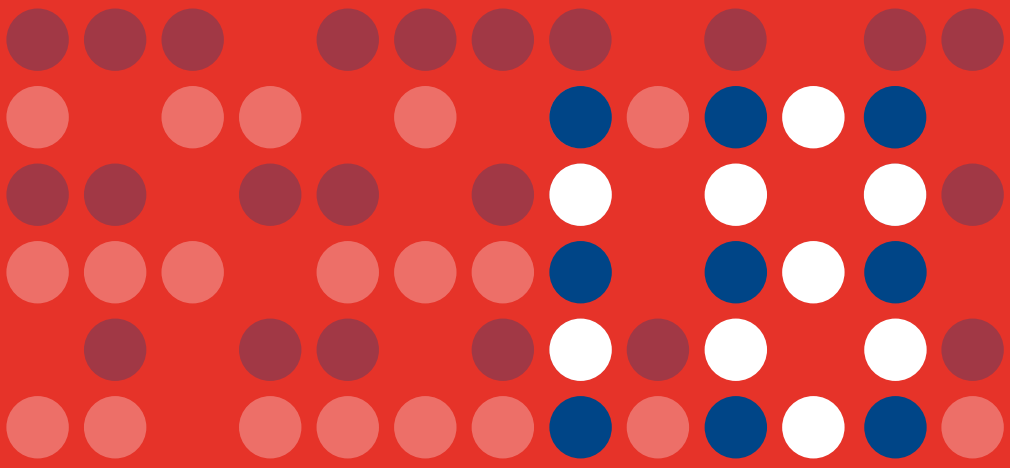
Human Immunodeficiency Virus (HIV)
infection in the Netherlands

HIV Monitoring

HIV Monitoring Report 2018

Summary and Recommendations

The Monitoring Report 2018 is now available online at www.hiv-monitoring.nl



About Stichting HIV Monitoring

Stichting HIV Monitoring (SHM), the Dutch HIV monitoring foundation, was founded in 2001 and appointed by the Dutch minister of Health, Welfare and Sport as the executive organisation for the registration and monitoring of HIV-positive individuals in the Netherlands.

SHM comprehensively maps the HIV epidemic and HIV treatment outcomes in the Netherlands, thereby contributing to the knowledge of HIV. In collaboration with the HIV treatment centres in the Netherlands, SHM has developed a framework for systematically collecting HIV data for the long-term follow up of all registered individuals. The Netherlands is the only country in the world to have such a framework, which enables healthcare professionals to aspire to the highest standard of HIV care.

In addition to national reports, healthcare professionals are provided with treatment centre-specific reports to enable them to monitor and optimise care provided in their centres. Moreover, upon request, SHM data are also made available for use in HIV-related research, both in the Netherlands and internationally. The outcome of SHM's research and international collaborations provides tangible input into policy guidelines and further improves HIV care in the Netherlands.

For further information about SHM or to sign up for our newsletter, please visit our website: **www.hiv-monitoring.nl** or send us an email: **hiv.monitoring@amc.uva.nl.**

HIV Monitoring

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Foreword

This Summary and Recommendations highlights the key trends over time in the HIV epidemic in the Netherlands and makes a number of important recommendations based on the findings published in the Monitoring Report 2018 on Human Immunodeficiency Virus (HIV) infection in the Netherlands.

The full Monitoring Report and all accompanying figures are available online (www.hiv-monitoring.nl). The 17th Monitoring Report comprises a section on the HIV Monitoring Programme that provides an update on the number of newly-registered HIV diagnoses, the changes over time in the characteristics of the HIV-positive population at the time of diagnosis, the effects of combination antiretroviral therapy (cART), cART prescription trends, the development of resistance to antiretroviral drugs, and morbidity and mortality in the HIV-positive population. This section also contains information on specific populations, including those with viral hepatitis co-infections and HIV-1-positive children, along with a chapter on quality of care in the 26 HIV treatment centres. As in previous years, the Special Reports section includes a chapter on the results from the Amsterdam Cohort Studies and one on HIV in Curaçao.

The Monitoring Report is the culmination of a great deal of hard work by many people both within and outside SHM. I would therefore like to thank the HIV treating physicians, HIV nurse consultants, and staff of the diagnostic laboratories, along with the data collecting and monitoring staff. Without their ongoing efforts, our work would not be possible. My thanks also go to our group of reviewers whose in-depth knowledge on relevant chapter topics has helped shape the content of this report. Their input is highly valuable and further improves the report's clinical and public health relevance. Finally, I extend my gratitude to the people living with HIV who generously agree to provide data to SHM. It is only through this partnership between both professionals and affected communities that we can further our insight into the many facets of HIV and HIV treatment, and thereby continue to not only improve the care for people living with HIV in the Netherlands, but also provide guidance for prevention.

