the last calendar year for which we have national data at the time of analysis (*Table 6.5 & Figure 6.5*). In men the prevalence of diabetes was significantly lower in nearly all age strata, while in women aged up to 65 year old the observed prevalence of diabetes was higher compared to the reference values in the general population.

Table 6.4: Crude incidence of diabetes mellitus per 1,000 person years of follow up in 2000-2009, 2010-2019 and 2020-2025 and age-standardised incidence ratio (indirect method) with 95% confidence intervals.

Calendar year	Male		Female	
	Incidence/1000PY (95%CI)	Standardized Inc. Ratio (95%CI)	Incidence/1000PY (95%CI)	Standardized Inc. Ratio (95%CI)
2000-2009	5.1 (4.6-5.7)	1.21 (1.09-1.33)	5.7 (4.7-6.8)	0.69 (0.56-0.82)
2010-2019	5.1 (4.7-5.4)	0.98 (0.91-1.05)	6.7 (5.8-7.6)	0.81 (0.70-0.92)
2020-2025	5.9 (5.4-6.4)	1 (reference)	8.4 (7.3-9.7)	1 (reference)

Figure 6.4: Age-standardised incidence ratio (indirect method) with 95% confidence intervals of diabetes mellitus per 1,000 person years of follow up in 2000-2009, 2010-2019 and 2020-2025.



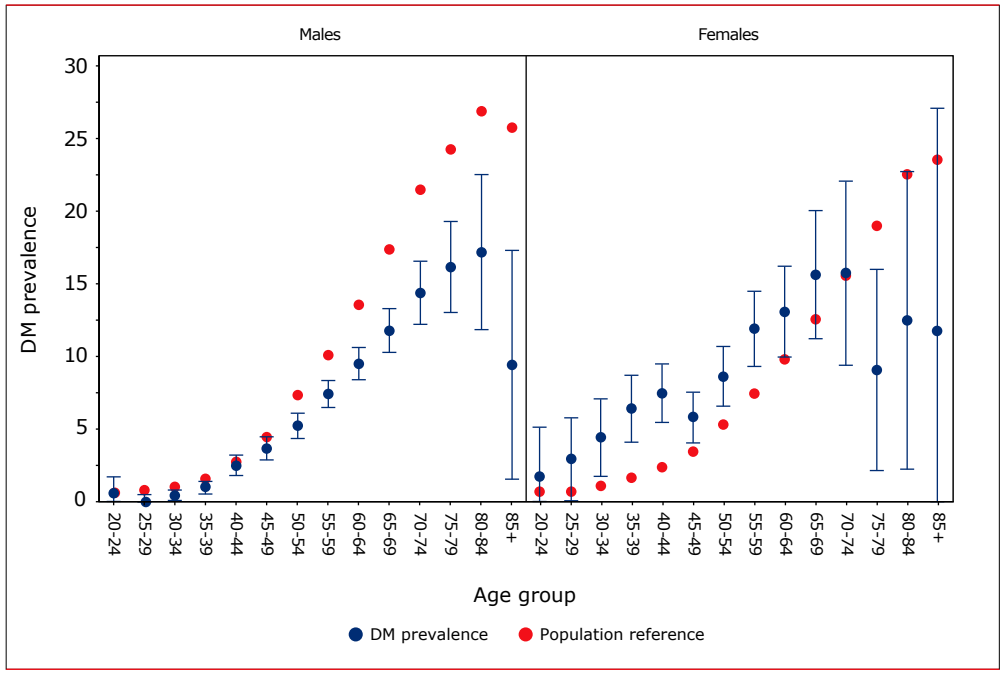
**Standardised according to the observed age distribution between 2020-2025.*

***Legend:** CI = confidence intervals; PY = person years.*

Table 6.5: Prevalence of diabetes mellitus in people with HIV stratified by age and sex in 2024, compared to the prevalence of diabetes mellitus type 2 in the general Dutch population in 2024 (https://www.vzinfo.nl/diabetes-mellitus/leeftijd-en-geslacht, accessed 17-9-2026).

Age group (years)	Males				Females			
	Events (n)	Group size (n)	Prevalence % (95%CI)	General population prevalence (%)	Events (n)	Group size (n)	Prevalence % (95%CI)	General population prevalence (%)
20-24	1	172	0.6 (0.0-1.7)	0.7	1	57	1.8 (0.0-5.2)	0.72
25-29	1	572	0.2 (0.0-0.5)	0.81	4	135	3.0 (0.1-5.8)	0.94
30-34	6	1,335	0.4 (0.1-0.8)	1.19	10	226	4.4 (1.7-7.1)	1.15
35-39	17	1,753	1.0 (0.5-1.4)	1.7	28	436	6.4 (4.1-8.7)	1.68
40-44	47	1,862	2.5 (1.8-3.2)	2.73	48	641	7.5 (5.5-9.5)	2.36
45-49	77	2,082	3.7 (2.9-4.5)	4.42	40	690	5.8 (4.1-7.5)	3.47
50-54	128	2,441	5.2 (4.4-6.1)	7.37	62	718	8.6 (6.6-10.7)	5.31
55-59	219	2,952	7.4 (6.5-8.4)	10.11	71	596	11.9 (9.3-14.5)	7.45
60-64	252	2,645	9.5 (8.4-10.6)	13.56	58	443	13.1 (10.0-16.2)	9.8
65-69	201	1,706	11.8 (10.3-13.3)	17.37	41	262	15.6 (11.2-20.0)	12.58
70-74	143	994	14.4 (12.2-16.6)	21.46	20	127	15.7 (9.4-22.1)	15.56
75-79	86	532	16.2 (13.0-19.3)	24.26	6	66	9.1 (2.2-16.0)	19
80-84	33	192	17.2 (11.9-22.5)	26.89	5	40	12.5 (2.3-22.7)	22.54
85+	5	53	9.4 (1.6-17.3)	25.77	2	17	11.8 (0.0-27.1)	23.53

Figure 6.5: Prevalence of diabetes mellitus in people with HIV stratified by age and sex in 2024, compared to the prevalence of diabetes mellitus type 2 in the general Dutch population in 2024 (https://www.vzinfo.nl/diabetes-mellitus/leeftijd-en-geslacht, accessed 17-9-2026).



Cardiovascular disease

- From January 2000 onwards, 2,321 individuals (2,055 men and 266 women) experienced one or more fatal or non-fatal cardiovascular event. Of these individuals:
- 1,115 had a myocardial infarction;
- 880 had a stroke;
- 173 had a coronary artery bypass graft;
- 875 had a coronary angioplasty or stenting; and
- 25 had a carotid endarterectomy.

The crude incidence over time remained stable and was lower in women than in men (*Figure 6.3B*). The age-standardised incidence ratio in men and women declined over time (*Table 6.6 & Figure 6.6*).

In the analysis of risk factors, those associated with cardiovascular disease were:

- older age group;
- male gender, MSM had lower risk than other men;
- a latest CD4 cell count below 350 cells/mm^3
- a prior AIDS diagnosis; as well as having a longer duration of severe immunodeficiency defined as cumulative number of years with a CD4 count <200 cells/mm^3;
- treatment with NRTI mono or dual treatment prior to the modern combination ART era;
- use of abacavir (either currently or in the last six months);
- current use of dolutegravir, raltegravir or bictegravir (borderline significant) (but not elvitegravir or cabotegravir);
- current and past smoking;
- the presence of diabetes mellitus; and
- the presence of hypertension.

Estimated cardiovascular risk using the D:A:D algorithm was also higher during 2000-2009 and 2010-2019 than during 2020-2025, independent of other variables included in the analysis (*Appendix Table 6.5*). The strong positive association between use of abacavir and CVD was independent of renal function. When eGFR, estimated using the Cockcroft-Gault method (available from 2007 onwards), was included in the model the abacavir effect was only slightly attenuated, decreasing from an incidence risk ratio (IRR) of 1.52 to 1.45, p<0.001.

From January 2000 onwards, 325 men and 35 women experienced a fatal or non-fatal secondary cardiovascular event: 191 had a myocardial infarction, 179 had a stroke (note that 10 persons experienced both a secondary MI and a secondary stroke). The crude incidence per 1,000 PYFU over the whole period between 2000 and 2025 in men and women with a prior cardiovascular event was 25.1 (22.4-28.0) and 21.0 (14.6-29.2), respectively. The crude rate and age-standardised incidence ratio (SIR; indirect method) of secondary myocardial infarction and stroke per 1,000 PYFU decreased significantly over time in men while it increased in women (*Table 6.7 & Figure 6.7*).

We compared the age- and sex-stratified prevalence of coronary artery disease (which includes myocardial infarction, angina pectoris) in the population of people with HIV with that observed in the general Dutch population (*Table 6.8 & Figure 6.8*). In men and women the prevalence of coronary artery disease was fairly equal in all age strata compared to the reference values in the general population.

Table 6.6 & Figure 6.6: *Crude incidence of primary cardiovascular disease per 1,000 person years of follow up in 2000-2009, 2010-2019, and 2020-2025 and age-standardised incidence ratio with 95% confidence intervals.*

Calendar year	Male		Female	
	Incidence/1000PY (95%CI)	Standardized Inc. Ratio (95%CI)	Incidence/1,000PY (95%CI)	Standardized Inc. Ratio (95%CI)
2000-2009	6.2 (5.7-6.8)	1.65 (1.50-1.80)	2.6 (1.9-3.4)	1.42 (1.03-1.81)
2010-2019	6.3 (5.9-6.8)	1.20 (1.12-1.28)	3.5 (2.9-4.2)	1.19 (0.97-1.40)
2020-2025	6.8 (6.3-7.3)	1 (reference)	4.1 (3.3-4.9)	1 (reference)

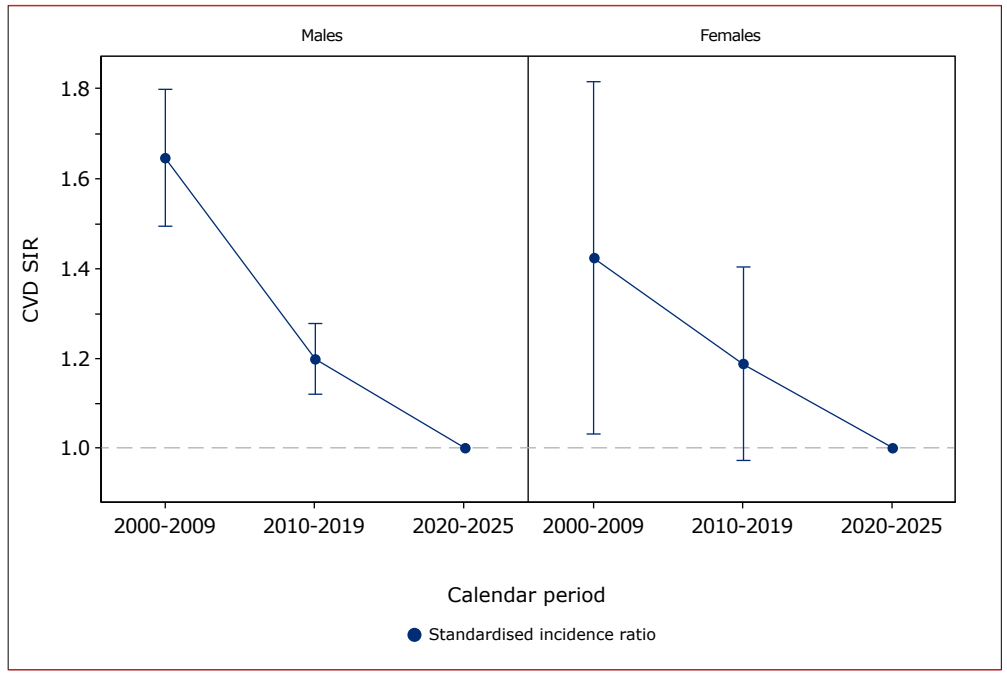
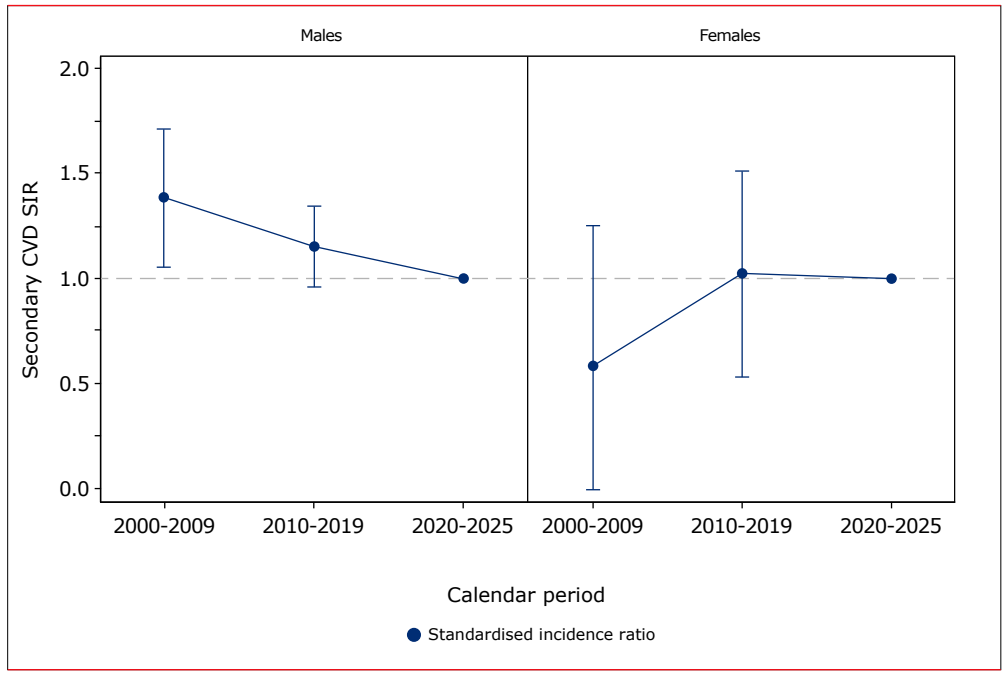


