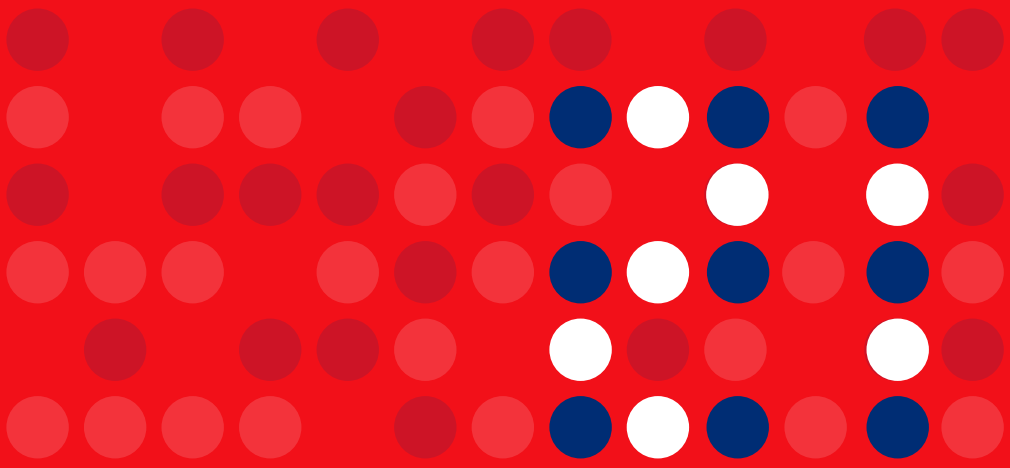
Human Immunodeficiency Virus (HIV)
Infection in the Netherlands

HIV Monitoring

HIV Monitoring Report 2021

Special report: COVID-19 in people living with HIV in the Netherlands



Special report

COVID-19 in people living with HIV in the Netherlands

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In this special chapter, we report on the consequences of the COVID-19 pandemic on the population of people living with HIV in the Netherlands. In the first section, we focus on the incidence of, and risk factors for severe COVID-19 in people living with HIV. The second section discusses the impact the COVID-19 pandemic has had on HIV care in general.

Incidence, risk factors, and outcomes of COVID-19 in people living with HIV

Background

The first documented case of SARS-CoV-2 infection in the Netherlands was on 27 February 2020[1]. By September 2021, an estimated cumulative 1.9 million Dutch individuals had acquired a SARS-CoV-2 infection, resulting in about 18,000 deaths[1]. The majority of SARS-CoV-2 infections result in a self-limiting disease with minor or mild symptoms. However, certain groups are at increased risk of severe COVID-19, hospitalisation, and death; for example, older individuals, men, certain ethnic groups, people with lower socio-economic status, and people diagnosed with certain ageing-associated, non-communicable comorbidities like obesity, hypertension, renal dysfunction, diabetes mellitus, and cardiovascular disease. People with certain inborn immunodeficiency syndromes, haematological malignancies, solid organ transplants, and people receiving immunosuppressive treatment are also at increased risk of severe outcomes. Currently, there are insufficient data available to confirm whether people living with HIV are at greater risk of developing severe COVID-19 than the general population: some studies suggest the risk is similar[2-8], while others suggest an increased risk of severe outcomes[9-13]. However, while most of these studies adjusted their analyses for age, sex, ethnicity, and comorbidities, many were conducted using data from general COVID cohorts, and missed detailed information on important HIV-related parameters, like use of antiretroviral therapy, plasma HIV-1 viremia, prior AIDS diagnoses, and current and nadir CD4 cell counts. Therefore, it also remains unclear whether, if people living with HIV are at greater risk of developing severe COVID-19, those risks are driven by differences in demographic characteristics, a high prevalence of non-HIV-related comorbidities, and/or HIV-related parameters. Many of the risk factors for severe COVID-19 in the general population are more prevalent in people living with HIV.

We describe the incidence, risk factors, and outcomes of COVID-19 in people living with HIV in the Netherlands using data collected up to 6 September 2021.