Professor Peter Reiss, MD

Director, Stichting HIV Monitoring

The HIV epidemic in the Netherlands in 2017

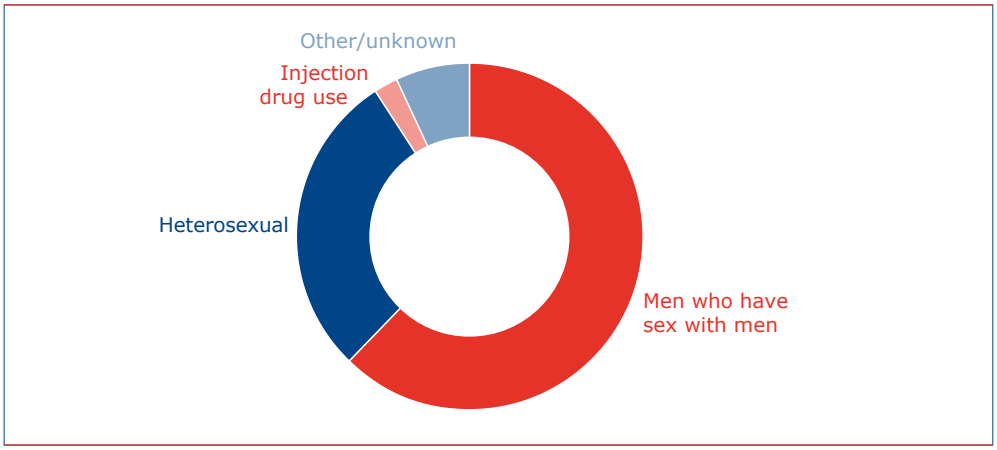
Trend of fewer new HIV diagnoses continues in 2017

Since 2008 there has been a decreasing trend in the annual number of new HIV diagnoses to below 900 new diagnoses in recent years. This decreasing trend continued in 2017. The projected number of new diagnoses for 2017 is 749, although this may change as registration of HIV diagnoses for 2017 has not yet been finalised.

Majority of new diagnoses continue to be in men who have sex with men

In 2017, the majority (69%) of newly-diagnosed infections were in men who have sex with men (MSM), while 23% were acquired through heterosexual contact and around 7% through other or unknown modes of transmission (*Figure 1*).

Figure 1: *Most likely route of HIV transmission in people in HIV care in the Netherlands in 2017.*



People newly-diagnosed with HIV rapidly receive specialised care

Over 95% of people newly-diagnosed with HIV entered specialised HIV care within 6 weeks after diagnosis. This rate was more or less the same regardless of where the diagnosis was made (i.e., hospital, general practice, sexually transmitted infections clinic, or other test location).

HIV testing is becoming more common

The rates of testing for HIV appear to be increasing in the Netherlands. This conclusion is based on the following observations. Firstly, our data show that the proportion of individuals with a previously negative HIV test has increased (73% of MSM, 33% of other men and 49% of women diagnosed in 2017 had a reported previous negative test). In addition, the proportion of individuals who are diagnosed with HIV relatively early in their infection (including during primary HIV infection) continues to increase, particularly among MSM. This is reflected in the CD4 count at diagnosis gradually having risen over time to a median of 380 cells/mm^3 in 2017.

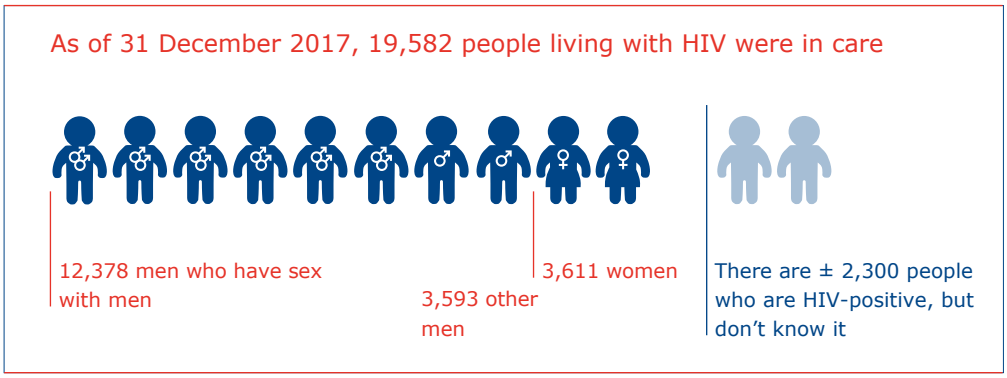
Late presentation for care remains a problem that needs attention

Despite the observed earlier diagnosis among certain groups, too many people still present late for care, i.e., with an already markedly impaired immune system (CD4 count below 350 cells/mm^3) or even AIDS; in 2017, this was the case for 37% of MSM, 63% of other men and 52% of women.

How many people were in HIV care in 2017?

As of 31 December 2017, a total of 19,582 people living with HIV in the Netherlands (19,390 adults and 192 children and adolescents) were known to be in care in one of the 26 adult or 4 paediatric HIV treatment centres (*Figure 2*).