Table 6.7 & Figure 6.7: *Crude incidence of secondary cardiovascular disease per 1,000 person years of follow up in 2000-2009, 2010-2019, and 2020-2025 and age-standardised incidence ratio with 95% confidence intervals.*

Calendar year	Male		Female	
	Incidence/1,000PY (95%CI)	Standardized Inc. Ratio (95%CI)	Incidence/1,000PY (95%CI)	Standardized Inc. Ratio (95%CI)
2000-2009	30.9 (24.0-39.0)	1.38 (1.06-1.71)	14.1 (2.9-41.2)	0.59 (0.00-1.25)
2010-2019	25.7 (21.6-30.3)	1.15 (0.96-1.34)	22.8 (13.3-36.6)	1.02 (0.54-1.51)
2020-2025	22.0 (18.2-26.4)	1 (reference)	21.1 (11.8-34.9)	1 (reference)



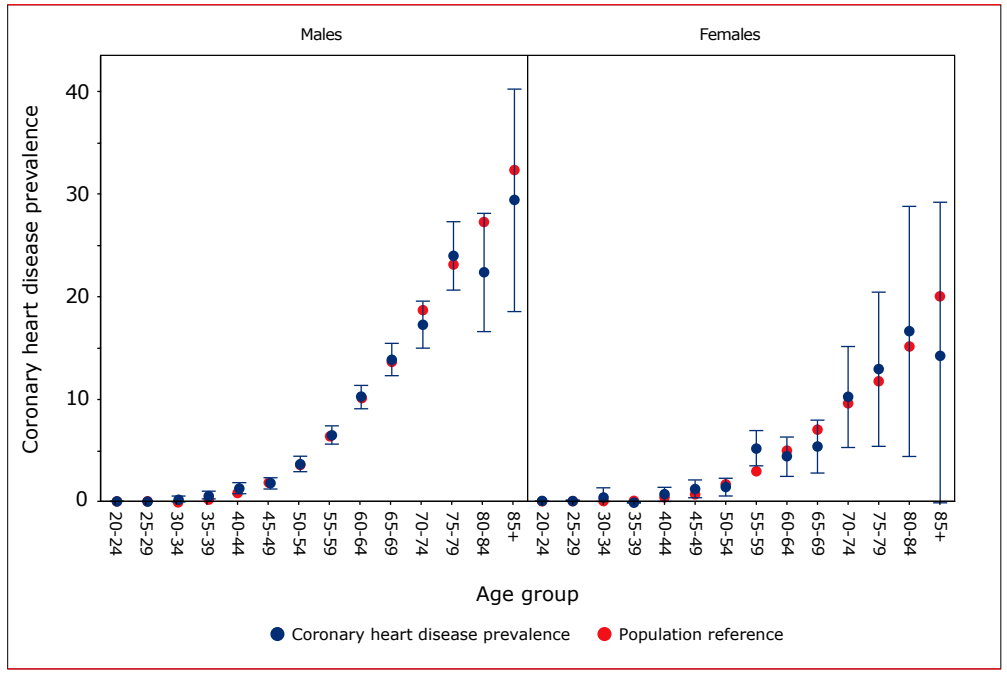
**Standardised according to the observed age distribution in 2020-2025.*

Legend: *CI = confidence intervals; PY = person years.*

Table 6.8 & Figure 6.8 : *Prevalence of coronary artery disease in people with HIV stratified by age and sex in 2025, compared to the prevalence observed in the general Dutch population in 2025 (https://www.staatvenz.nl/kerncijfers/coronaire-hartziekten-aantal-patiënten-bekend-bij-de-huisarts, accessed 17-9-2026).*

Age group (years)	Males				Females			
	Events (n)	Group size (n)	Prevalence % (95%CI)	General population prevalence (%)	Events (n)	Group size (n)	Prevalence % (95%CI)	General population prevalence (%)
20-24	0	150	0.0 (0.0-0.0)	0.03	0	62	0.0 (0.0-0.0)	0.04
25-29	0	583	0.0 (0.0-0.0)	0.05	0	134	0.0 (0.0-0.0)	0.04
30-34	4	1,257	0.3 (0.0-0.6)	0.13	1	213	0.5 (0.0-1.4)	0.07
35-39	12	1,735	0.7 (0.3-1.1)	0.26	0	390	0.0 (0.0-0.0)	0.14
40-44	25	1,805	1.4 (0.8-1.9)	0.79	5	637	0.8 (0.1-1.5)	0.37
45-49	39	2,085	1.9 (1.3-2.5)	1.7	9	673	1.3 (0.5-2.2)	0.85
50-54	86	2,303	3.7 (3.0-4.5)	3.6	11	736	1.5 (0.6-2.4)	1.74
55-59	191	2,907	6.6 (5.7-7.5)	6.45	33	627	5.3 (3.5-7.0)	2.99
60-64	284	2,765	10.3 (9.1-11.4)	10.15	20	449	4.5 (2.5-6.4)	4.92
65-69	257	1,846	13.9 (12.3-15.5)	13.75	16	294	5.4 (2.8-8.0)	7.11
70-74	175	1,011	17.3 (15.0-19.6)	18.64	15	146	10.3 (5.3-15.2)	9.65
75-79	151	629	24.0 (20.7-27.3)	23.26	10	77	13.0 (5.5-20.5)	11.81
80-84	45	201	22.4 (16.6-28.2)	27.31	6	36	16.7 (4.5-28.8)	15.14
85+	20	68	29.4 (18.6-40.2)	32.33	3	21	14.3 (0.0-29.3)	20.04

Legend: *CI = confidence intervals.*



Trends in cardiovascular risk factors

Figures 6.9A and *6.9B* show that the distribution of body mass index (BMI) of both men and women in the HIV-1-positive population has increased over time. In 2025, the proportion of men with available BMI data who were overweight (25-30 kg/m^2) or obese (WHO class I: 30-35 kg/m^2 and WHO class II/III: 35 kg/m^2 or over), was 37.9%, 10.4% and 2.9%, respectively. In women, these proportions were 31.3%, 20.5% and 13.5%, respectively.

Using mixed-effects modelling, we investigated whether the increase in BMI over time could be ascribed to changes in the demographic characteristics and ageing of the population with HIV. This analysis revealed that the increase was at least partially driven by changes over time in population demographic characteristics (age, non-Western region of origin, HIV transmission category) and time since first initiating ART, and that this effect was more marked in men than in women. With regard to specific antiretroviral drugs, the use of bictegravir, dolutegravir, rilpivirine and tenofovir alafenamide were all independently associated with higher body weight.

Figure 6.9A-B: *Distribution of the body mass index (BMI) at the end of each calendar year in (A) men, and (B) women, as a percentage of the total number of men and women with a known BMI in each year. For each individual, the last available weight measurement in each year was selected. The numbers at the top of each bar represent the number of individuals contributing data during that calendar year.*

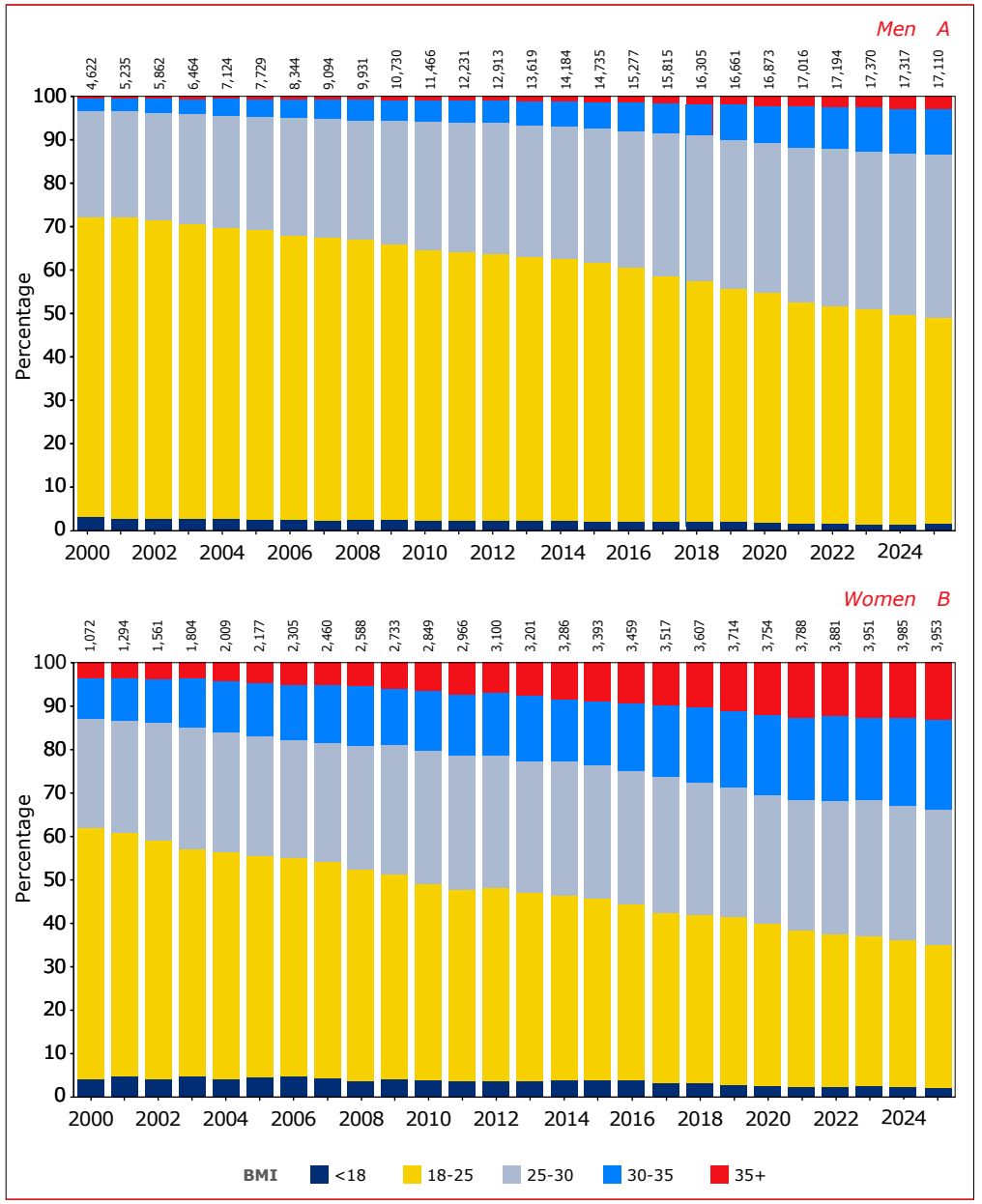


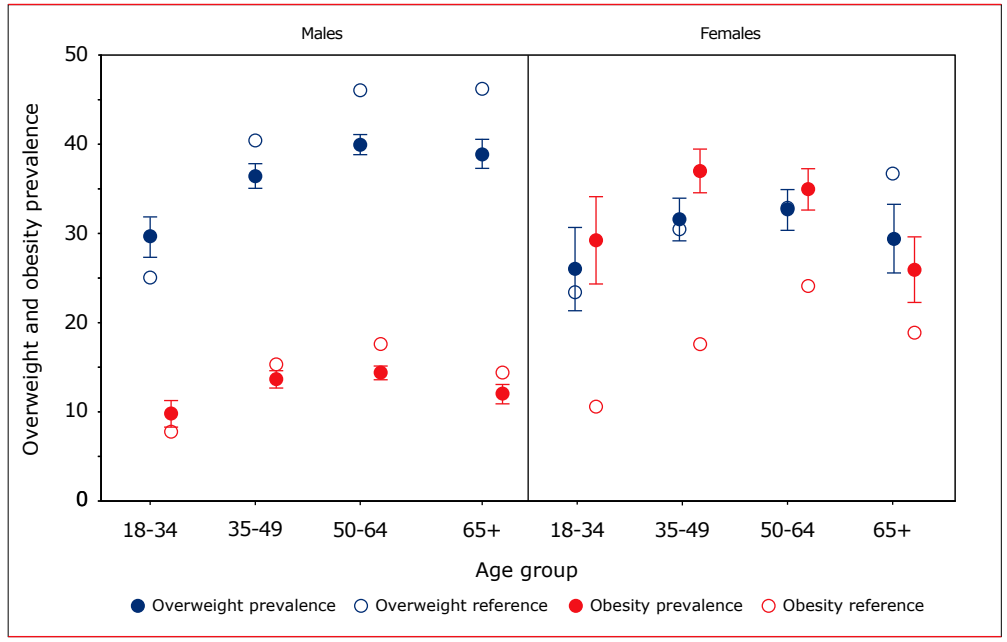
Table 6.9 and *Figure 6.10* shows a comparison with the general Dutch population of the age- and sex-stratified prevalence of overweight and obesity in 2025. Males aged 35 and older were significantly less often overweight or obese than the general Dutch male population, while women in all age strata were more likely to be obese. Whereas in adult men of all age groups, the proportion classified as obese (14.0%) was similar to the proportion found in the general Dutch male population (13.7%), in women of all age groups there was more obesity (34.0%) than in the general Dutch female population (17.7%)[47].

There were substantial differences between those of Dutch origin, Western migrants and non-Western migrants: among males, 12.0% of Dutch men, 14.0% of Western migrants and 16.2% of non-Western migrants were obese. In females, however, those figures were 23.8%, 24.1%, and 40.8%, respectively. Being overweight (a BMI between 25-30) or being obese (a BMI over 30) were both independently associated with an increased risk of diabetes (overweight IRR 2.13, 95%CI 1.90-2.38, p<0.001; obese IRR 5.04, 95%CI 4.44-5.72, p<0.001), as well as with CKD (overweight IRR 1.18, 95%CI 1.09-1.28, p<0.001; obese IRR 1.13, 95%CI 1.01-1.28, p=0.036) (*Appendix Table 6.5*). Overweight and obesity were not associated with an increased risk of CVD and non-AIDS malignancies.

