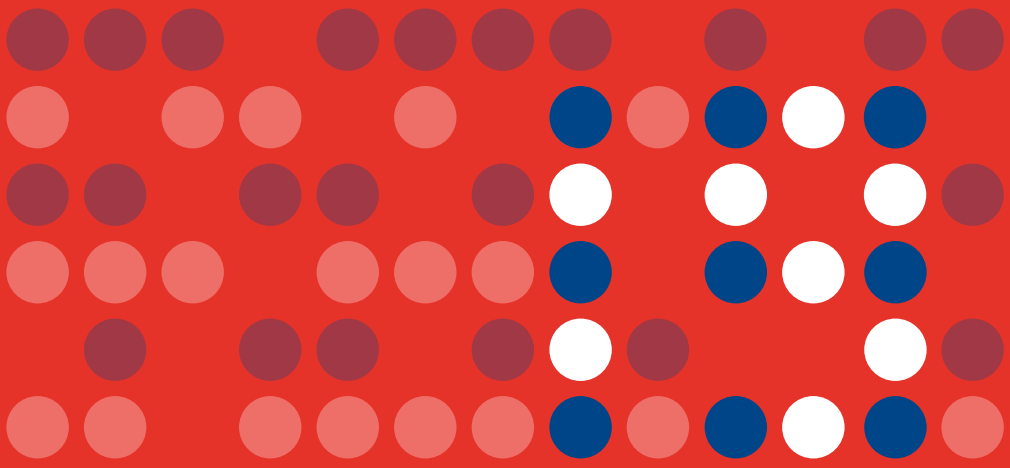
Human Immunodeficiency Virus (HIV)
Infection in the Netherlands

HIV Monitoring

HIV Monitoring Report 2019

Summary and Recommendations

The Monitoring Report 2019 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 2019 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 18th 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, HIV-1-positive children, and pregnant women living with HIV, along with a chapter on quality of care in the 24 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

HIV in the Netherlands: key findings from our 2019 HIV Monitoring Report

This chapter provides a summary of the key findings from the latest HIV Monitoring Report that was published on 13 November 2019. The full report is available on our website.

The HIV epidemic in the Netherlands in 2018

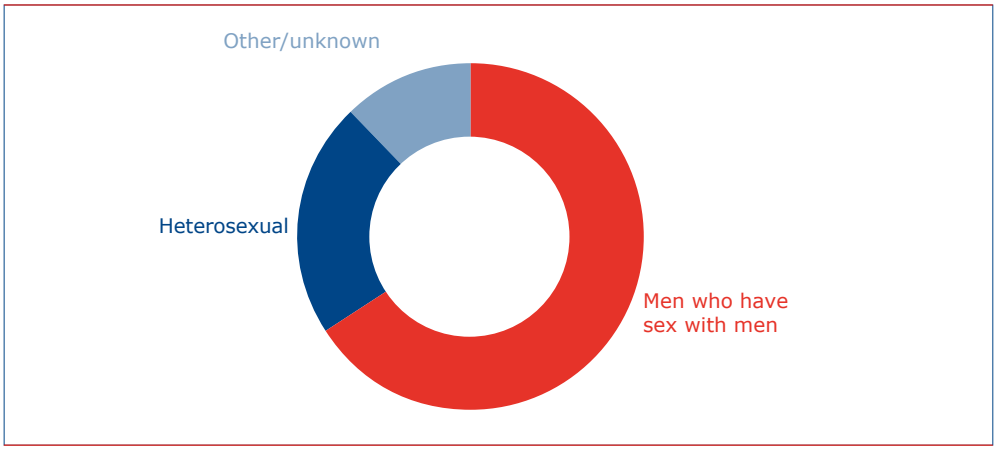
Trend of fewer new HIV diagnoses continues in 2018

Since 2008 there has been a decreasing trend in the annual number of newly-diagnosed HIV infections. This decreasing trend continued in 2018. The projected number of new diagnoses for 2018 is 664, compared with 749 in 2017.

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

In 2018, the majority (66%) of newly-diagnosed infections were in men who have sex with men (MSM), while 22% were acquired through heterosexual contact and around 12% through other or unknown modes of transmission

Figure 1: Most likely route of HIV transmission in people newly-diagnosed in 2018.