***Figure 2:** Number of people living with HIV and in care in the Netherlands in 2017.*



Continuum of HIV care in 2017: 90-93-95

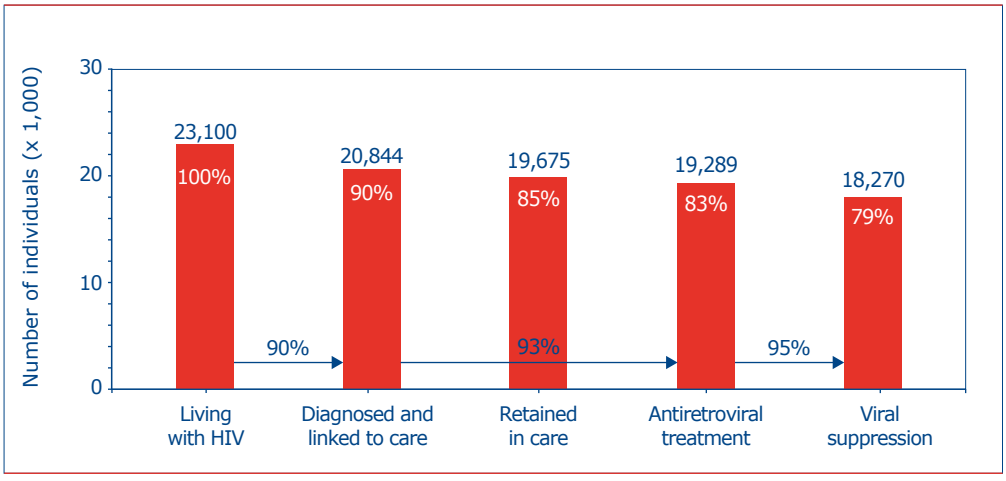
One of the goals of HIV treatment is to achieve viral suppression. The key steps that need to be achieved to reach viral suppression are illustrated in a continuum of HIV care. A continuum of care also gives a measure of progress towards achieving the UNAIDS 90-90-90 goals for HIV care by 2020.

The continuum of care in *Figure 3* shows that the Netherlands has reached these goals (90-93-95 in 2017):

- By the end of 2017, 23,100 individuals were estimated to be living with HIV, of whom an estimated 2,300 were still undiagnosed.
- In total, 20,844 individuals (**90%** of the total number estimated to be living with HIV) had been diagnosed, linked to care, and registered by SHM.
- Of the individuals who had been diagnosed, linked to care, and registered by SHM, the majority (19,289; **93%**), had started antiretroviral treatment, and 18,270 of those (**95%**) had achieved viral suppression.

This means that overall, 79% of the total estimated population living with HIV and 88% of those diagnosed and linked to care had a suppressed viral load by the end of 2017.

Figure 3: Continuum of HIV care for the total estimated HIV-positive population in the Netherlands by the end of 2017, based on UNAIDS 90-90-90 goals for 2020: 90-93-95.



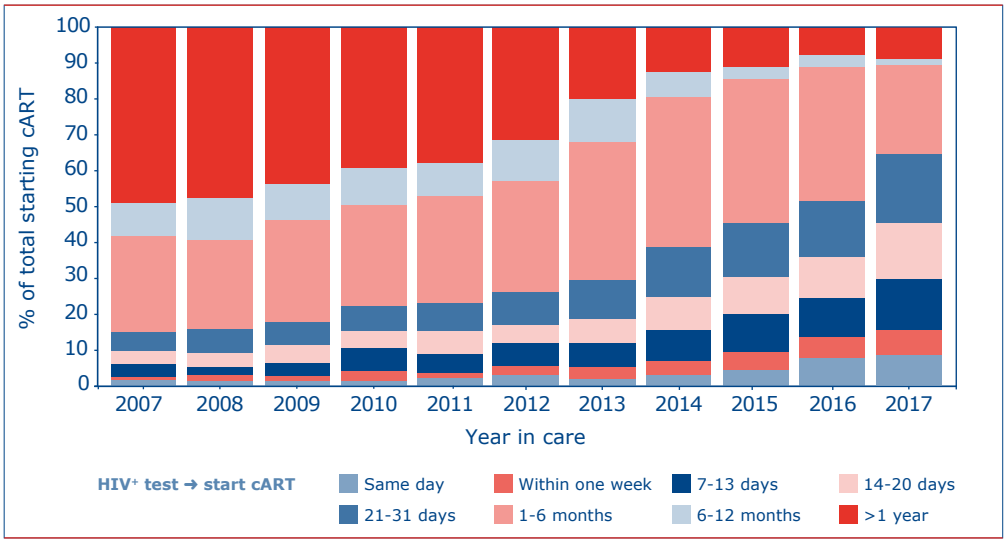
The figures for the Netherlands are impressive compared with other parts of the world. Nonetheless, in 2017 there were around 750 new diagnoses and an estimated 2,300 people who remained undiagnosed. To achieve a significant decline in these numbers, novel trans-disciplinary strategies are needed to simultaneously reduce the likelihood of HIV transmission in key populations at risk, identify individuals with HIV infection early, rapidly link all people living with HIV to care, and immediately offer them the possibility of starting combination antiretroviral therapy.

Combination antiretroviral therapy in adults

In 2017, most people started HIV treatment within a month of diagnosis

People are increasingly starting cART sooner after being diagnosed with HIV. Of those starting cART in 2017 more than half did so within one month, and 90% within 6 months after diagnosis (*Figure 4*). Importantly, this was the case irrespective of the CD4 cell count at diagnosis.

Figure 4: *Time between HIV diagnosis and starting combination antiretroviral therapy (cART) for those starting cART between 2007–2017.*



Legend: *cART=combination antiretroviral therapy.*

People are increasingly starting treatment with a less impaired immune system

People are increasingly starting cART at higher CD4 counts. The proportion of people who had a CD4 count of 500 cells/mm^3 or above at diagnosis and who had begun cART within 6 months of diagnosis rose from 87% in 2015 to 91% in 2017.