Table 6.9: *Age- and sex-stratified prevalence of overweight and obesity in 2025, compared to the general Dutch population in 2025 (source: https://www.vzinfo.nl/overgewicht/volwassenen, accessed 17-9-2026).*

Age group (years)	Group size (n)	Over-weight (n)	Overweight prevalence % (95%CI)	General population overweight prevalence (%)	Obesity (n)	Obesity prevalence % (95%CI)	General population obesity prevalence (%)
Males							
18-34	1,510	448	29.7 (27.4-32.0)	25.1	149	9.9 (8.4-11.4)	7.8
35-49	4,793	1,749	36.5 (35.1-37.9)	40.5	657	13.7 (12.7-14.7)	15.4
50-64	7,317	2,931	40.1 (38.9-41.2)	46.1	1,055	14.4 (13.6-15.2)	17.7
65+	3,490	1,361	39.0 (37.4-40.6)	46.3	422	12.1 (11.0-13.2)	14.5
Females							
18-34	338	88	26.0 (21.4-30.7)	23.4	99	29.3 (24.4-34.1)	10.6
35-49	1,431	452	31.6 (29.2-34.0)	30.5	530	37.0 (34.5-39.5)	17.6
50-64	1,641	536	32.7 (30.4-34.9)	32.9	574	35.0 (32.7-37.3)	24.1
65+	543	160	29.5 (25.6-33.3)	36.7	141	26.0 (22.3-29.7)	18.9

Figure 6.10: *Distribution of the body mass index (BMI) over the age groups for men, and women, in 2025, compared to the general Dutch population in 2025.*



Legend: *BMI = body mass index.*

Chapter 12 on Quality of Care contains more information on the prevalence and treatment of hypertension; the proportion of treated hypertensive individuals attaining treatment goals; the proportion of individuals with a SCORE2 or SCORE2-OP predicted 10-year risk greater than 10%, without a history of CVD, that received a prescription for statins; the proportion of high-risk individuals receiving statins who attained treatment goals.

Chronic kidney disease

Glomerular filtration rate (GFR) is a marker of renal function and is commonly estimated by one of three formulae, namely the Cockcroft-Gault, the Modification of Diet in Renal Disease (MDRD), or the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations[48]. As all three equations used to estimate GFR (eGFR) are based on serum creatinine, they may be markedly affected by rapid changes in muscle mass, as is seen in some individuals with advanced HIV disease who commence ART. Of these equations, both the Cockcroft-Gault and the CKD-EPI equations have been validated in individuals with HIV[48, 49]. However, because the CKD-EPI equation is the one most often used in clinical practice, we have chosen to report eGFR values as estimated by this equation. The distribution of eGFR categories in ml/min/1.73m^2 (90 or above, normal kidney function; 60-89, mildly reduced; 30-59, moderately reduced; 15-29, severely reduced; and below 15, very severely reduced kidney function) is shown in *Figures 6.11A* and *6.11B* for men and women. The percentage of men with normal kidney function decreased over time from 74.5% in 2007, to 39.0% in 2025, and this pattern was similar in women. Typically, eGFR decreases with increased age, as shown in *Figure 6.12*, and therefore the decrease in the proportion of individuals with normal function over time is likely due, in part, to the increasing age of individuals in care.

CKD incidence and risk factors

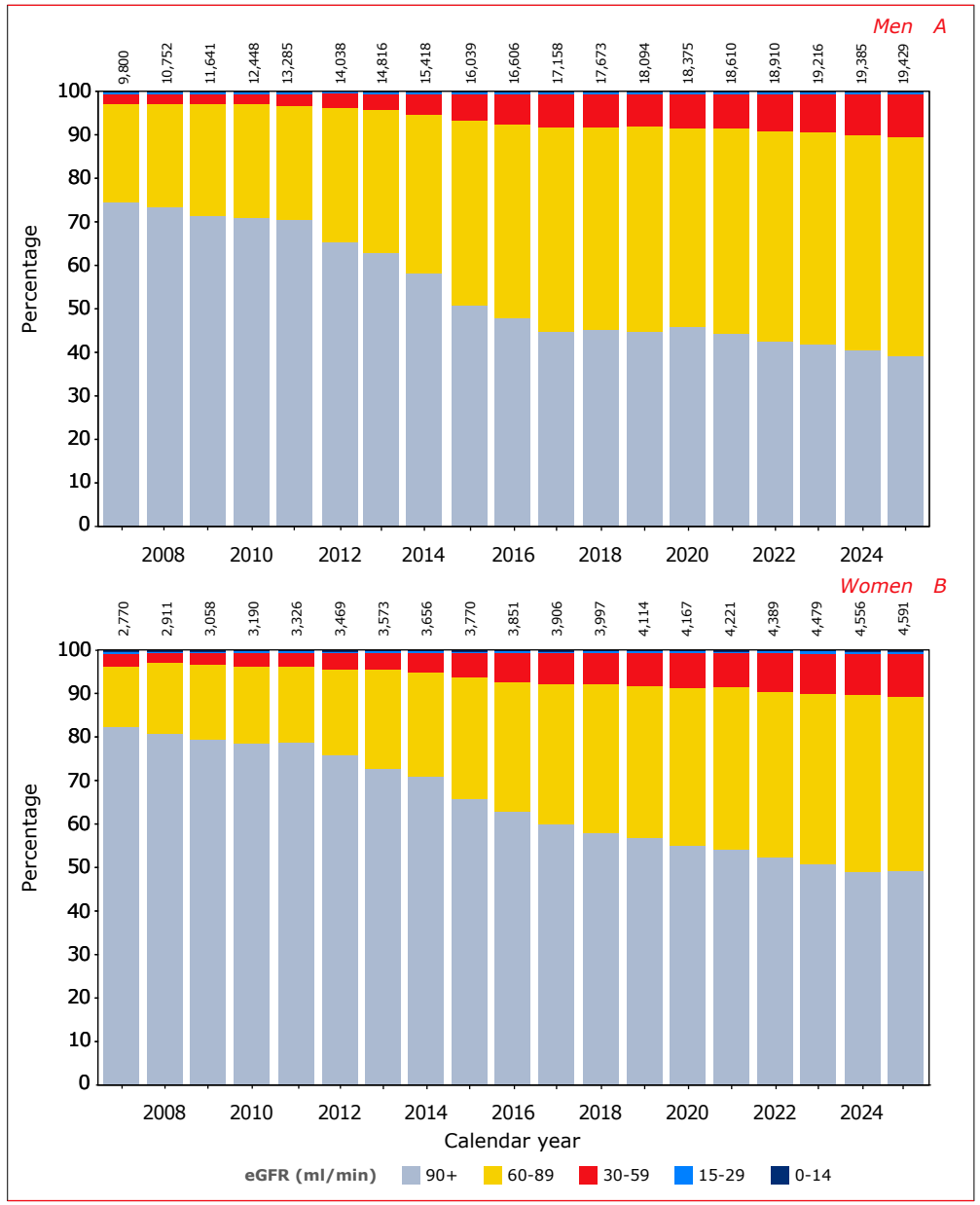
In individuals with an eGFR above 60ml/min/1.73m^2 at the time of inclusion in the analyses, who did not have a previously confirmed CKD, the crude incidence of CKD (defined as eGFR below 60ml/min/1.73m^2 confirmed by a second test at least 26 weeks later) varied over time (*Figure 6.3C*). Routine collection of serum creatinine measurements commenced in 2007. To avoid misclassifying prevalent CKD as incident CKD, we used serum creatinine levels measured in 2007 to distinguish between prevalent (i.e. CKD already present in 2007) versus new-onset incident cases of CKD (i.e. no CKD observed in 2007) from 2008 onwards. In men, the incidence rose from 9.9 cases per 1,000 PYFU in the period 2008-19 to 10.4 in 2020-2025. In women, the incidence rose from 10.4 to 10.8 cases per 1,000 PYFU during the same periods (*Table 6.10*). However, the age-standardised incidence ratio in both men and women was significantly lower in the 2020-2025 period (*Table 6.10*).

Risk factors for CKD included:

- female gender;
- Dutch origin;
- low current CD4 cell count (below 350 cells/mm^3);
- a prior AIDS diagnosis;
- belonging to the HIV transmission risk group of people who inject drugs;
- older age group;
- being underweight or overweight / obese;
- hypertension;
- diabetes mellitus;
- cardiovascular disease;
- treatment with NRTI mono or dual treatment prior to the modern combination ART era; and
- chronic HBV and HCV co-infection (*Appendix Table 6.5*).

When current use of cobicistat, rilpivirine, dolutegravir, and bictegravir were added to the model, the increased risk of CKD over calendar time completely disappeared (even reversed). This strongly suggests that the increase in CKD seen in recent years is largely due to increases in serum creatinine caused by ARV-induced reversible inhibition of two transporters that mediate tubular secretion of creatinine, without affecting the true glomerular filtration rate (namely, organic cation transporter 2 [OCT2], and multidrug and toxin extrusion transporter [MATE1]) and is therefore not a true increase in CKD.

Figure 6.11A–B: *Distribution of categories of estimated glomerular filtration rate (eGFR) at the end of each calendar year in (A) men, and (B) women. For each individual, the last available measurement in each year was selected. The numbers at the top of each bar represent the number of individuals contributing data during that calendar year.*



Legend: *eGFR = estimated glomerular filtration rate; eGFR 90+ ml/min/1.73m^2: normal kidney function; 60–89 ml/min/1.73m^2: mildly reduced; 30–59 ml/min/1.73m^2: moderately reduced; 15–29 ml/min/1.73m^2: severely reduced; 0–15 ml/min/1.73m^2 very severely reduced kidney function.*

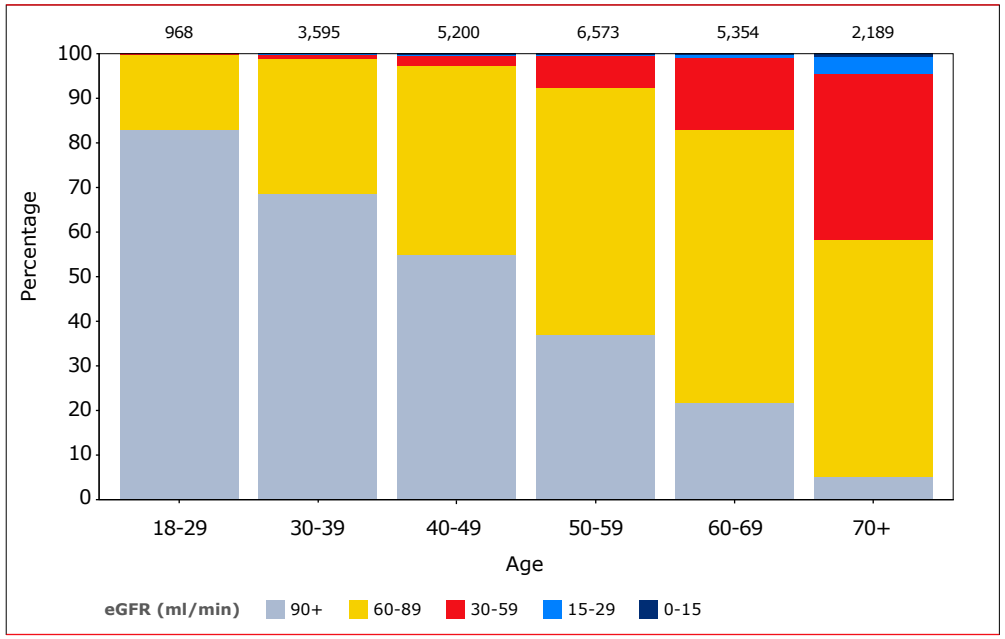
Table 6.10: Crude chronic kidney disease incidence per 1,000 person years of follow up in 2008–2019, and 2020–2025, and age-standardised incidence ratio with 95% confidence intervals.

Calendar year	Male		Female	
	Incidence/1,000PY (95%CI)	Standardized Inc. Ratio (95%CI)	Incidence/1,000PY (95%CI)	Standardized Inc. Ratio (95%CI)
2008–2019	9.9 (9.3–10.5)	1.28 (1.20–1.36)	10.4 (9.0–11.9)	1.38 (1.19–1.57)
2020–2025	10.4 (9.7–11.2)	1 (reference)	10.8 (9.2–12.6)	1 (reference)

**Standardised according to the observed age distribution in 2020–2025.*

***Legend:** CI = confidence interval; PYFU = person years.*

Figure 6.12: Distribution of categories of estimated glomerular filtration rate (eGFR) in 2025 for different age categories. For each individual, the last available measurement in 2025 was selected. The numbers at the top of each bar represent the number of individuals contributing data to that age category.



***Legend:** eGFR = estimated glomerular filtration rate; eGFR 90+ ml/min/1.73m²: normal kidney function; 60–89 ml/min/1.73m²: mildly reduced; 30–59 ml/min/1.73m²: moderately reduced; 15–29 ml/min/1.73m²: severely reduced; 0–15 ml/min/1.73m² very severely reduced kidney function.*

Non-AIDS-defining malignancies

Between 2000 and 2025, 2,874 diagnoses of non-AIDS-defining malignancies (NADM) in 2,626 unique individuals were recorded in SHM's database. An additional 1,128 patients were diagnosed with one or more non-melanoma skin cancers, but these were not included in the present analysis. *Table 6.11* shows the most common types of non-AIDS-defining cancer. *Figure 6.13A* shows the changes in types of non-AIDS-defining cancers over time. The proportion of individuals with intestinal, prostate, and renal cancer has increased over time, likely reflecting the increasing age of the study population. This is further illustrated in *Figure 6.13B*, which shows the distribution of non-AIDS-defining malignancies with increasing age at cancer diagnosis.

Risk factors for non-AIDS-defining malignancies

The crude incidence over time of NADM in men and women is shown in *Figure 6.3D*. The age-standardised incidence in men statistically significantly decreased over time (*Table 6.12* & *Figure 6.14*). This lower age-standardised incidence in men may be due to a reduction over time in risk factors such as smoking, and a higher proportion of individuals living with high CD4 cell counts. The temporal trend for women was similar – the age-standardised incidence decreased (although not significantly) over time.