People newly-diagnosed with HIV rapidly receive specialised care

Just 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, sexual health centre, 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 a number of observations. Firstly, our data show that the proportion of individuals with a previously negative HIV test has increased (74% of MSM, 30% of other men and 41% of women diagnosed in 2018 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 390 cells/mm^3 in 2018.

Number of newly-acquired infections is declining

The estimated number of newly-acquired HIV infections is declining and reached 320 in 2018 (compared with 440 in 2017). This downward trend over the years confirms that the Netherlands is on track to achieving the UNAIDS' fast-track target for 2020 of a 75% reduction in annual newly-acquired HIV infections since 2010.

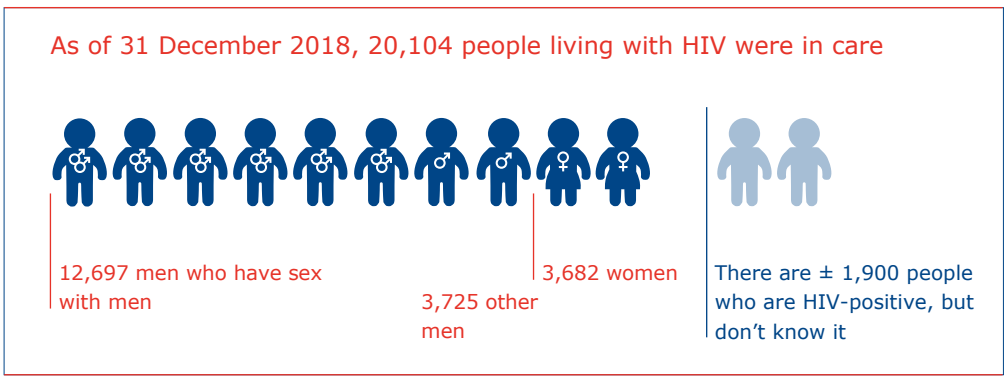
Late presentation for care remains a problem that needs attention

Despite the observed earlier diagnosis in certain groups, 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 2018, this was the case for 41% of MSM, 66% of other men and 45% of women.

How many people were in HIV care in 2018?

As of 31 December 2018, a total of 20,104 people living with HIV in the Netherlands (19,910 adults and 194 children and adolescents) were known to be in care in one of the 24 adult or 4 paediatric HIV treatment centres.

Figure 2: Number of people living with HIV and in care in the Netherlands in 2018.



Continuum of HIV care in 2018: 92-93-96

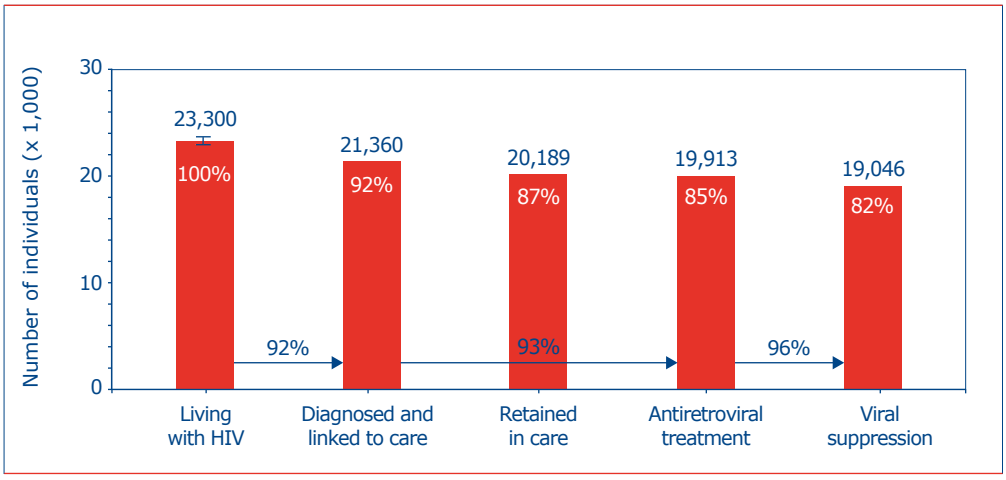
One of the goals of HIV treatment is to achieve viral suppression. The key steps that need to be achieved to reach viral suppression are illustrated in a continuum of HIV care. A continuum of care also gives a measure of progress towards achieving the UNAIDS 90-90-90 goals for HIV care by 2020.