Most common cART regimens in 2017

Initial regimens

More than 80% of people started on an integrase inhibitor-containing regimen in 2017, with abacavir/lamivudine/dolutegravir and tenofovir alafenamide/emtricitabine/cobicistat-boosted elvitegravir being the most frequently prescribed initial regimens in 2017.

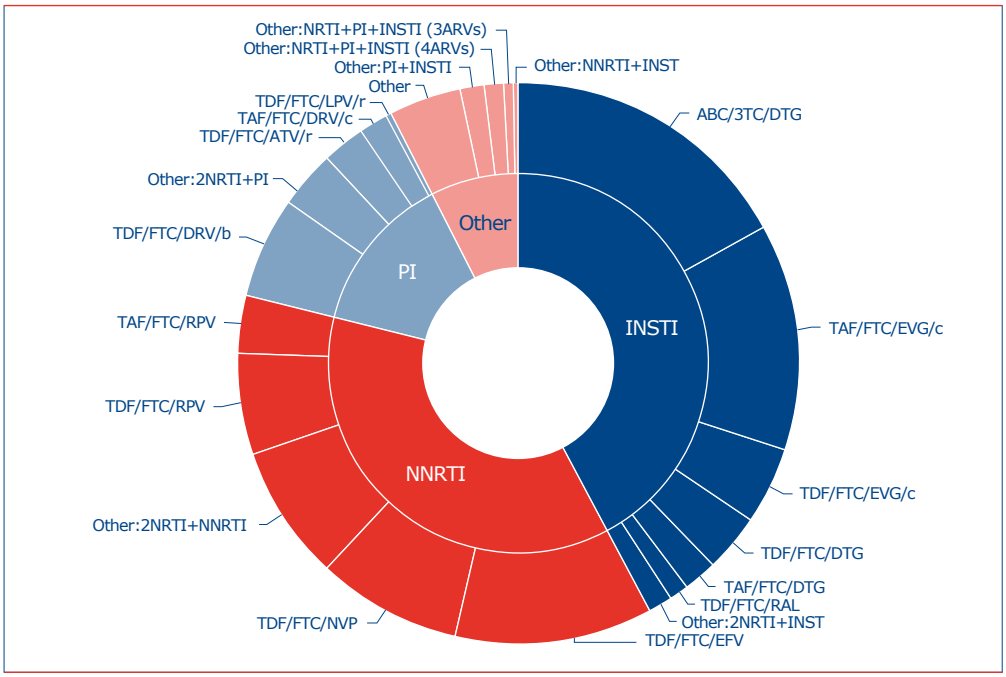
The likelihood of discontinuing or switching the initial regimens has been decreasing since 1996. As in previous years, toxicity continued to be a main reason for discontinuing or switching the initial regimen during the first year of treatment. Toxicity-related discontinuations were often due to neuropsychiatric, gastrointestinal, or renal problems, or medication-related skin rash. Other, more recent, important reasons for discontinuation or regimen switch during the first year of treatment include regimen simplification or the availability of new drugs.

Integrase inhibitor–based cART used increasingly frequently

Since its introduction a few years ago, integrase inhibitor-based cART has been implemented on a large scale in the Netherlands: in 2017, 42% of all adults in care and on cART received an integrase inhibitor, compared to 27% in 2015. Half of the population on cART in 2017 received a backbone consisting of tenofovir disoproxil fumarate/emtricitabine, although the availability of new fixed-dose combinations has led to an increase in the use of abacavir/lamivudine and tenofovir alafenamide/emtricitabine.

Among all HIV-positive individuals in care and on treatment in 2017, the majority received a cART regimen based on two nucleoside analogue reverse transcriptase inhibitors (NRTIs), combined with an integrase inhibitor (42%), a non-nucleoside reverse transcriptase inhibitor (NNRTI, 36%), or a protease inhibitor (14%) *(Figure 5)*. The most commonly-prescribed regimens in 2017 were abacavir/lamivudine/dolutegravir (17%), tenofovir alafenamide/emtricitabine/cobicistat-boosted elvitegravir (13%), and tenofovir disoproxil/emtricitabine combined with efavirenz (11%) or nevirapine (8%).

Figure 5: Combination antiretroviral therapy (cART) use in 2017 by all HIV-positive individuals in care.



Legend: 3TC=lamivudine; b=boosted (cobicistat or ritonavir); /r=ritonavir-boosted; /c=cobicistat-boosted; ABC=abacavir; ATV=atazanavir; DRV=darunavir; DTG=dolutegravir; EFV=efavirenz; EVG=elvitegravir; FTC=emtricitabine; INSTI=integrase inhibitor; LPV=lopinavir; NRTI=nucleoside analogue reverse transcriptase inhibitor; NNRTI=non-nucleoside reverse transcriptase inhibitor; NVP=nevirapine; PI=protease inhibitor; RAL=raltegravir; RPV=rilpivirine; TAF=tenofovir alafenamide; TDF=tenofovir disoproxil fumarate.

Excellent virological response, including in long-term survivors

Both short-term and long-term viral suppression rates remain high and continue to improve. Of all adults in care and on cART in 2017, 97% had an undetectable viral load (<200 copies/ml). Individuals who had been diagnosed with HIV before 1996 and who remained in care and on cART in 2017 (i.e., long-term survivors) had equally high levels of viral suppression.