Demographic and clinical factors independently associated with an increased risk of a first non-AIDS-defining malignancy were (*Appendix Table 6.5*):

- older age group;
- people born in the Netherlands, and migrants from Western countries;
- low body mass index;
- lower current CD4 cell count (CD4 below 350 cells/mm^3);
- prior AIDS;
- chronic HBV co-infection; and
- current or past smoking.

In the period from 1 January 2000 to 31 December 2025, the overall five-year survival rate following the most common non-AIDS-defining malignancies are shown in *Table 6.11* and *Figure 6.15*. *Table 6.11* also shows the distribution and crude 5-year survival rates of the subgroup of NADM diagnosed in the last 10 years of follow-up. For nearly all NADM we observed no clinically significant change in the crude 5-year survival rates (but with slightly improved survival for lung cancer and malignant melanoma).

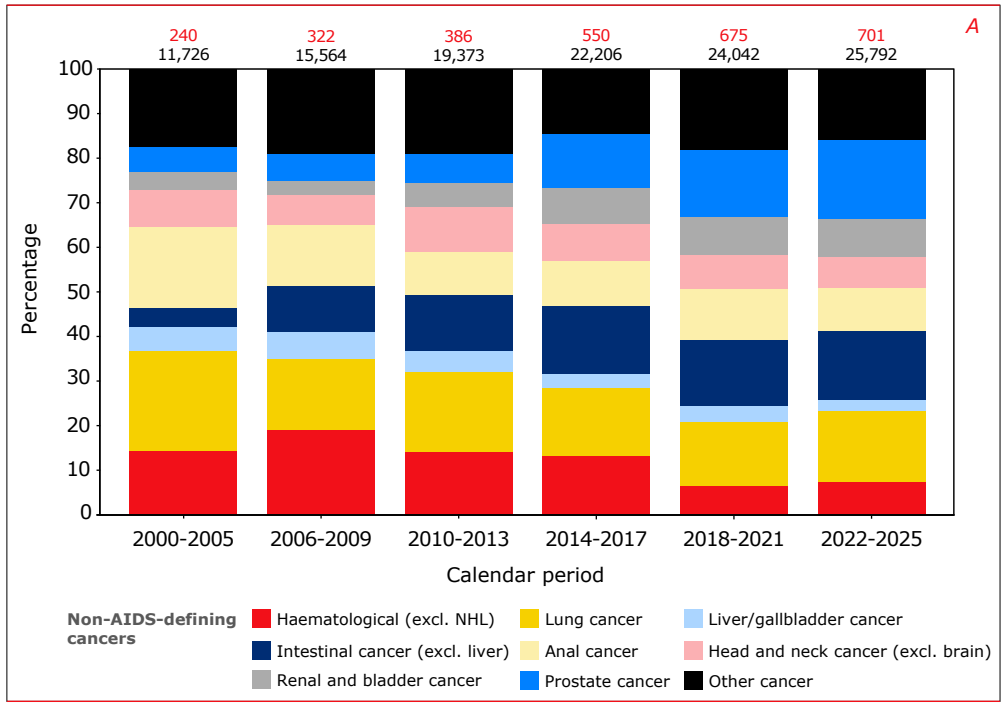
We calculated the age- and sex-stratified incidence of non-AIDS-defining malignancy (including non-melanoma skin cancer) per 1,000 person years of follow up in the 10-year period 2016-2025, and compared with the incidence in the general Dutch population in 2025 (*Table 6.13* & *Figure 6.16*). The incidence of NADM in all age groups (with at least 15 events) in men was significantly higher than the observed cancer incidence in the general Dutch male population. The relatively low cumulative follow-up time and number of events per age group in women limits the statistical power of the analysis. However, the observed incidence in each age group appears to be rather similar to the observed cancer incidence in the general Dutch female population.

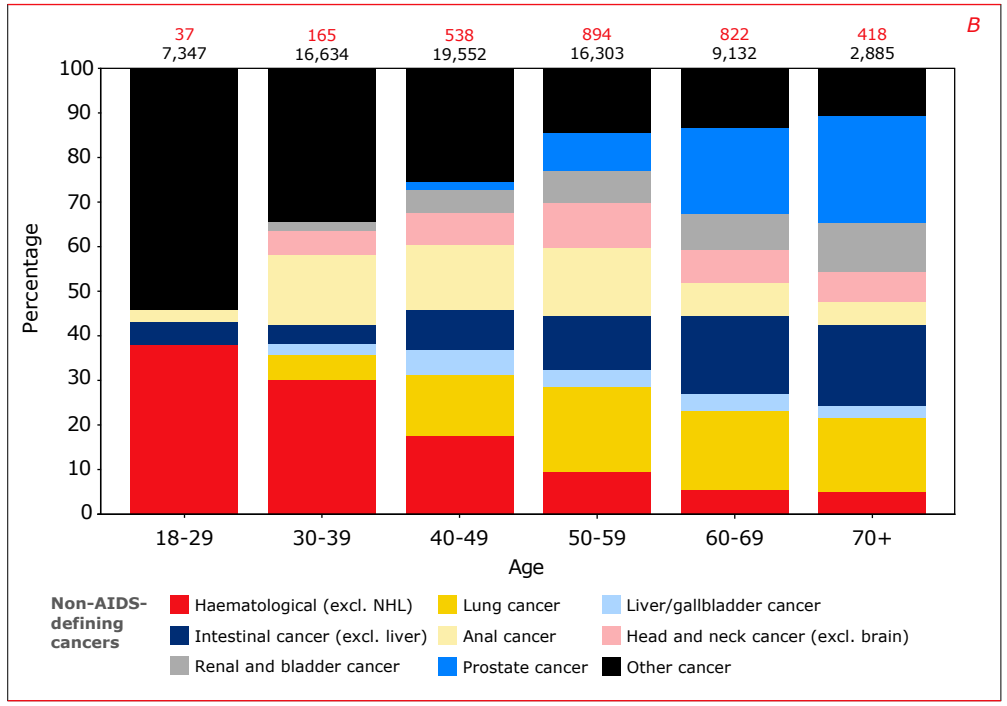
Table 6.11: *Most common non-AIDS-defining malignancies diagnosed in 2000-2025, and a subgroup diagnosed in the last 10 year between 2016-2025, excluding non-melanoma skin cancer and pre-malignant lesions found by cervical and anal screening.*

	2000-2025			2016-2025		
Non-AIDS malignancy	**# of malignancies**	**%**	**Five-year survival (%)**	**# of malignancies**	**%**	**Five-year survival (%)**
Lung cancer	466	16.2	17.2	257	15.3	22.1
Intestinal cancer (excl. liver)	385	13.4	34.3	254	15.1	33.1
Prostate cancer	350	12.2	76.0	263	15.7	74.5
Anal cancer	325	11.3	67.3	171	10.2	70.4
Hematological (excl. NHL)	313	10.9	64.8	133	7.9	61.7
Head and neck cancer (excl. brain)	228	7.9	54.5	128	7.6	52.8
Renal and bladder cancer	205	7.1	62.0	146	8.7	58.7
Other cancers	138	4.8	42.3	68	4.0	38.0
Malignant melanoma	134	4.7	79.8	83	4.9	87.0
Liver/gallbladder cancer	111	3.9	12.9	51	3.0	14.4
Breast cancer	83	2.9	79.2	47	2.8	63.1
Testicular cancer	53	1.8	89.5	26	1.5	91.1
CNS cancer	43	1.5	48.7	36	2.1	37.8
Gynecological cancer (excl. cervical)	40	1.4	71.9	17	1.0	73.3

Legend: *CNS = central nervous system; excl. = excluding; NHL = non-Hodgkin's lymphoma.*

Figure 6.13A-B: *Relative changes in non-AIDS-defining malignancies (A) between 2000 and 2025 and (B) with increasing age, in PWH in the Netherlands. The numbers at the top of each bar represent the number of non-AIDS-defining cancer diagnoses (top number) and the total number of individuals in care during that calendar period (bottom number).*

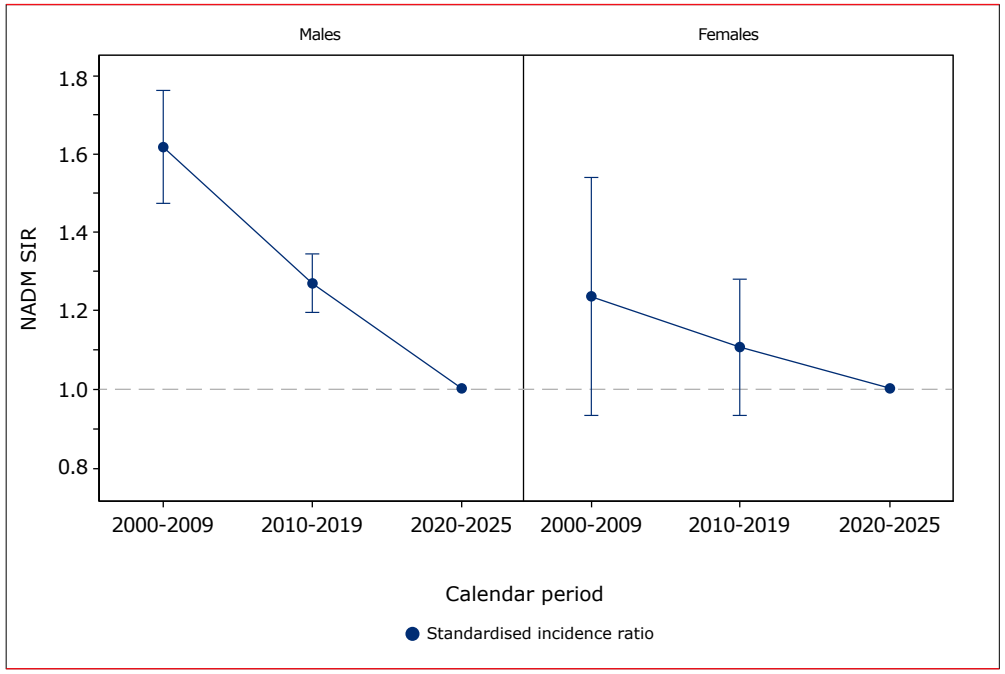




Legend: *excl. NHL = excluding non-Hodgkin's lymphoma.*

Table 6.12 & Figure 6.14: *Crude non-AIDS-defining malignancy incidence per 1,000 person years of follow up in 2000-2009, 2010-2019, and 2020-2025, and age-standardised incidence ratio with 95% confidence intervals.*

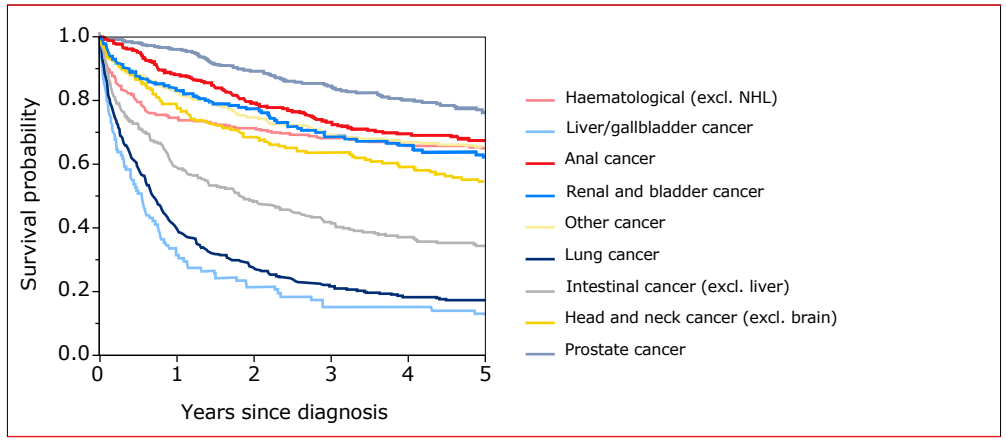
Calendar year	Male		Female	
	Incidence/1,000PY (95%CI)	Standardized Inc. Ratio (95%CI)	Incidence/1,000PY (95%CI)	Standardized Inc. Ratio (95%CI)
2000-2009	6.4 (5.9-7.0)	1.62 (1.47-1.76)	3.1 (2.4-4.0)	1.24 (0.93-1.54)
2010-2019	7.5 (7.1-8.0)	1.27 (1.20-1.34)	4.4 (3.8-5.2)	1.11 (0.93-1.28)
2020-2025	8.1 (7.5-8.6)	1 (reference)	5.5 (4.6-6.5)	1 (reference)



**Standardised according to the observed age distribution in 2020-2025.*

Legend: *CI = confidence intervals; PY = person years.*

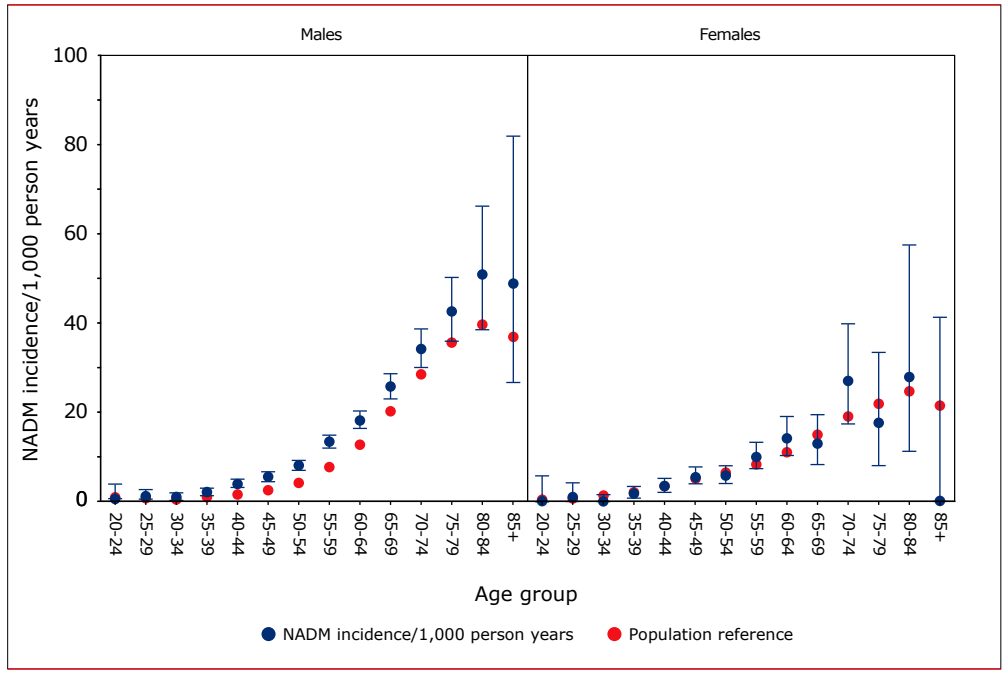
Figure 6.15: *Estimated five-year survival following the diagnosis of the most common non-AIDS-defining malignancies diagnosed between 1 January 2000 and 31 December 2025.*



Legend: *KM = Kaplan-Meier; excl. NHL = excluding non-Hodgkin's lymphoma.*

Table 6.13 & Figure 6.16: Age- and sex-stratified incidence of non-AIDS-defining malignancy (including non-melanoma skin cancer) per 1,000 person years of follow up in 2016-2025, compared to the incidence in the general Dutch population in 2025 (https://www.vzinfo.nl/kanker/leeftijd-en-geslacht, accessed 18-9-2026).