The continuum of care for the Netherlands confirms that we have reached these goals (92-93-96 in 2018, see *Figure 3*):

- By the end of 2018, 23,300 individuals were estimated to be living with HIV, of whom an estimated 1,900 were still undiagnosed.
- In total, 21,360 individuals (**92%** 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 (19,913; **93%**), had started antiretroviral treatment, and 19,046 of those (**96%**) had achieved viral suppression.

This means that overall, 82% of the total estimated population living with HIV and 89% of those diagnosed and linked to care had a suppressed viral load by the end of 2018.

Figure 3: Continuum of HIV care for the total estimated HIV-positive population in the Netherlands by the end of 2018, based on UNAIDS 90-90-90 goals for 2020: 92-93-96.



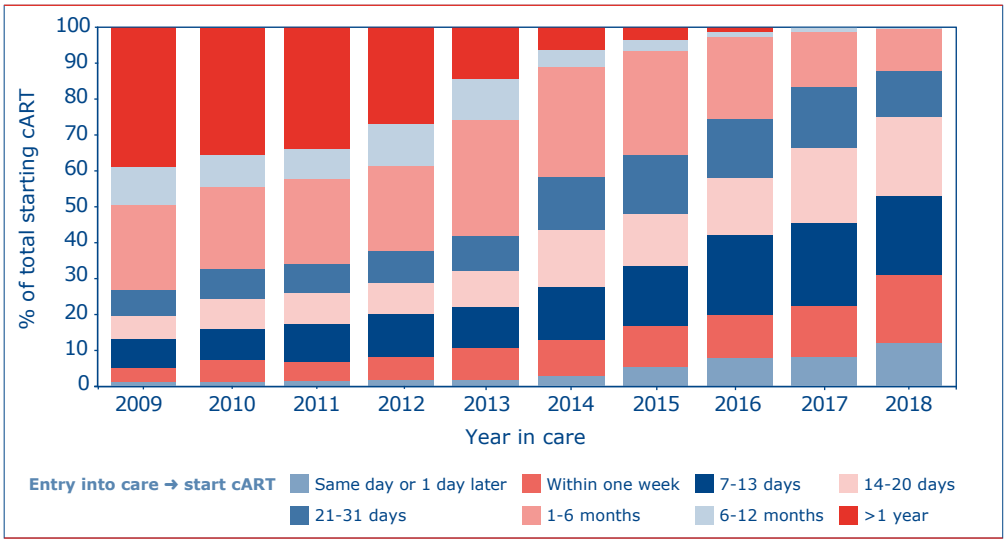
The figures for the Netherlands are impressive compared with other parts of the world. Nonetheless, in 2018 there were 664 new diagnoses and an estimated 1,900 people who remained undiagnosed. To achieve a significant decline in these numbers, novel transdisciplinary strategies are needed to simultaneously reduce the likelihood of HIV transmission in key populations at risk (including by provision of pre-exposure prophylaxis or PrEP), 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 2018, most people started HIV treatment within a month of entry into care

People are increasingly starting combination antiretroviral therapy (cART) soon after being diagnosed with HIV and entering care. In 2018, close to 90% of people started cART within one month of entry into care. Importantly, this was the case irrespective of the CD4 cell count at entry into care. In addition, in 2018, 3.5% started cART on the same day or the day after their HIV infection was diagnosed.

Figure 4: Time between entry into care and starting combination antiretroviral therapy (cART) for those starting cART between 2009–2018.



Legend: cART=combination antiretroviral therapy.

Most common cART regimens in 2018

Initial regimens

Just over 75% people started on an integrase inhibitor-containing regimen in 2018, with abacavir/lamivudine/dolutegravir and tenofovir alafenamide/emtricitabine/cobicistat-boosted elvitegravir being the most frequently-prescribed initial regimens in 2018.