Changing cART landscape

Following revised HIV treatment guidelines, prompt cART initiation has continued to become more common in 2017. In recent years, the introduction of new integrase inhibitor-based once-daily fixed-dose combinations has changed the landscape of cART use in the Netherlands. All currently-recommended regimens are durable.

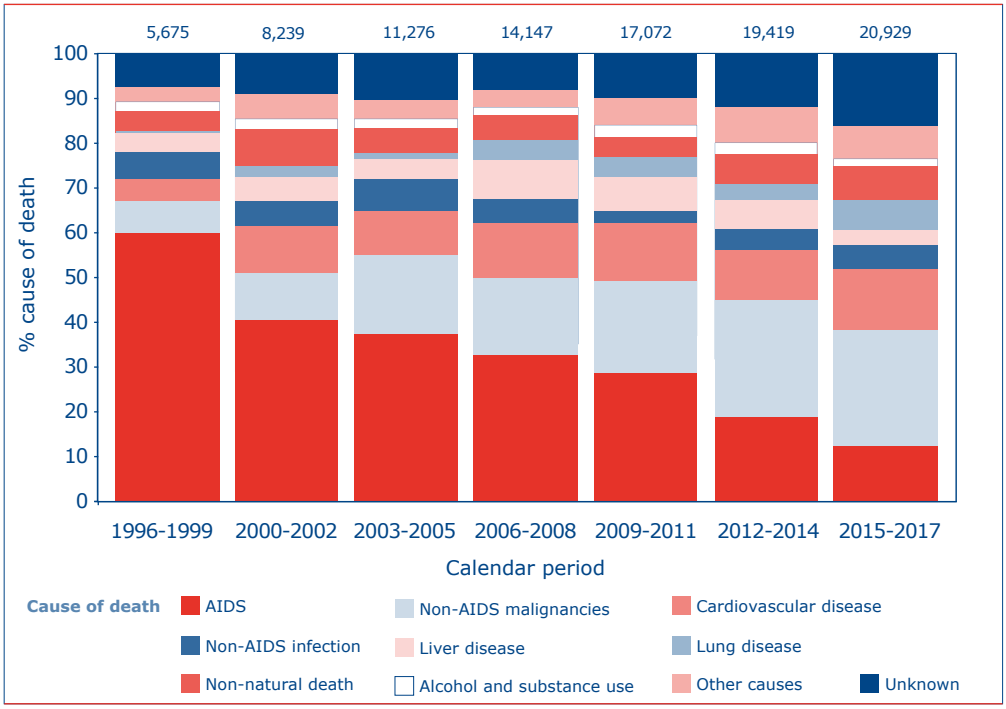
Morbidity and mortality

Sustained decline in AIDS-related death

Mortality remains low in HIV-positive individuals in care in the Netherlands. There has been a sustained decline in the risk of death from AIDS, with a shift towards death from non-AIDS comorbidities, including non-AIDS-defining malignancies (NADM), cardiovascular disease (CVD) and chronic liver disease *(Figure 6)*.

Those cases of AIDS-related death that do occur are largely driven by late entry into care, which once again stresses the importance of identifying and linking individuals to care earlier in the course of the infection.

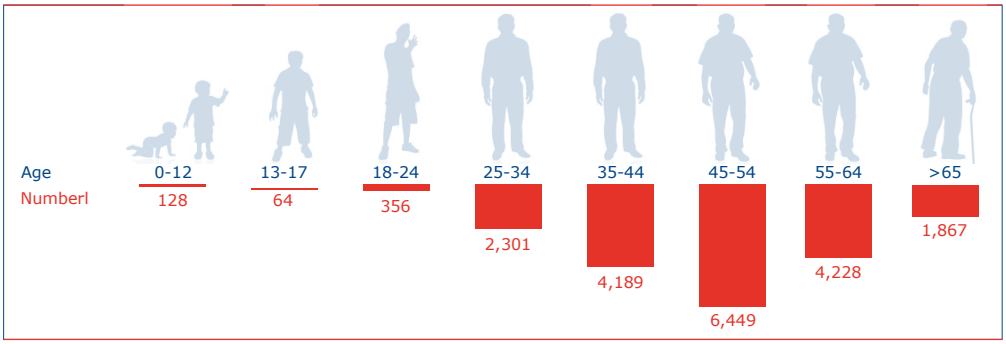
Figure 6: *Relative changes in cause of death in different calendar periods since the introduction of combination antiretroviral therapy (cART) in the Netherlands. Numbers above each bar represent the number of people at risk during that calendar period.*