Age categories	Males				Females			
	Person-years of follow-up	Number of NADM	Incidence/ 1,000PY (95%CI)	Incidence general population	Person-years of follow-up	Number of NADM	Incidence/ 1,000PY (95%CI)	Incidence general population
20-24	1,861	2	1.1 (0.1-3.9)	0.37	643	0	0.0 (0.0-5.7)	0.36
25-29	6,705	9	1.3 (0.6-2.5)	0.6	1,334	1	0.7 (0.0-4.2)	0.7
30-34	12,472	14	1.1 (0.6-1.9)	0.87	2,807	0	0.0 (0.0-1.3)	1.38
35-39	15,515	33	2.1 (1.5-3.0)	1.15	4,744	8	1.7 (0.7-3.3)	2.24
40-44	18,202	73	4.0 (3.1-5.0)	1.58	6,021	20	3.3 (2.0-5.1)	3.37
45-49	22,098	121	5.5 (4.5-6.5)	2.5	6,553	36	5.5 (3.8-7.6)	5.06
50-54	27,067	217	8.0 (7.0-9.2)	4.33	6,119	35	5.7 (4.0-8.0)	6.54
55-59	26,901	360	13.4 (12.0-14.8)	7.87	4,724	47	9.9 (7.3-13.2)	8.34
60-64	19,975	364	18.2 (16.4-20.2)	12.71	3,112	44	14.1 (10.3-19.0)	10.98
65-69	12,493	321	25.7 (23.0-28.7)	20.25	1,768	23	13.0 (8.2-19.5)	14.85
70-74	7,237	247	34.1 (30.0-38.7)	28.49	927	25	27.0 (17.5-39.8)	19.08
75-79	3,379	144	42.6 (35.9-50.2)	35.63	512	9	17.6 (8.0-33.4)	21.9
80-84	1,100	56	50.9 (38.5-66.1)	39.64	251	7	27.9 (11.2-57.5)	24.7
85+	287	14	48.8 (26.7-81.9)	36.81	89	0	0.0 (0.0-41.3)	21.45



Multimorbidity

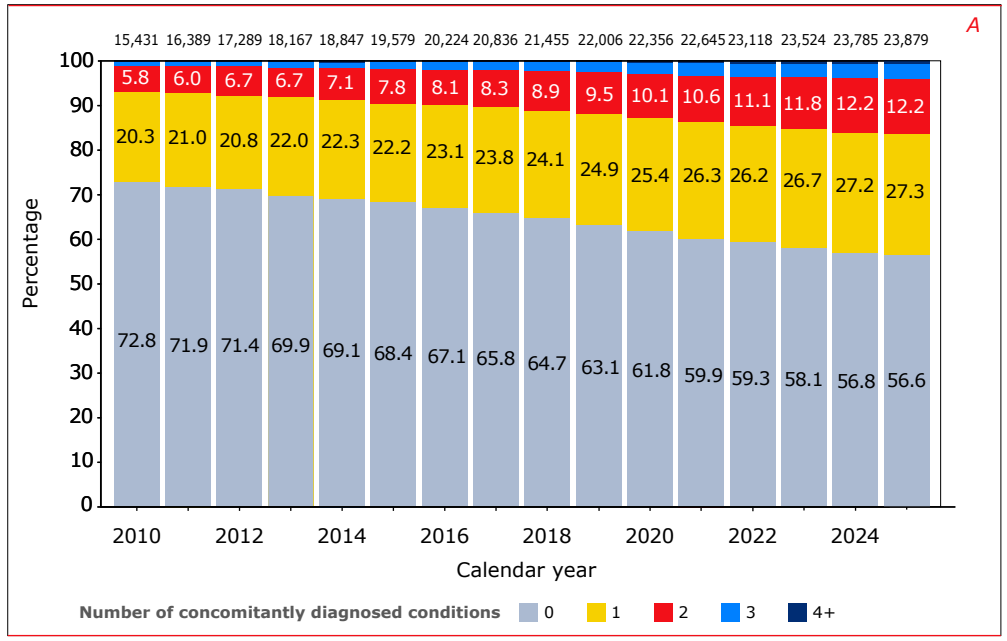
We investigated changes over time in the prevalence of non-AIDS multimorbidity. HIV infections and AIDS diagnoses did not contribute to the multimorbidity count. The following comorbidities and conditions were taken into account:

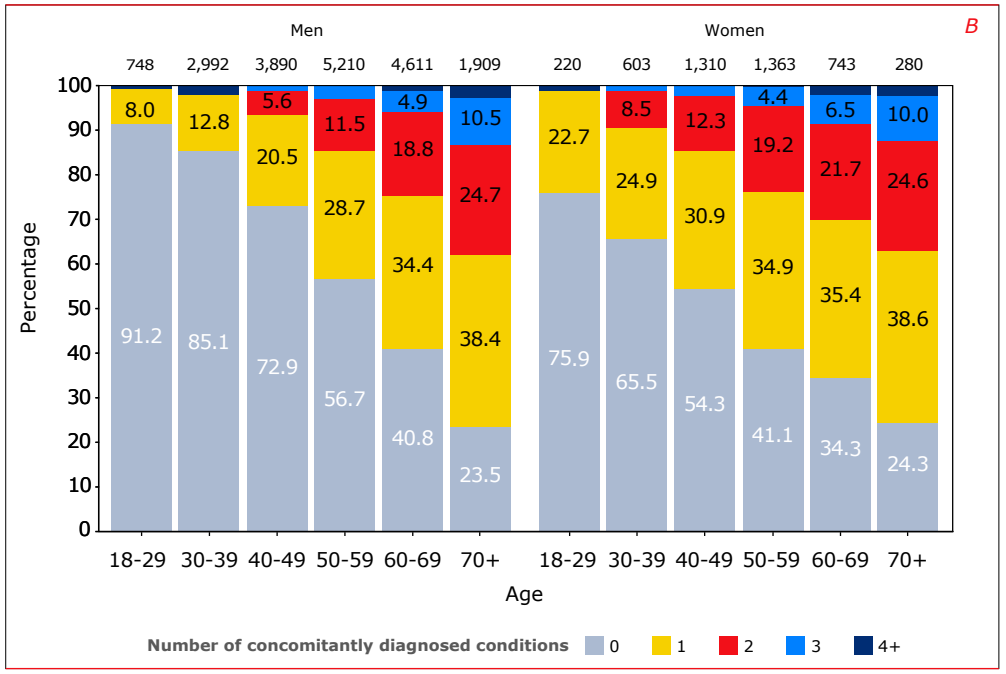
1. **Cardiovascular disease** (either myocardial infarction, coronary artery bypass grafting, coronary angioplasty or stenting, and carotid endarterectomy)
2. **Stroke**
3. **Non-AIDS-defining malignancies**, excluding non-melanoma skin cancers and pre-malignant lesions found at cervical/anal screening
4. **Chronic kidney disease** (eGFR below 30 ml/min/1.73 m^2)
5. **Diabetes mellitus** (according to D:A:D diagnostic criteria)
6. **Hypertension**, defined as the use of antihypertensive drugs and/or measured grade 2 (or higher) hypertension with systolic pressure at or above 160 mmHg and/or diastolic pressure at or above 100 mmHg
7. **Obesity** (BMI over 30).

Note that more stringent definitions of CKD and hypertension have been applied here than in the analyses presented earlier in this chapter; this is to avoid overdiagnosis of CKD in people using antiretroviral drugs that inhibit tubular secretion of creatinine, and hypertension in those with borderline hypertension. Recurrences and non-primary CVD, stroke, and non-AIDS-defining malignancy events were not considered. Finally, CKD, hypertension, and obesity could be reversible.

Figure 6.17A shows the prevalence of each individual comorbidity over calendar time. *Figure 6.17B* shows the distribution of the number of concomitantly-diagnosed conditions in various age categories of the adult male and female population in 2025. The number of concomitant conditions was slightly higher in women than in men for all age categories. After adjusting for the variables listed in *Appendix Table 6.2*, multimorbidity was independently associated with increased risk of mortality (RR 2.01 (1.94-2.07), p<0.001, per additional comorbidity diagnosed).

Figure 6.17A-B: *(A) Prevalence of non-AIDS multimorbidity in the adult population over calendar time. (B) Prevalence of non-AIDS multimorbidity by gender in the adult population in 2025. The numbers at the top of each bar represent the number of individuals contributing data to that age category. The numbers in the stacked bars represent percentages, with all stacked bars adding up to 100% per age category.*





Polypharmacy

Polypharmacy, commonly defined as the concomitant use of five or more medications, is associated with adverse health outcomes, prescription errors, lower adherence and an increased risk of clinically relevant pharmacological interactions and adverse drug reactions, especially in the elderly. At the end of each calendar year, we count the number of registered comedications for each individual in active follow up. Antiretroviral drugs are excluded from this count. We further excluded the ATC categories "Vitamins (A11)" and "Mineral supplements (A12)" for the count. We counted individual ATC codes (Anatomical Therapeutic Chemical classification system[a]) of the comedications. Note that coformulated combinations, such as cotrimoxazole, have a single ATC code and therefore increase the comedication count by one.

In 2025, 25.1% of adults in active follow up had no recorded comedication use, 25.3% used one comedication, 14.6% used two comedications, 10.4% used three comedications, and 6.8% used four comedications. A further 18.0% used five or more non-antiretroviral comedications in addition to their ART regimen, which qualifies as polypharmacy.

a https://www.whocc.no/atc_ddd_index/

The prevalence of polypharmacy among adults has increased over time (*Figure 6.18*): in 2000, just 3.4% of adults used five or more non-antiretroviral comedications in addition to their ART regimen. The main drivers for this increase are the rising age of the population and the growth in the number of chronic comorbidities. Older people (*Figure 6.19*) used more comedications, primarily because they have been diagnosed with a higher number of comorbidities. There were some differences between men and women, with women using slightly more comedications than men, while the most pronounced differences were to be found in the youngest age groups. Finally, in adults receiving ART in the period 2007-2025, polypharmacy was also associated with an increased risk of death (RR 2.35 (2.15-2.56), p<0.001) independent of demographic and HIV-related parameters, chronic HBV and HCV co-infections, smoking status, and number of comorbidities (i.e. multimorbidity). All comedications used by at least 250 adults with HIV in care in 2025 are listed in *Table 6.14*. A notable difference with what we reported last year is that in 2025 lipid lowering agents were used by 7,400 individuals compared to 6,209 individuals in 2024 and 5,155 individuals in 2023, a substantial increase caused by the guideline change for primary CVD prophylaxis based on the findings of the REPRIEVE study[9].

Table 6.14: *Use of comedications in 2025.*

Comedication use in 2025	N	%
ATC group		
Lipid modifying agents	7,400	11.2
Vitamins	6,707	10.1
Drugs for acid related disorders	4,466	6.8
Agents acting on the renin-angiotensin system	4,255	6.4
Psycholeptics drugs (antipsychotics, anxiolytics, hypnotics, sedatives)	3,700	5.6
Antithrombotic agents	3,494	5.3
Drugs for obstructive airway diseases	3,324	5.0
Drugs used in diabetes	3,293	5.0
Psychoanaleptics (antidepressants, psychostimulants)	2,759	4.2
Urological drugs	2,139	3.2
Calcium channel blockers	2,131	3.2
Beta blocking agents	1,929	2.9
Mineral supplements	1,753	2.7
Antibacterial drugs	1,553	2.3
Diuretic drugs	1,459	2.2
Antianemic drugs	1,420	2.1
Analgesic drugs	1,368	2.1
Sex hormones and modulators of the genital system	1,310	2.0
Topical dermatological corticosteroids	1,272	1.9
Corticosteroids systemic	1,186	1.8
Cardiac therapy	957	1.4
Nasal preparations	831	1.3
Antiviral drugs	801	1.2
Antidiarrheals, intestinal anti-inflammatory/anti-infective agents	552	0.8
Antiepileptic drugs	541	0.8
Antimycotic drugs	525	0.8
Drugs affecting bone structure and mineralization	488	0.7
Immunosuppressants drugs	465	0.7
Thyroid therapy	413	0.6
Ophthalmological drugs	405	0.6
Anti-inflammatory and antirheumatic drugs	273	0.4
Antineoplastic drugs	262	0.4
Other nervous system drugs	260	0.4

Figure 6.18: Number of comedications used over calendar time. The numbers at the top of each bar represent the number of individuals contributing data to that period. The numbers in the stacked bars represent percentages, with all stacked bars adding up to 100% per period.