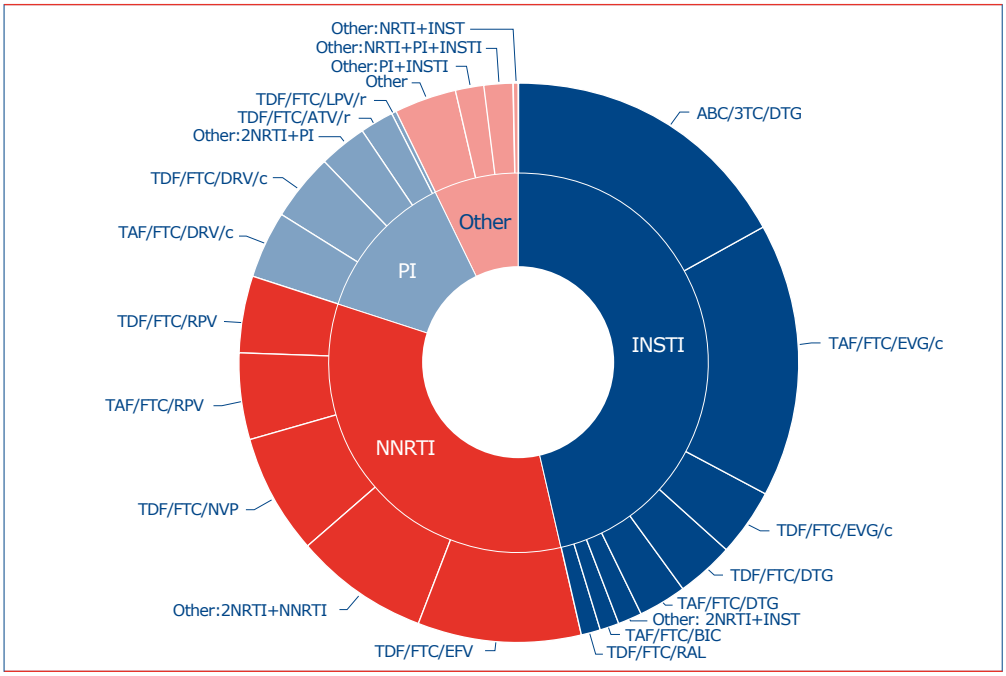
The likelihood of discontinuing or switching the initial regimen has been decreasing since 1996. As in previous years, toxicity continued to be a main reason for discontinuing or switching the initial regimen during the first year of treatment. Toxicity-related discontinuations were often due to neuropsychiatric,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

Integrase inhibitor–based cART used increasingly frequently

Integrase inhibitor-based cART continues to be further implemented on a large scale in the Netherlands: in 2018, 46% of all adults in care and on cART received an integrase inhibitor, compared with 39% in 2017. While 35% of the population on cART in 2018 received a backbone containing tenofovir disoproxil fumarate, new fixed-dose combinations have also led to an increase in the use of abacavir (35%) and tenofovir alafenamide (33%).

Among all HIV-positive individuals in care and on treatment in 2018, the majority (92.8%) received a cART regimen based on two nucleoside analogue reverse transcriptase inhibitors (NRTIs), combined with an integrase inhibitor (46.6%), a non-NRTI (NNRTI, 33.4%), or a protease inhibitor (14%) (*Figure 5*). The most commonly-prescribed regimens in 2018 were abacavir/lamivudine/dolutegravir (17.2%), tenofovir alafenamide/emtricitabine/cobicistat-boosted elvitegravir (15.6%), and tenofovir disoproxil /emtricitabine combined with efavirenz (9.4%) or nevirapine (7%).

Figure 5: Combination antiretroviral therapy (cART) use in 2018 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; BIC=bictegravir; 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 receiving cART for at least 12 months and in care in 2018, 98% had achieved viral suppression (viral load <200 copies/ml). Individuals who had been diagnosed with HIV before 1996 and who remained in care and on cART in 2018 (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 2018. 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.