Ageing and comorbidities

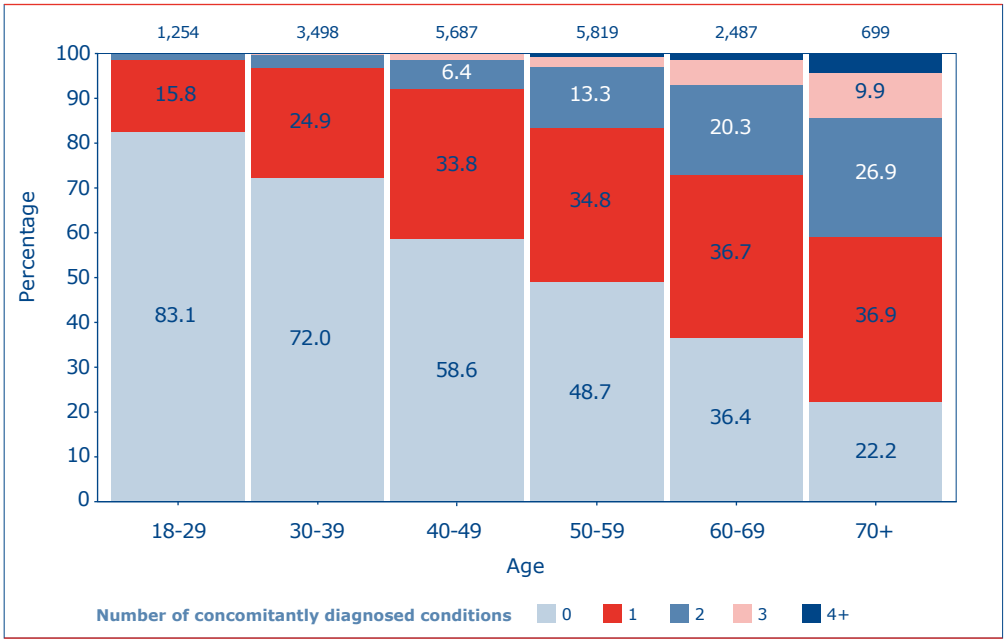
A substantial proportion of those people who were newly-diagnosed with HIV and entered HIV care in 2017 were older individuals; 27% were 50 years or older. At the same time, the overall population of people with HIV in care in the Netherlands also continues to age, with 48% currently older than 50 years compared with 39% in 2013 *(Figure 7)*.

Figure 7: Age distribution of people living with HIV and in care in the Netherlands in 2017.



As in the general population, older age was an important risk factor for comorbidities such as cardiovascular disease and non-AIDS malignancies. Of particular concern is the increasing proportion of individuals with multiple comorbidities, the risk of which appears to be increased in those with HIV *(Figure 8)*.

Figure 8: Prevalence of non-HIV/AIDS multimorbidity in adults in HIV care in 2017. Numbers on top of the bars represent the number of individuals contributing data to that age category.



Cardiovascular risk

Despite the increasing age of the HIV-positive population, the proportion at high or very high cardiovascular risk only increased slightly over the period 2000-2017. This suggests that cardiovascular risk management may have improved over time. Significant room for further improvement remains, however, given the suboptimal use of statin therapy, antihypertensive therapy and antiplatelet therapy as secondary prevention following a myocardial infarction or ischaemic stroke, and the limited uptake of these medications in the prevention of primary cardiovascular disease in high-risk individuals.

Non-AIDS malignancies

The most common non-AIDS malignancies are lung cancer, Hodgkin's lymphoma, anal, gastrointestinal, prostate, and head and neck cancers. Although the incidence rate of non-AIDS malignancies in the Netherlands has remained stable over time, the number of deaths due to these malignancies has increased. However, when taking the increasing age of the HIV-positive population into account, we did observe a decline in the risk of new non-AIDS malignancies in men, including anal cancer. This may be the result of a reduction in risk factors such as smoking, as well as expanded screening and treatment for early stages of anal cancer, together with a higher proportion of individuals living with higher CD4 cell counts in more recent years.

Improved awareness of risk factors may reduce comorbidity

Resilient ageing in people living with HIV and a lower comorbidity burden can be achieved by increasing awareness of the role of modifiable and often lifestyle-related risk factors among both physicians and the people living with HIV themselves. This is particularly relevant for older individuals and those at increased risk of comorbidity, and applies not only to conditions such as cardiovascular disease and diabetes mellitus, but also to cancer, chronic kidney disease and loss of bone mineral density.

Hepatitis B and C virus co-infections

Hepatitis B and C virus screening is now universal

Hepatitis C (HCV) and hepatitis B (HBV) co-infections are far more prevalent in HIV-positive individuals than in the general population due to shared routes of transmission. Screening for HCV and HBV co-infection is part of standard HIV care in the Netherlands, the presence or absence of these co-infections is now documented for almost all HIV-positive individuals.

Hepatitis C virus co-infection

Approximately 12% of all individuals monitored by SHM had evidence of ever having been exposed to HCV, with 6% having documented evidence of chronic infection and 2% having evidence of acute HCV infection at the time of the first diagnosis. Most individuals with HCV infection were male and from the Netherlands or other European countries.

Hepatitis B virus co-infection

The prevalence of chronic HBV infection has decreased over time as a result of increased HBV vaccination rates, together with the HBV-prophylactic effect of tenofovir for treatment of HIV. Six percent of individuals ever in care were found to have chronic HBV infection.

HBV vaccination remains a priority

An estimated 29% of HIV-positive individuals overall and 21% of MSM had not been exposed to HBV and had not been successfully vaccinated and therefore may remain at risk of acquiring HBV. These findings illustrate the importance of continuing our efforts to increase successful HBV vaccination rates in this subgroup, particularly in those who are not receiving a tenofovir-containing antiretroviral regimen.