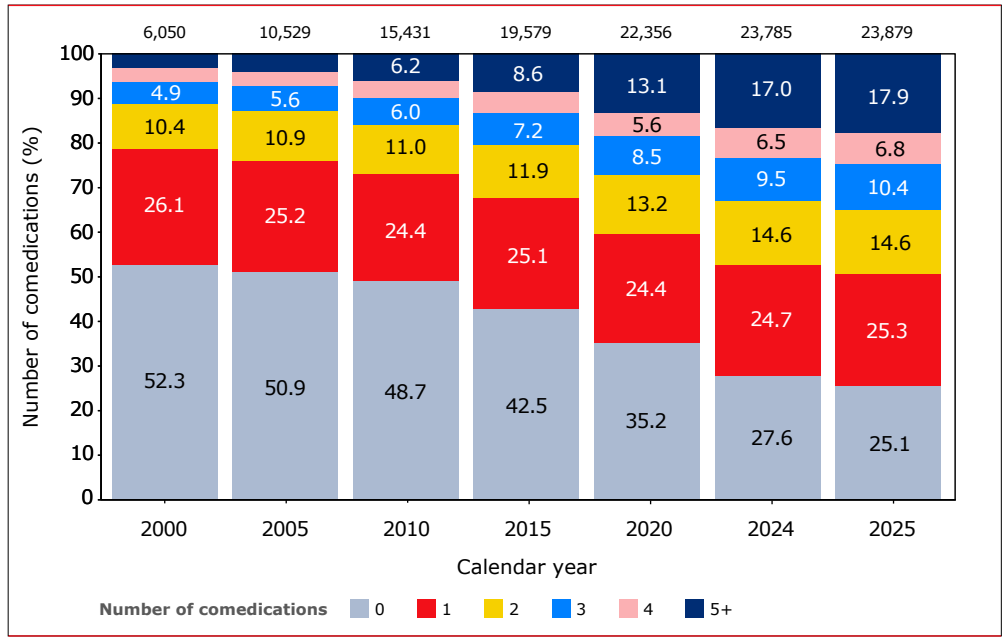
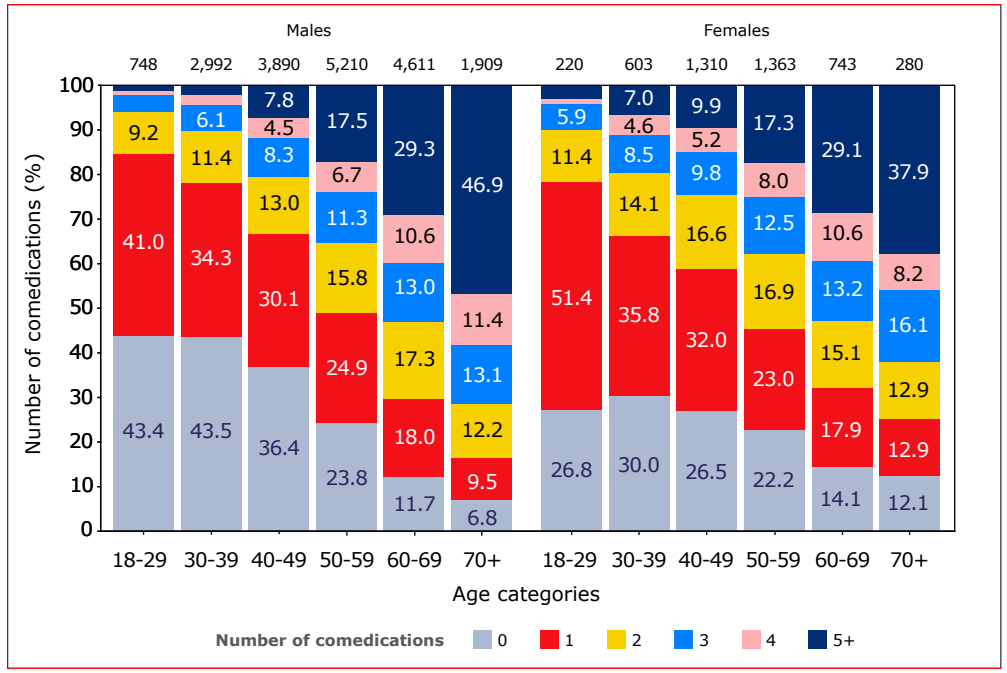


Figure 6.19: Number of comedications used by age group and gender in 2025. The numbers at the top of each bar represent the number of individuals contributing data to that age/gender category. The numbers in the stacked bars represent percentages, with all stacked bars adding up to 100% per age category.



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Appendix: supplementary tables

Appendix Table 6.1: *Absolute number of causes of death among PWH during the periods 1996–2025.*

Cause of death	1996–2001		2002–2004		2005–2007		2008–2010		2011–2013		2014–2016		2017–2019		2020–2022		2023–2025	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
AIDS (subtotal)	258	54.0	148	36.9	157	37.7	132	29.9	110	24.4	79	15.4	63	12.1	52	8.0	71	9.2
Infection	83	17.4	70	17.5	102	24.5	88	19.9	79	17.5	32	6.3	16	3.1	13	2.0	30	3.9
Malignancy	73	15.3	34	8.5	46	11.1	37	8.4	27	6.0	27	5.3	35	6.7	29	4.5	32	4.2
Unclassifiable	102	21.3	44	11.0	9	2.2	7	1.6	4	0.9	20	3.9	12	2.3	10	1.5	9	1.2
Non-AIDS malignancies	40	8.4	60	15.0	66	15.9	88	19.9	109	24.2	127	24.8	183	35.2	194	30.0	212	27.5
CVD (subtotal)	31	6.5	45	11.2	45	10.8	49	11.1	50	11.1	77	15.0	59	11.3	95	14.7	81	10.5
MI	15	3.1	13	3.2	16	3.8	13	2.9	18	4.0	20	3.9	16	3.1	34	5.3	17	2.2
Stroke	4	0.8	8	2.0	6	1.4	8	1.8	8	1.8	11	2.1	8	1.5	18	2.8	18	2.3
Other CVD	12	2.5	24	6.0	23	5.5	28	6.3	24	5.3	46	9.0	35	6.7	43	6.6	46	6.0
Non-AIDS infection	25	5.2	37	9.2	14	3.4	18	4.1	14	3.1	19	3.7	21	4.0	59	9.1	33	4.3
Liver disease	20	4.2	14	3.5	28	6.7	34	7.7	26	5.8	22	4.3	16	3.1	10	1.5	9	1.2
Lung disease	9	1.9	8	2.0	11	2.6	14	3.2	17	3.8	30	5.9	36	6.9	27	4.2	39	5.1
Non-natural death (subtotal)	30	6.3	31	7.7	41	9.9	46	10.4	46	10.2	61	11.9	34	6.5	43	6.6	40	5.2
Accident / violence	8	1.7	8	2.0	9	2.2	15	3.4	9	2.0	13	2.5	7	1.3	11	1.7	19	2.5
Suicide	14	2.9	19	4.7	32	7.7	31	7.0	35	7.8	47	9.2	27	5.2	32	4.9	20	2.6
Euthanasia	8	1.7	4	1.0	.	.	.	.	2	0.4	1	0.2	.	.	.	.	1	0.1
Alcohol, substance abuse, psychiatric disease	14	2.9	8	2.0	15	3.6	20	4.5	17	3.8	16	3.1	24	4.6	33	5.1	24	3.1
Other causes	24	5.0	14	3.5	13	3.1	12	2.7	19	4.2	28	5.5	33	6.3	55	8.5	89	11.6
Unknown	27	5.6	36	9.0	26	6.3	29	6.6	43	9.5	52	10.2	51	9.8	60	9.3	62	8.1
Sudden death	.	.	.	.	.	.	.	.	.	.	1	0.2	.	.	19	2.9	110	14.3
Total	**478**	**100**	**401**	**100**	**416**	**100**	**442**	**100**	**451**	**100**	**512**	**100**	**520**	**100**	**647**	**100**	**770**	**100**

Legend: *CVD = cardiovascular disease.*

Appendix Table 6.2: *Adjusted risk factors for death and AIDS among PWH.*

			Death			AIDS
Risk factors	**RR (95%CI)**	**p-value**	**Overall p-value**	**RR (95%CI)**	**p-value**	**Overall p-value**
Region of birth						
Native Dutch	1 (reference)		0.006	1 (reference)		0.015
Western migrants	0.95 (0.84-1.07)	0.370		1.30 (1.11-1.51)	<.001	
non-Western migrants	0.87 (0.79-0.96)	0.005		1.06 (0.94-1.19)	0.363	
Unknown origin	1.78 (1.03-3.08)	0.038		1.12 (0.58-2.18)	0.733	
HIV-1 transmission route						
MSM	1 (reference)		<.001	1 (reference)		0.140
Other men	1.19 (1.08-1.30)	<.001		0.98 (0.86-1.11)	0.749	
Women	0.89 (0.78-1.00)	0.051		0.92 (0.80-1.06)	0.261	
Transgender	0.83 (0.48-1.43)	0.497		1.33 (0.83-2.12)	0.238	
IDU	1.46 (1.24-1.72)	<.001		0.73 (0.58-0.93)	0.011	
Blood contact	0.89 (0.69-1.16)	0.404		0.81 (0.58-1.14)	0.234	
Pediatric transmission	1.41 (0.70-2.84)	0.339		0.84 (0.45-1.56)	0.580	
Age*						
18-29	0.86 (0.62-1.17)	0.333	<.001	1.04 (0.85-1.27)	0.681	<.001
30-39	1 (reference)			1 (reference)		
40-49	1.59 (1.38-1.83)	<.001		1.03 (0.91-1.16)	0.648	
50-59	2.77 (2.41-3.18)	<.001		1.21 (1.06-1.39)	0.004	
60-69	4.96 (4.29-5.73)	<.001		1.41 (1.20-1.65)	<.001	
70+	11.97 (10.27-13.94)	<.001		1.86 (1.48-2.36)	<.001	
CD4 cell count**						
0-50	7.70 (6.52-9.09)	<.001	<.001	6.41 (5.27-7.79)	<.001	<.001
050-199	3.62 (3.22-4.07)	<.001		2.73 (2.36-3.17)	<.001	
200-349	1.80 (1.61-2.01)	<.001		1.61 (1.40-1.86)	<.001	
350-499	1.32 (1.18-1.46)	<.001		1.17 (1.02-1.36)	0.030	
500-749	1 (reference)			1 (reference)		
750+	0.85 (0.77-0.95)	0.004		1.10 (0.94-1.28)	0.244	
Per year longer on ART with HIV RNA>1,000 cp/mL	1.06 (1.05-1.08)	<.001	<.001	1.05 (1.02-1.07)	<.001	<.001
Treatment status						
Treatment-experienced at start ART	0.93 (0.86-1.02)	0.135		0.68 (0.61-0.77)	<.001	
Treatment-naive at start	1 (reference)			1 (reference)		
Prior AIDS event	1.59 (1.47-1.71)	<.001				
Hepatitis B virus positive	1.26 (1.12-1.42)	<.001		0.94 (0.79-1.11)	0.441	
Hepatitis C virus positive	1.54 (1.36-1.74)	<.001		1.14 (0.96-1.35)	0.134	
Body mass index *						
0-18	3.31 (2.96-3.70)	<.001	<.001			
18-25	1 (reference)					
25-30	0.67 (0.61-0.73)	<.001				
30+	0.81 (0.71-0.93)	0.002				
Smoking status						
Current smoker	1.26 (1.13-1.39)	<.001	<.001	0.74 (0.67-0.83)	<.001	<.001
Never smoker	1 (reference)			1 (reference)		
Past smoker	1.89 (1.72-2.08)	<.001		0.91 (0.80-1.03)	0.154	
Early ART***	0.75 (0.58-0.97)	0.027		1.15 (0.91-1.46)	0.255	

**Time-updated.*

***Time-updated and lagged by three months.*

****ART started within 12 months of the last HIV-negative test.*

Legend: *ART = combination antiretroviral therapy; IDU = people who inject drugs; MSM = men who have sex with men; CI = confidence interval; RR = risk ratio.*

Appendix Table 6.3: *Lost to care (no recorded follow up after 31 December 2024) by region of origin and time-updated CD4 cell count.*

	Total population			Native Dutch			Western migrants			non-Western migrants		
Last CD4 count	**N**	**PY**	**Incidence/ 1,000PY (95%CI)**	**N**	**PY**	**Incidence/ 1,000PY (95%CI)**	**N**	**PY**	**Incidence/ 1,000PY (95%CI)**	**N**	**PY**	**Incidence/ 1,000PY (95%CI)**
0-50	82	3,359	24.4 (19.4-30.3)	6	1,792	3.3 (1.2-7.3)	17	342	49.7 (29.0-79.6)	59	1,225	48.2 (36.7-62.1)
050-199	298	13,162	22.6 (20.1-25.4)	40	7,191	5.6 (4.0-7.6)	73	1,578	46.3 (36.3-58.2)	185	4,393	42.1 (36.3-48.6)
200-349	541	29,402	18.4 (16.9-20.0)	86	16,971	5.1 (4.1-6.3)	131	2,763	47.4 (39.6-56.3)	324	9,668	33.5 (30.0-37.4)
350-499	780	56,972	13.7 (12.7-14.7)	147	33,405	4.4 (3.7-5.2)	205	5,908	34.7 (30.1-39.8)	428	17,659	24.2 (22.0-26.6)
500-749	1,220	137,970	8.8 (8.4-9.4)	296	81,006	3.7 (3.2-4.1)	350	14,152	24.7 (22.2-27.5)	574	42,812	13.4 (12.3-14.6)
750+	1,115	195,613	5.7 (5.4-6.0)	301	113,737	2.6 (2.4-3.0)	395	23,402	16.9 (15.3-18.6)	419	58,475	7.2 (6.5-7.9)

Legend: *n = number; PY = person years of follow up; CI = confidence interval.*

Appendix Table 6.4: *Absolute number of first AIDS events among PWH during the periods 1996–1999, 2000–2004, 2005–2009, 2010–2014, 2015–2019, and 2020–2025.*