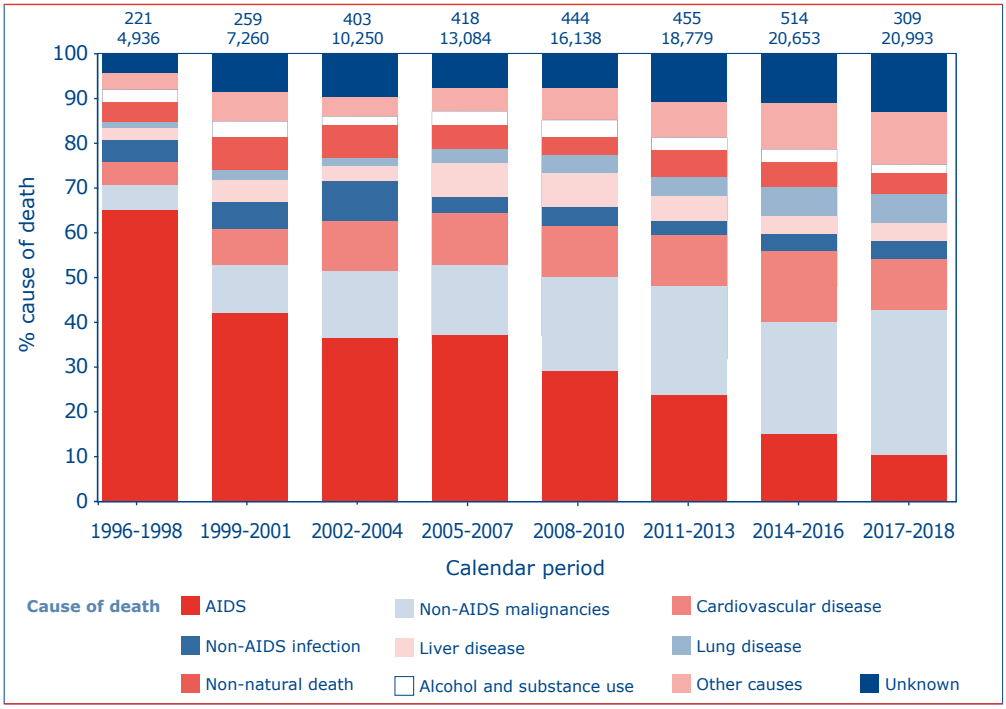
Morbidity and mortality

Sustained decline in AIDS-related death

Mortality remains low in HIV-positive individuals in care in the Netherlands. Since cART became available in the Netherlands in 1996, there has been a sustained decline in the risk of death from AIDS. Death is now increasingly likely to be caused by 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.

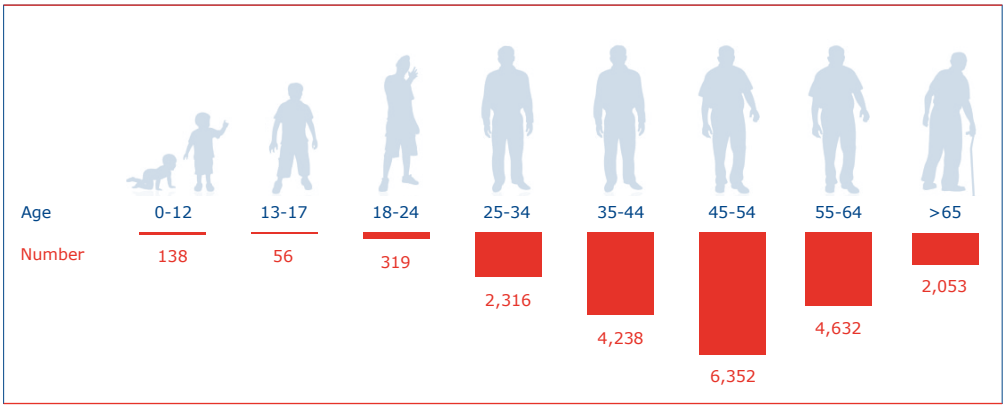


Ageing and comorbidities

A substantial proportion of those people who were newly-diagnosed with HIV and entered HIV care in 2018 were older individuals; 24% were 50 years or older. At the same time,