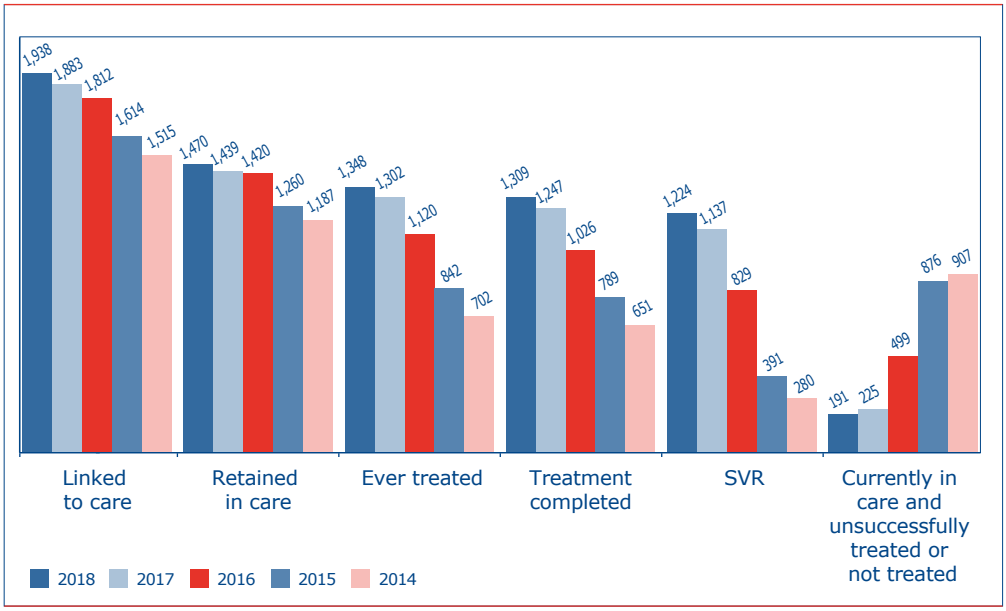
Risk of dying from HCV or HBV co-infection is decreasing

Overall, HIV-positive individuals with a chronic HCV or HBV co-infection remain at increased risk of liver-related morbidity and mortality. However, people diagnosed with chronic HCV or HBV after 2000 (i.e., after tenofovir was introduced), have a lower risk of liver-related death. For those with chronic HBV infection, this is likely a result of increasingly effective HBV treatment through the use of tenofovir-containing cART that became available in 2002.

Successful HCV treatment with direct-acting antivirals has progressed further

Our data clearly show that the large majority of HIV-positive individuals with HCV co-infection have now received treatment for HCV. By 31 December 2017, over 800 individuals had received or were receiving treatment with novel direct-acting antiviral agents (DAAs). Of all people treated with DAAs, 97% achieved a sustained virological response and no longer had evidence of an active HCV infection. These developments have resulted in fewer HCV co-infected individuals remaining in need of treatment than in previous years *(Figure 9)*.

Figure 9: Hepatitis C virus continuum of care.



***Legend:** SVR=sustained virological response.*

Successful HCV treatment prevents HCV transmission

Successful treatment of HCV may also prevent onward HCV transmission, as suggested by the lower number of acute HCV infections observed in the past year, together with the rapid decline in prevalence of active HCV infections. In MSM the prevalence of active HCV infections decreased to less than 1% in 2017. Although there has been a drop in the HCV re-infection rate in most recent years, re-infection following successful treatment continues to be reported, indicating that HCV transmission has not ceased completely.

Regular HCV screening among sexually-active MSM recommended

Over time, the rapidly expanding availability of DAA regimens for HCV, together with optimised screening for HCV co-infection, is expected to limit the impact of HCV co-infection on long-term liver-related morbidity and mortality; however, this effect should be monitored. To reduce new HCV infections among the key affected population of sexually-active MSM, regular screening for HCV among successfully-treated individuals is recommended for early detection of HCV re-infections, in combination with preventive behavioural interventions.

Children living with HIV

No new cases of perinatal transmission of HIV within the Netherlands since 2015

Of 603 children diagnosed with HIV before the age of 18 and ever registered by SHM, the majority (77%) remain in care.

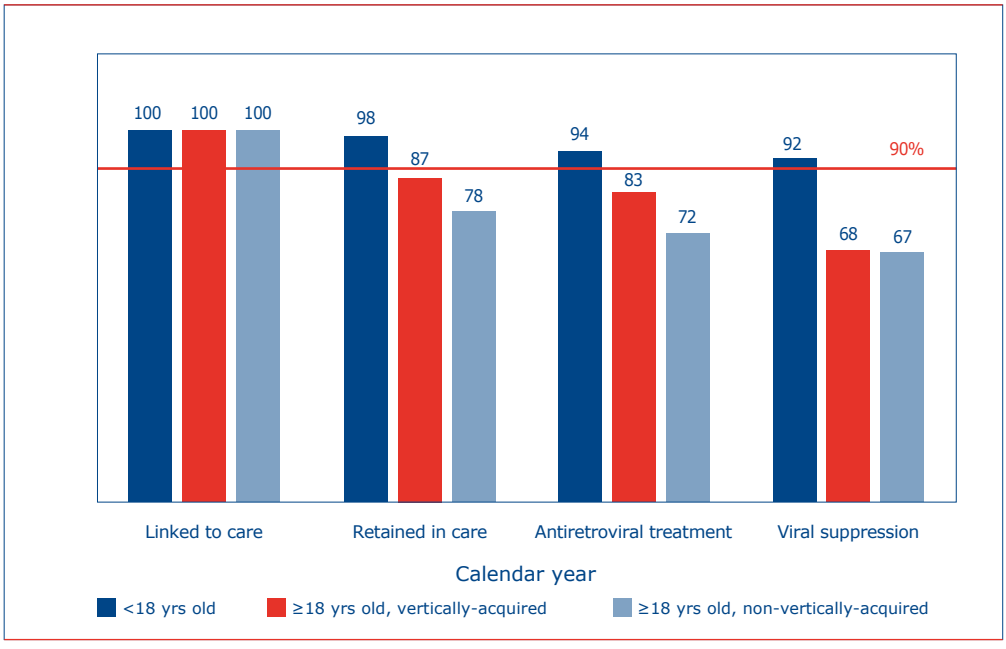
The majority (67%) of children who acquired HIV perinatally were born outside the Netherlands, Perinatal transmission of HIV within the Netherlands has become extremely rare, with no new cases reported since 2015.