CDC event	1996–1999	2000–2004	2005–2009	2010–2014	2015–2019	2020–2025	Total	
	N	N	N	N	N	N	N	%
AIDS Dementia Complex – HIV Encefalopathy	32	40	57	40	24	21	214	2.80
Aspergillosis, invasive extrapulmonary/disseminated	.	.	1	.	.	1	2	0.03
Aspergillosis, invasive pulmonary	.	.	2	.	7	6	15	0.20
Bacterial pneumonia, recurring	40	53	76	70	108	105	452	5.92
CMV colitis/proctitis	1	.	1	1	5	4	12	0.16
CMV disease, unspecified	21	33	29	34	7	.	124	1.62
CMV gastroenteritis	.	.	.	.	.	1	1	0.01
CMV meningo-encefalitis	.	.	.	.	1	.	1	0.01
CMV oesophagitis	.	.	.	.	.	3	3	0.04
CMV pneumonitis	.	.	.	1	12	22	35	0.46
CMV radiculomyelitis	.	1	.	.	.	.	1	0.01
CMV retinitis	25	19	16	13	12	4	89	1.16
Candidiasis lung/bronchial/trachea	4	13	9	7	5	4	42	0.55
Candidiasis oesophagitis	217	216	270	227	169	154	1,253	16.40
Cervical cancer	2	6	5	7	6	2	28	0.37
Coccidioimycosis, extrapulmonary/disseminated	.	.	1	.	.	.	1	0.01
Cryptococcosis, extrapulmonary/disseminated	18	29	39	12	15	2	115	1.51
Cryptosporidiosis	17	15	9	14	5	5	65	0.85
Cystoisosporiasis	1	11	5	1	.	.	18	0.24
HIV wasting	42	45	75	78	70	40	350	4.58
HSV chronic ulcer	1	.	4	4	24	31	64	0.84
HSV oesophagitis	.	.	.	.	.	1	1	0.01
HSV pneumonitis	.	.	1	.	.	1	2	0.03
Herpes simplex virus	26	33	57	44	15	.	175	2.29
Histoplasmosis, extrapulmonary/disseminated	5	13	12	8	2	1	41	0.54
Kaposi sarcoma	144	138	198	162	100	68	810	10.60
Leishmaniasis visceral	.	1	3	2	1	.	7	0.09
Microsporidiosis	11	1	2	2	.	1	17	0.22
Mycobacterium avium/kansasii, extrapulmonary/disseminated	21	22	23	14	9	4	93	1.22
Mycobacterium avium/kansasii, pulmonary	3	2	4	1	8	5	23	0.30
Mycobacterium other/unspecified, extrapulmonary/disseminated	17	13	7	11	7	5	60	0.79
Mycobacterium other/unspecified, pulmonary	2	2	7	11	4	7	33	0.43
Non-Hodgkin lymphoma (NHL)	53	74	98	94	93	59	471	6.16
Penicilliosis	.	.	1	.	.	.	1	0.01
Pneumocystis jirovecii extrapulmonary	.	1	3	1	1	1	7	0.09
Pneumocystis jirovecii pulmonary	264	297	309	294	215	168	1,547	20.25
Primairy CBS lymphoma	6	6	9	7	5	1	34	0.44
Progressive multifocal leucoencefalopathy	14	19	37	26	10	9	115	1.51
Salmonella sepsis, recurring	2	.	.	1	.	.	3	0.04
Toxoplasmosis cerebral	55	94	62	55	33	19	318	4.16
Tuberculosis, extrapulmonary/disseminated	56	113	91	61	43	34	398	5.21
Tuberculosis, pulmonary	80	168	135	99	72	46	600	7.85
Total	**1,180**	**1,478**	**1,658**	**1,402**	**1,088**	**835**	**7,641**	**100.00**

Legend: *CDC = Centers for Disease Control and Prevention; CMV = cytomegalovirus; MAI = mycobacterium avium intracellulare complex.*

Appendix Table 6.5: *Adjusted risk factors for non-AIDS-defining morbidity.*

	Non-AIDS-defining disease			Cardiovascular disease			Non-AIDS-defining malignancy			Diabetes mellitus			CKD		
	IRR (95%CI)	p-value	Overall p-value	IRR (95%CI)	p-value	Overall p-value	IRR (95%CI)	p-value	Overall p-value	IRR (95%CI)	p-value	Overall p-value	IRR (95%CI)	p-value	Overall p-value
Region of birth															
Native Dutch	1 (reference)	.	<.001	1 (reference)	.	0.195	1 (reference)	.	<.001	1 (reference)	.	<.001	1 (reference)	.	<.001
Western migrants	0.94 (0.85-1.03)	0.188	.	0.98 (0.85-1.14)	0.804	.	0.97 (0.83-1.13)	0.678	.	0.95 (0.80-1.12)	0.517	.	0.95 (0.83-1.08)	0.427	.
non-Western migrants	1.14 (1.06-1.23)	<.001	.	0.88 (0.78-0.99)	0.033	.	0.79 (0.70-0.90)	<.001	.	1.80 (1.61-2.00)	<.001	.	0.70 (0.63-0.77)	<.001	.
Unknown origin	0.63 (0.33-1.21)	0.168	.	1.08 (0.49-2.42)	0.844	.	0.18 (0.02-1.26)	0.083	.	0.60 (0.19-1.87)	0.380	.	1.34 (0.76-2.36)	0.317	.
HIV-1 transmission route															
MSM	1 (reference)	.	<.001	1 (reference)	.	<.001	1 (reference)	.	0.034	1 (reference)	.	<.001	1 (reference)	.	<.001
Other men	1.19 (1.11-1.28)	<.001	.	1.19 (1.06-1.33)	0.003	.	1.04 (0.92-1.18)	0.492	.	1.33 (1.19-1.50)	<.001	.	1.10 (1.00-1.22)	0.057	.
Women	0.93 (0.86-1.02)	0.127	.	0.74 (0.63-0.86)	<.001	.	0.98 (0.84-1.13)	0.765	.	0.99 (0.87-1.13)	0.912	.	1.53 (1.37-1.71)	<.001	.
Transgender	0.88 (0.63-1.24)	0.458	.	1.39 (0.86-2.24)	0.185	.	0.33 (0.12-0.89)	0.028	.	0.93 (0.58-1.51)	0.780	.	1.01 (0.60-1.68)	0.976	.
IDU	1.20 (1.01-1.42)	0.043	.	0.99 (0.76-1.31)	0.969	.	1.27 (0.98-1.65)	0.070	.	1.38 (1.03-1.86)	0.033	.	1.73 (1.36-2.20)	<.001	.
Blood contact	1.13 (0.92-1.38)	0.255	.	1.07 (0.78-1.48)	0.662	.	1.32 (0.97-1.80)	0.080	.	1.28 (0.95-1.72)	0.106	.	1.32 (1.01-1.73)	0.041	.
Pediatric transmission	0.71 (0.29-1.74)	0.457	.	0.00 (0.00-99.99)	0.998	.	1.16 (0.28-4.88)	0.840	.	0.63 (0.20-2.00)	0.430	.	2.78 (0.83-9.33)	0.098	.
Age *															
18-29	0.61 (0.47-0.80)	<.001	<.001	0.51 (0.28-0.93)	0.028	<.001	0.65 (0.39-1.09)	0.101	<.001	0.66 (0.46-0.93)	0.019	<.001	0.26 (0.12-0.59)	0.001	<.001
30-39	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.
40-49	2.05 (1.83-2.30)	<.001	.	2.87 (2.29-3.60)	<.001	.	2.45 (1.95-3.07)	<.001	.	1.54 (1.31-1.81)	<.001	.	2.58 (2.02-3.30)	<.001	.
50-59	3.74 (3.33-4.19)	<.001	.	5.84 (4.68-7.30)	<.001	.	4.58 (3.67-5.72)	<.001	.	2.44 (2.07-2.88)	<.001	.	7.46 (5.91-9.43)	<.001	.
60-69	6.30 (5.58-7.12)	<.001	.	9.37 (7.43-11.81)	<.001	.	9.95 (7.93-12.49)	<.001	.	3.56 (2.97-4.27)	<.001	.	18.80 (14.87-23.78)	<.001	.
70+	9.88 (8.57-11.39)	<.001	.	15.77 (12.26-20.29)	<.001	.	17.19 (13.45-21.98)	<.001	.	3.79 (2.99-4.80)	<.001	.	34.89 (27.26-44.64)	<.001	.
CD4 cell count **															
0-50	3.36 (2.72-4.15)	<.001	<.001	2.66 (1.83-3.87)	<.001	<.001	2.39 (1.58-3.64)	<.001	<.001	4.72 (3.50-6.37)	<.001	<.001	2.58 (1.75-3.82)	<.001	<.001
050-199	1.77 (1.55-2.02)	<.001	.	1.62 (1.31-2.00)	<.001	.	1.96 (1.58-2.44)	<.001	.	1.73 (1.39-2.15)	<.001	.	1.90 (1.57-2.30)	<.001	.
200-349	1.23 (1.11-1.35)	<.001	.	1.23 (1.06-1.44)	0.007	.	1.37 (1.18-1.59)	<.001	.	1.17 (0.99-1.37)	0.062	.	1.18 (1.04-1.35)	0.011	.
350-499	1.07 (0.99-1.16)	0.096	.	1.12 (0.99-1.28)	0.083	.	1.09 (0.96-1.24)	0.168	.	1.07 (0.93-1.22)	0.357	.	1.08 (0.98-1.20)	0.131	.
500-749	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.
750+	1.15 (1.08-1.24)	<.001	.	1.22 (1.09-1.36)	<.001	.	1.00 (0.89-1.12)	0.978	.	1.26 (1.12-1.41)	<.001	.	0.92 (0.84-1.01)	0.076	.
Per year longer with CD4<200 cells/mm^3	1.00 (0.99-1.02)	0.645	.	1.03 (1.00-1.05)	0.020	.	0.99 (0.96-1.02)	0.419	.	1.00 (0.97-1.03)	0.880	.	0.98 (0.96-1.01)	0.165	.
Prior AIDS event	1.22 (1.14-1.29)	<.001	.	1.10 (1.00-1.21)	0.057	.	1.15 (1.05-1.27)	0.004	.	1.32 (1.20-1.45)	<.001	.	1.14 (1.05-1.23)	0.002	.
Per year longer on cART while HIV RNA>1000 cp/mL	1.01 (0.99-1.03)	0.196	.	1.01 (0.98-1.03)	0.629	.	1.00 (0.97-1.02)	0.760	.	0.99 (0.97-1.02)	0.517	.	0.97 (0.94-0.99)	0.005	.
Treatment status															
Not (yet) started cART	1.34 (1.19-1.51)	<.001	<.001	1.15 (0.94-1.42)	0.180	0.086	1.38 (1.13-1.69)	0.002	<.001	1.65 (1.37-1.99)	<.001	<.001	0.32 (0.22-0.45)	<.001	<.001
Treatment-experienced at start cART	1.28 (1.18-1.38)	<.001	.	1.13 (0.99-1.28)	0.065	.	1.16 (1.02-1.32)	0.023	.	1.26 (1.10-1.46)	0.001	.	1.07 (0.96-1.20)	0.227	.
Treatment-naive at start	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.
Per year longer on cART	1.01 (1.00-1.01)	0.016	.	1.00 (0.99-1.01)	0.814	.	1.01 (1.00-1.02)	0.053	.	1.00 (0.99-1.01)	0.650	.	0.99 (0.98-1.00)	0.010	.