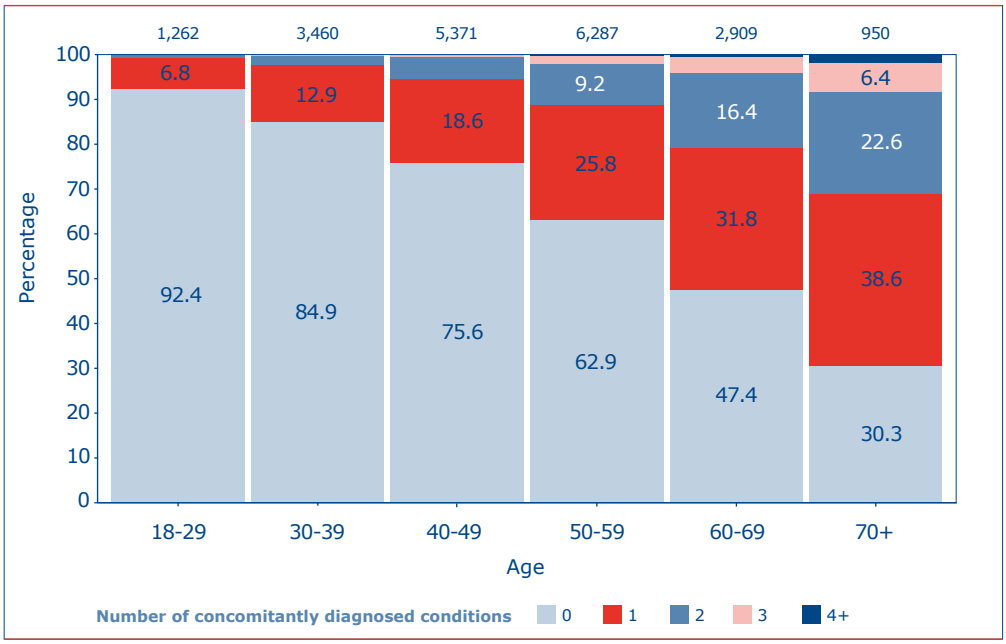
the overall population of people with HIV in care in the Netherlands also continues to age, with 50% currently older than 50 years (*Figure 7*).

Figure 7: *Age distribution of people living with HIV and in care in the Netherlands in 2018.*



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 2018. 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 cardiovascular risk only increased slightly over the period 2000-2018. This suggests that cardiovascular risk management has improved over time. Nonetheless, there remains significant room for further improvement, given the suboptimal use of statin therapy, antihypertensive therapy and low-dose acetylsalicylic acid use as secondary prevention following a myocardial infarction or ischaemic stroke, as well as the low, albeit slowly improving, uptake of these medications in the prevention of primary cardiovascular disease.

Non-AIDS malignancies

The most common non-AIDS malignancies are lung, anal, and head and neck cancers, as well as Hodgkin's lymphoma. The incidence rate of non-AIDS malignancies in the Netherlands has remained stable over time. However, when the increasing age of the HIV-positive population is taken into account, we observe a decline in the age-adjusted 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. Individuals who initiated ART within 12 months after their last HIV-negative test had a lower risk of being diagnosed with a non-AIDS-defining malignancy, independent of their current CD4 cell count and other risk factors, suggesting an additional health benefit of early initiation of ART.

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, 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.

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 the standard of HIV care in the Netherlands, and 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 5% having documented evidence of chronic infection and 3% 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 and tenofovir alafenamide for the treatment of HIV. Six percent of individuals ever in care were found to have, or have had, chronic HBV infection.

HBV vaccination remains a priority

An estimated 34% of HIV-positive individuals overall had not been exposed to HBV and had not been successfully vaccinated. These individuals remain at risk of acquiring HBV if they are not taking a cART regimen including tenofovir or tenofovir alafenamide. These findings illustrate the importance of continuing our efforts to increase successful HBV vaccination rates, particularly in those who are not receiving tenofovir-containing cART.