Of the children who are currently in care, 115 (25%) were born outside the Netherlands and adopted by Dutch parents.

Favourable outcomes for HIV-positive children

There is a high retention-in-care rate among children currently under the age of 18. Outcomes for children who are receiving cART are generally favourable and have resulted in a low mortality rate and good long-term immunological responses *(Figure 10)*.

Figure 10: *Cascade of care by age and mode of HIV acquisition, as of 31 December 2017. The numbers on top of the bars indicate the proportion of individuals.*



Poorer viral suppression around transition to adult care

Of those individuals who were originally registered as a child, 77% were still in care in 2017, 61% of whom were older than 18 as of 31 December 2017. Of the children who had transitioned from paediatric to adult care, 21% did not have suppressed viraemia at the time of transition, suggesting challenges for these adolescents with respect to adherence to treatment around the time of transition to adult care.

Optimisation of long-term care for young people

The relatively large proportion of adolescents who have inadequately-suppressed viraemia at the time of transitioning to adult care illustrates that long-term care for this particularly vulnerable and difficult-to-manage group of young individuals clearly needs to be further optimised.

Quality of care

High overall retention in care

The quality of care provided in Dutch adult HIV treatment centres was explored using indicators based on the national guidelines issued by the Dutch Association of HIV-Treating Physicians. Overall, retention in care was found to be high in most HIV treatment centres in the Netherlands, although it was lower for people not born in the Netherlands.

Earlier start of cART and high rates of viral suppression

In addition, across most centres, people are starting cART sooner after entering into care, confirming that most centres are following the guideline to offer cART to everyone with newly-diagnosed HIV regardless of CD4 count. However, there are some centres in which this policy could be improved further for people who enter care with CD4 cell counts above 350 cells/mm^3. Regardless of time since entering care, a median proportion of 99% of all individuals who entered care between 2012 and 2016 and who were retained in care in 2017 had initiated cART.

Viral suppression rates in the first 6 months on cART, as well as during longer term use of treatment, were high across all centres, regardless of the number of people receiving care at a particular centre.

Heterogeneity in repeat HCV screening

Greater heterogeneity was observed in repeat HCV screening in MSM. This variation is thought to be a difference in screening policy, with centres screening partly on the basis of elevated liver enzymes. Given that HCV transmission still occurs, continued monitoring of (repeat) HCV screening rates is certainly warranted.

HIV in Curaçao

In recent years, individuals with HIV in care at the St Elisabeth Hospital in Willemstad in Curaçao appear to be diagnosed increasingly earlier in their infection, as shown by a declining proportion of individuals presenting late for care. As a consequence, cART is being started at increasingly higher CD4 cell counts. However, although early start of treatment appears to be possible, data also suggest that long-term retention in care needs to be improved to optimise the sustained effect of treatment.

Amsterdamse Cohort Studies

The Amsterdam Cohort Studies (ACS) on HIV infection and AIDS were started in 1984 a few years after the first cases of AIDS were diagnosed in the Netherlands. By enrolling men who have sex with men (MSM) in a prospective cohort study, the ACS aimed to investigate the prevalence and incidence of HIV-1 infection and AIDS, the associated risk factors, the natural history and pathogenesis of HIV-1 infection, and the effects of interventions. A second cohort involving people who use drugs (PWUD) was initiated in 1985. Follow up of PWUD ended in 2016. In 2017, the cohorts reached 33 years of follow up.

As of 31 December 2017, 2,796 MSM had been included in the ACS, of whom 607 were HIV-positive when they entered the study and 253 seroconverted during follow up. In 2017, 701 HIV-negative and 73 HIV-positive MSM remained in active follow up at the GGD Amsterdam, with an additional 256 HIV-positive MSM being followed at the MC Jan van Goyen or the DC Klinieken Lairesse-Hiv Focus Centrum in Amsterdam. In 2017, 60 additional HIV-negative MSM were recruited. The median age in this group was 29.5 years, while that of the total group of MSM in active follow up was 42.5 years at their last visit. The majority (85.0%) of the total group were born in the Netherlands and 83.8% were residents of Amsterdam. Finally, 75.3% of the participants had a college degree or higher. In 2017, 2 MSM participating in the ACS seroconverted for HIV. The observed HIV incidence among MSM has remained relatively stable and low in recent years and was 0.5 per 100 person years in 2017.