	Non-AIDS-defining disease			Cardiovascular disease			Non-AIDS-defining malignancy			Diabetes mellitus			CKD		
	IRR (95%CI)	p-value	Overall p-value	IRR (95%CI)	p-value	Overall p-value	IRR (95%CI)	p-value	Overall p-value	IRR (95%CI)	p-value	Overall p-value	IRR (95%CI)	p-value	Overall p-value
Early cART within 12 months after last HIV-negat	0.83 (0.70-0.97)	0.024		0.99 (0.78-1.25)	0.922	.	0.79 (0.61-1.04)	0.096	.	0.59 (0.43-0.82)	0.002	.	1.01 (0.84-1.20)	0.947	.
Body mass index*															
0-18	1.48 (1.25-1.75)	<.001	<.001	1.26 (0.97-1.65)	0.085	0.034	1.91 (1.54-2.38)	<.001	<.001	1.34 (0.95-1.87)	0.094	<.001	1.27 (0.99-1.64)	0.060	<.001
18-25	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.
25-30	1.19 (1.11-1.27)	<.001	.	1.00 (0.91-1.11)	0.990	.	0.84 (0.76-0.93)	0.001	.	2.13 (1.90-2.38)	<.001	.	1.18 (1.09-1.28)	<.001	.
30+	1.87 (1.72-2.04)	<.001	.	1.05 (0.90-1.22)	0.549	.	0.83 (0.70-0.98)	0.027	.	5.04 (4.44-5.72)	<.001	.	1.13 (1.01-1.28)	0.036	.
Hepatitis B virus positive	1.18 (1.06-1.31)	0.002	.	0.97 (0.82-1.16)	0.775	.	1.51 (1.29-1.76)	<.001	.	1.11 (0.93-1.32)	0.240	.	1.29 (1.12-1.49)	<.001	.
Hepatitis C virus positive	1.04 (0.93-1.15)	0.509	.	1.02 (0.86-1.20)	0.850	.	1.05 (0.89-1.24)	0.582	.	1.04 (0.87-1.25)	0.672	.	1.09 (0.96-1.25)	0.191	.
Hypertension	1.12 (1.06-1.18)	<.001	.	1.18 (1.08-1.29)	<.001	.	0.93 (0.85-1.02)	0.130	.	1.18 (1.08-1.29)	<.001	.	1.06 (0.99-1.14)	0.103	.
Smoking status															
Current smoker	1.40 (1.30-1.50)	<.001	<.001	1.84 (1.65-2.06)	<.001	<.001	1.53 (1.36-1.72)	<.001	<.001	1.07 (0.96-1.20)	0.236	<.001	0.80 (0.73-0.88)	<.001	<.001
Never smoker	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.
Past smoker	1.36 (1.27-1.47)	<.001	.	1.48 (1.32-1.66)	<.001	.	1.63 (1.46-1.83)	<.001	.	1.22 (1.09-1.37)	<.001	.	0.99 (0.91-1.08)	0.893	.
Calendar year period															
2000-2009	1.19 (1.08-1.31)	<.001	<.001	1.50 (1.26-1.78)	<.001	<.001	1.03 (0.87-1.22)	0.733	<.001	1.45 (1.21-1.73)	<.001	<.001	2.09 (1.73-2.51)	<.001	<.001
2010-2019	1.17 (1.09-1.25)	<.001	.	1.21 (1.07-1.36)	0.002	.	1.20 (1.08-1.34)	<.001	.	1.19 (1.05-1.34)	0.007	.	1.77 (1.63-1.94)	<.001	.
2020-2025	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.	1 (reference)	.	.
Recent use of ABC ***		.	.	1.52 (1.37-1.69)	<.001	.		.	.		.	.		.	.
Per year longer on LOP/r		.	.	1.00 (0.99-1.01)	0.798	.		.	.		.	.		.	.
Per year longer on IDV		.	.	1.00 (0.99-1.01)	0.897	.		.	.		.	.		.	.
Prior diabetes		.	.	1.95 (1.70-2.24)	<.001	.		.	.		.	.	1.29 (1.14-1.46)	<.001	.
Current use of bictegravir		.	.	1.43 (1.18-1.72)	<.001	.		.	.	1.70 (1.42-2.03)	<.001	.	2.59 (2.28-2.95)	<.001	.
Current use of dolutegravir		.	.	1.25 (1.10-1.42)	<.001	.		.	.	1.56 (1.39-1.77)	<.001	.	2.80 (2.58-3.04)	<.001	.
Current use of elvitegravir		.	.	1.06 (0.88-1.27)	0.546	.		.	.	1.11 (0.92-1.33)	0.277	.		.	.
Current use of raltegravir		.	.	1.67 (1.41-1.99)	<.001	.		.	.	2.29 (1.92-2.72)	<.001	.		.	.
Current use of cabotegravir		.	.	1.04 (0.56-1.95)	0.893	.		.	.	0.98 (0.52-1.84)	0.953	.	0.44 (0.21-0.94)	0.035	.
Per year longer on ZDV		.	.		.	.		.	.	1.02 (1.01-1.03)	0.003	.		.	.
Per year longer on d4T		.	.		.	.		.	.	1.03 (1.00-1.05)	0.051	.		.	.
Per year longer on ddI		.	.		.	.		.	.	1.04 (1.02-1.06)	<.001	.		.	.
Per year longer on TAF		.	.		.	.		.	.		.	.	1.00 (0.99-1.00)	0.315	.
Per year longer on TDF		.	.		.	.		.	.		.	.	1.01 (1.00-1.01)	0.067	.
Prior cardiovascular event		.	.		.	.		.	.		.	.	1.62 (1.45-1.82)	<.001	.
Current use of cobicistat		.	.		.	.		.	.		.	.	1.35 (1.21-1.49)	<.001	.
Current use of rilpivirine		.	.		.	.		.	.		.	.	1.29 (1.11-1.49)	<.001	.

**Time-updated.*

***Time-updated and lagged by three months.*

****Current use or recently used in the past six months.*

***Legend:** CKD = chronic kidney disease; IDU = injecting drug use; ART = combination antiretroviral therapy; LOP/r = lopinavir/ritonavir; IDV = indinavir; ABC = abacavir; ZDV = zidovudine; d4T = stavudine; ddI = didanosine; BMI: <18 kg/m² = underweight; 18-25 kg/m² = normal; 25-30 kg/m² = overweight;>30 kg/m² = severely overweight.*

Appendix Table 6.6: *Specific CDC-B and CDC-C (AIDS) events occurring in individuals on ART with undetectable viral load between 2000 and 2025.*

				CD4 category									
		All events		0-50		050-199		200-349		350-499		500-749		750+	
	CDC event	n	%	n	%	n	%	n	%	n	%	n	%	n	%
CDC-B events	Bacillary Angiomatosis	1	0.0%	0	0.0%	1	0.1%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	Candidiasis oropharyngeal	1,109	27.5%	136	30.1%	294	33.8%	214	28.0%	170	24.1%	173	22.3%	122	26.3%
	Candidiasis vulvovaginal, recurring/persistent	57	1.4%	2	0.4%	5	0.6%	12	1.6%	13	1.8%	20	2.6%	5	1.1%
	Cardiomyopathy, HIV-associated	37	0.9%	2	0.4%	6	0.7%	4	0.5%	5	0.7%	11	1.4%	9	1.9%
	Cardiomyopathy, HIV-related	6	0.1%	0	0.0%	2	0.2%	1	0.1%	0	0.0%	1	0.1%	2	0.4%
	Diarrea, HIV-related >=30 days	66	1.6%	2	0.4%	9	1.0%	12	1.6%	19	2.7%	16	2.1%	8	1.7%
	Fever e.c.i. HIV-related	6	0.1%	0	0.0%	1	0.1%	2	0.3%	0	0.0%	1	0.1%	2	0.4%
	HIV-associeerd nephropathy (HIVAN)	27	0.7%	5	1.1%	4	0.5%	4	0.5%	6	0.9%	5	0.6%	3	0.6%
	Herpes zoster, multidermatomal	45	1.1%	4	0.9%	3	0.3%	8	1.0%	10	1.4%	11	1.4%	9	1.9%
	Herpes zoster, recurrent/multidermatomal	209	5.2%	10	2.2%	38	4.4%	45	5.9%	41	5.8%	47	6.1%	28	6.0%
	Herpes zoster, unidermatomaal recurring	60	1.5%	4	0.9%	9	1.0%	4	0.5%	9	1.3%	21	2.7%	13	2.8%
	Listeriosis	1	0.0%	0	0.0%	0	0.0%	1	0.1%	0	0.0%	0	0.0%	0	0.0%
	Myelopathy, HIV-related	10	0.2%	0	0.0%	4	0.5%	2	0.3%	0	0.0%	2	0.3%	2	0.4%
	Neuropathy, HIV-associated	145	3.6%	0	0.0%	12	1.4%	19	2.5%	38	5.4%	44	5.7%	32	6.9%
	Neuropathy, HIV-related	134	3.3%	2	0.4%	9	1.0%	19	2.5%	33	4.7%	44	5.7%	27	5.8%
	Nocardiosis	2	0.0%	1	0.2%	0	0.0%	0	0.0%	1	0.1%	0	0.0%	0	0.0%
	Oral Hairy Leukoplakia (OHL)	59	1.5%	2	0.4%	16	1.8%	14	1.8%	8	1.1%	11	1.4%	8	1.7%
	Pelvic inflammatory disease (PID)	13	0.3%	0	0.0%	0	0.0%	5	0.7%	0	0.0%	5	0.6%	3	0.6%
	Trombocytopenia, HIV-associated	44	1.1%	8	1.8%	4	0.5%	12	1.6%	5	0.7%	13	1.7%	2	0.4%
	Trombocytopenia, HIV-related	144	3.6%	8	1.8%	27	3.1%	29	3.8%	32	4.5%	35	4.5%	13	2.8%
	Weight loss >10% HIV-related/unknown cause	37	0.9%	5	1.1%	5	0.6%	6	0.8%	8	1.1%	5	0.6%	8	1.7%
Subtotal		**2212**	**54.9%**	**191**	**42.3%**	**449**	**51.6%**	**413**	**54.1%**	**398**	**56.5%**	**465**	**60.0%**	**296**	**63.8%**
CDC-C events	AIDS Dementie Complex - HIV Encefalopathy	48	1.2%	7	1.5%	8	0.9%	8	1.0%	11	1.6%	10	1.3%	4	0.9%
	Aspergillosis, invasive extrapulmonary/ disseminated	2	0.0%	0	0.0%	1	0.1%	0	0.0%	0	0.0%	1	0.1%	0	0.0%
	Aspergillosis, invasive pulmonary	20	0.5%	3	0.7%	5	0.6%	3	0.4%	0	0.0%	5	0.6%	4	0.9%
	Bacterial pneumonia, recurring	376	9.3%	13	2.9%	75	8.6%	84	11.0%	94	13.3%	74	9.5%	36	7.8%
	CMV colitis/proctitis	2	0.0%	1	0.2%	1	0.1%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	CMV disease, unspecified	19	0.5%	4	0.9%	4	0.5%	3	0.4%	5	0.7%	1	0.1%	2	0.4%
	CMV meningo-encefalitis	2	0.0%	1	0.2%	0	0.0%	1	0.1%	0	0.0%	0	0.0%	0	0.0%
	CMV oesophagitis	2	0.0%	1	0.2%	0	0.0%	0	0.0%	1	0.1%	0	0.0%	0	0.0%
	CMV pneumonitis	2	0.0%	1	0.2%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.2%
	CMV retinitis	27	0.7%	9	2.0%	11	1.3%	2	0.3%	4	0.6%	1	0.1%	0	0.0%
	Candidiasis lung/bronchial/trachea	12	0.3%	2	0.4%	1	0.1%	6	0.8%	1	0.1%	2	0.3%	0	0.0%

		All events		0–50		CD4 category: 050–199		200–349		350–499		500–749		750+	
	CDC event	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Candidiasis oesophagitis	332	8.2%	52	11.5%	79	9.1%	70	9.2%	44	6.2%	57	7.4%	30	6.5%
	Cervical cancer	13	0.3%	0	0.0%	3	0.3%	3	0.4%	2	0.3%	4	0.5%	1	0.2%
	Coccidioimycosis, extrapulmonary/disseminated	1	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.1%	0	0.0%
	Cryptococcosis, extrapulmonary/disseminated	18	0.4%	10	2.2%	5	0.6%	2	0.3%	0	0.0%	1	0.1%	0	0.0%
	Cryptosporidiosis	12	0.3%	3	0.7%	1	0.1%	1	0.1%	4	0.6%	2	0.3%	1	0.2%
	Cystoisosporiasis	2	0.0%	0	0.0%	1	0.1%	1	0.1%	0	0.0%	0	0.0%	0	0.0%
	HIV wasting	30	0.7%	13	2.9%	13	1.5%	1	0.1%	2	0.3%	1	0.1%	0	0.0%
	HSV chronic ulcer	50	1.2%	3	0.7%	8	0.9%	2	0.3%	7	1.0%	17	2.2%	13	2.8%
	HSV oesophagitis	3	0.1%	0	0.0%	1	0.1%	0	0.0%	1	0.1%	0	0.0%	1	0.2%
	HSV pneumonitis	2	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	2	0.4%
	Herpes simplex virus	66	1.6%	10	2.2%	8	0.9%	14	1.8%	19	2.7%	10	1.3%	5	1.1%
	Histoplasmosis, extrapulmonary/disseminated	3	0.1%	2	0.4%	0	0.0%	0	0.0%	0	0.0%	1	0.1%	0	0.0%
	Kaposi sarcoma	159	3.9%	11	2.4%	24	2.8%	36	4.7%	28	4.0%	38	4.9%	22	4.7%
	Leishmaniasis visceral	5	0.1%	1	0.2%	3	0.3%	1	0.1%	0	0.0%	0	0.0%	0	0.0%
	Microsporidiosis	6	0.1%	2	0.4%	3	0.3%	0	0.0%	0	0.0%	0	0.0%	1	0.2%
	Mycobacterium avium/kansasii, extrapulmonary/disseminated	34	0.8%	12	2.7%	12	1.4%	4	0.5%	4	0.6%	1	0.1%	1	0.2%
	Mycobacterium avium/kansasii, pulmonary	8	0.2%	1	0.2%	3	0.3%	1	0.1%	0	0.0%	1	0.1%	2	0.4%
	Mycobacterium other/unspecified, extrapulmonary/disseminated	14	0.3%	6	1.3%	4	0.5%	3	0.4%	1	0.1%	0	0.0%	0	0.0%
	Mycobacterium other/unspecified, pulmonary	7	0.2%	1	0.2%	2	0.2%	0	0.0%	2	0.3%	1	0.1%	1	0.2%
	Non-Hodgkin lymphoma (NHL)	219	5.4%	13	2.9%	51	5.9%	48	6.3%	45	6.4%	41	5.3%	21	4.5%
	Pneumocystis jirovecii extrapulmonary	1	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.2%
	Pneumocystis jirovecii pulmonary	104	2.6%	40	8.8%	36	4.1%	13	1.7%	8	1.1%	6	0.8%	1	0.2%
	Primary CBS lymphoma	10	0.2%	1	0.2%	4	0.5%	4	0.5%	0	0.0%	1	0.1%	0	0.0%
	Progressive multifocal leukoencephalopathy	24	0.6%	9	2.0%	8	0.9%	4	0.5%	2	0.3%	1	0.1%	0	0.0%
	Toxoplasmosis cerebral	33	0.8%	14	3.1%	12	1.4%	6	0.8%	0	0.0%	1	0.1%	0	0.0%
	Tuberculosis, extrapulmonary/disseminated	65	1.6%	9	2.0%	15	1.7%	11	1.4%	7	1.0%	11	1.4%	12	2.6%
	Tuberculosis, pulmonary	85	2.1%	6	1.3%	19	2.2%	19	2.5%	15	2.1%	20	2.6%	6	1.3%
Subtotal		**1,818**	**45.1%**	**261**	**57.7%**	**421**	**48.4%**	**351**	**45.9%**	**307**	**43.5%**	**310**	**40.0%**	**168**	**36.2%**
Total		**4,030**	**100.0%**	**452**	**100.0%**	**870**	**100.0%**	**764**	**100.0%**	**705**	**100.0%**	**775**	**100.0%**	**464**	**100.0%**

Legend: *CDC = Centers for Disease Control and Prevention; CNS = Central Nervous System; MAI = mycobacterium avium intracellulare complex.*