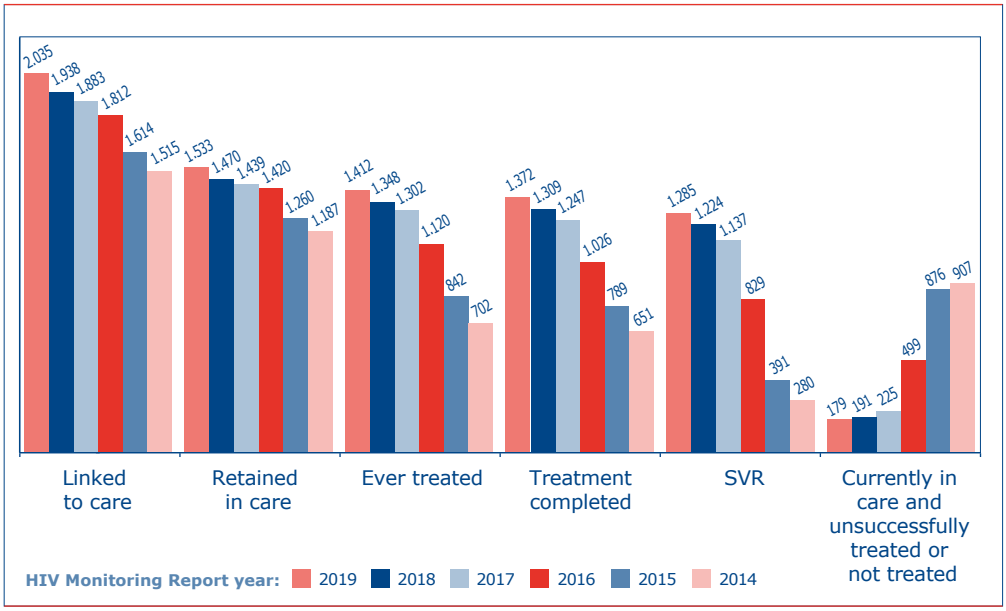
Risk of dying from HCV or HBV co-infection is decreasing

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 have had a steadily decreasing risk of liver-related death since 2010. 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 more widespread 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 effective treatment for HCV. By 31 December 2018, over 950 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*). However, not all individuals in need of treatment have yet received treatment with DAAs; this underlines the need for additional efforts to reach these people.

Figure 9: Hepatitis C virus continuum of care in people with HIV/HCV co-infection.



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 2018. 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 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 interventions to reduce HCV risk behaviours.

Pregnancies in women living with HIV-1 in the Netherlands

A total of 2,705 pregnancies were documented in 1,517 women in HIV care in the Netherlands. Of these women, 81% were born outside the Netherlands, mainly in sub-Saharan Africa (68%). Women who were born in the Netherlands were more likely to be aware of their HIV-positive status prior to conception than those born elsewhere (78% and 62%, respectively). In both groups, the most common mode of HIV acquisition was heterosexual contact (94%).

Fewer pregnancies

The number of pregnancies among women living with HIV-1 has been decreasing since 2009. This may be due to the increasing age of the women in HIV care, as well as a drop in national birth rates.

Higher detectable HIV RNA rates at the time of delivery

Almost all women (99%) were treated with antiretroviral therapy during pregnancy. As a result, maternal HIV RNA levels were below 50 copies/ml (i.e., undetectable) in 85% of the deliveries, and between 50-500 copies/ml in a further 10% of deliveries. However, we did see an increase in the proportion of women with detectable HIV RNA levels in 2018. This was primarily in women who were newly-diagnosed with HIV during pregnancy and consequently only started treatment during pregnancy. Therefore, it is important that women who are newly-diagnosed with HIV during pregnancy are closely monitored.

Perinatal transmission of HIV now very rare in the Netherlands

Due to the high rates of successful treatment in women living with HIV, perinatal transmission of HIV is rare in the Netherlands, with only one reported case since 2015. The majority (69%) of children who acquired HIV perinatally were born outside the Netherlands. In the Netherlands, in women who receive treatment and have undetectable HIV RNA levels, the rate of vertical transmission is 0.18%.

Suboptimal viral suppression rates during the post-partum period

Following the new guideline recommendation in 2015 to prescribe cART to all individuals regardless of CD4 count, it is now also recommended that all pregnant women continue cART after pregnancy. Since 2015, of those women who continued using antiretroviral therapy after delivery, 12% had at least one detectable HIV RNA measurement in the year following delivery. This may reflect poorer treatment compliance during the post-partum period.

To achieve viral suppression during delivery and maintain treatment compliance in the post-partum period, women living with HIV who start cART during pregnancy require additional support, not only during pregnancy but also post-partum.

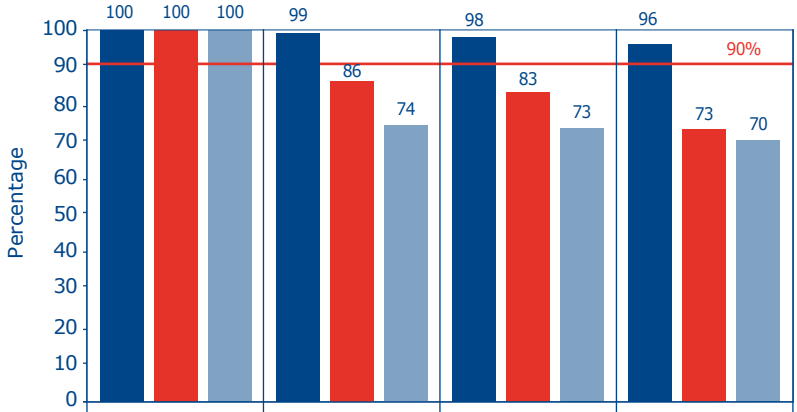
Children living with HIV

Of 504 children ever registered by SHM and who entered HIV care in the Netherlands, the majority (81%) remain in care. Of the children who are currently in care, 136 (27%) 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*).

Figuur 10: *Cascade of care by age and mode of HIV acquisition in people who acquired HIV in childhood, as of 31 December 2018. The numbers on top of the bars indicate the proportion of individuals.*



	Linked to care	Retained in care	On antiretroviral treatment	Virologically suppressed
Current age <18 years	195	194	191	187
Current age ≥18 years vertical transmission	140	121	116	102
Current age ≥18 years non-vertical transmission	125	93	91	88

Poorer viral suppression around transition to adult care

Of those individuals who were originally registered as a child, 81% were still in care in 2018, 52% of whom were older than 18 as of 31 December 2018. Of the children who had transitioned from paediatric to adult care, 20% 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 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

Comparing indicators to the national average

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. In this year's report, we also compared each centre's indicator to the national average, in a manner that takes into account the diverse mix of patients' geographical origin and routes of transmission that are found across centres.

In all centres the proportion of patients in care in 2018 who had initiated cART and had viral suppression were within the expected range of the national average.

High overall retention in care

Overall, retention in care was found to be high in most HIV treatment centres in the Netherlands, although in some centres 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. In fact, a median of 100% of all patients who entered care in 2016 and 2017 and who were retained in care in 2018 had initiated cART, while across all centres, more than 95% of patients in care in 2018 were on 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.

Amsterdam Cohort Studies

The Amsterdam Cohort Studies (ACS) on HIV infection and AIDS were started in 1984 shortly 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.

As of 31 December 2018, 2,888 MSM had been included in the ACS, of whom 607 were HIV-positive when they entered the study and 261 seroconverted during follow up. In 2018, 749 HIV-negative and 60 HIV-positive MSM remained in active follow up at the GGD Amsterdam, with an additional 197 HIV-positive MSM being followed at the MC Jan van Goyen or the DC Klinieken Lairesse-Hiv Focus Centrum in Amsterdam. In 2018, 92 additional HIV-negative MSM were recruited. The median age in this group was 28.1 years, while that of the total group of MSM in active follow up was 42.9 years at their last visit. The majority (83.7%) of the total group were born in the Netherlands and 85.7% were residents of Amsterdam. Finally, 75.9% of the participants had a college degree or higher. In 2018, 3 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 2018.

HIV in Curaçao

Over the years, an increasing proportion of individuals with HIV in care at the St Elisabeth Hospital in Willemstad in Curaçao have managed to achieve a suppressed viral load. 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. In addition, the proportion of people entering care with late-stage HIV infection remains high, although the proportion with advanced HIV disease appears to be decreasing.