Methods

Stichting hiv monitoring (SHM) records relevant HIV-related and ART-related data, including diagnosis of, and hospitalisations for COVID-19, for all consenting people living with HIV in the Netherlands. SHM uses automated electronic queries of electronic medical records (EMR) in the HIV treatment centres to quickly identify new diagnoses of, and hospitalisations for COVID-19 and prioritises data collection on these events. However, data collection does not happen in real time, so delays remain between the COVID-19 event happening, the information being recorded in the EMR in the treatment centres, and the moment the data is captured by SHM and becomes available for analysis.

Details regarding diagnosis, disease severity, hospitalisations, and outcomes of COVID-19 are also collected. SHM data collection of COVID-19 events is based on the WHO International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) COVID-19 case report forms[14]. Hospitalised patients are the main focus of our data collection, as individuals with COVID-19 who are not admitted to hospital, rarely have reliable, detailed information documented in their EMR in HIV treatment centres for SHM to capture. SHM has not (yet) established links to other COVID-19 providers and cohorts/datasets, so direct comparisons with other patient populations cannot currently be made. Data on SARS-CoV-2 vaccination are also not yet available.

Objective measures of COVID-19 disease severity could often not be recorded by SHM, as these data were not systematically recorded in EMRs, especially for people who weren't hospitalised. In addition, detailed information on COVID-19 disease severity was often not available for patients who had been hospitalised for COVID-19, if the hospital differed from the one in which they received their HIV care. Therefore, we used data on hospitalisation for COVID-19 as a proxy for COVID-19 disease severity: cases of COVID-19 were classified as 'very severe' (admission to an intensive care unit [ICU]), 'severe' (requiring hospitalisation but no ICU admission), 'moderate' (requiring a visit to the emergency room but no hospitalisation), or 'mild' (requiring no medical care, or care by the family practitioner only).

Risk factors for (very) severe COVID-19 (hospitalisation and death), were investigated using multivariable logistic regression including relevant demographics (age, sex, region of origin), general risk factors (comorbidities), and HIV-related parameters.

Findings

By 6 September 2021, SHM had collected data on 1,308 probable (SARS-CoV-2 PCR-negative but with a strong clinical suspicion, n=19, 1.5%), and definitively-diagnosed (SARS-CoV-2 PCR-positive, n=1,289, 98.5%) SARS-CoV-2 infections in people living with HIV (*Table SR1*). An additional 201 possible COVID-19 events were reported by individuals who experienced mild symptoms but had no positive SARS-CoV-2 PCR test; these mostly occurred in the early months of the pandemic in 2020, when SARS-CoV-2 testing was not (widely) available. None of the 201 possible events resulted in hospitalisation and they are not further considered in this report.

Of the 1,308 recorded COVID-19 events, 109 (8.3%) resulted in hospitalisation; 18 (1.4%) of which required ICU admission. An additional 37 (2.8%) individuals presented with COVID-19 at an emergency room but required no hospitalisation, and the remaining 1,162 (88.8%) individuals remained at home.

The characteristics of the overall population living with HIV in care in the Netherlands in 2020 is described in *Chapter 2*, *Table 2.2*. Compared to the total population living with HIV, those who were hospitalised for COVID-19 were older, were more likely to have acquired HIV through heterosexual contact (both men and women), and were more likely to be born in sub-Saharan Africa or Latin America (including the Caribbean). Overall, men were not more likely than women to be hospitalised for COVID-19; the percentage of men among hospitalised patients (75.9%) was even somewhat lower than in the total population living with HIV (82.2%).

Regarding HIV-related characteristics, there were only minor differences between people living with HIV who were diagnosed with COVID-19, and the total population living with HIV, with the overwhelming majority being on ART, with a plasma HIV-1 viral load below 200 cps/mL, and a high median CD4 cell count well above 500 cells/mm^3. There were, however, noticeable differences between people diagnosed with COVID-19 who were hospitalised and those who weren't hospitalised; for example, the former had generally been HIV-positive for longer, but this is most likely driven by the fact that those who were hospitalised were on average eight years older. Furthermore, those who were hospitalised had lower current and nadir CD4 cell counts, and had more frequently had a prior AIDS diagnosis, compared to those not hospitalised (*Table SR1*).

Table SR1: Characteristics of individuals diagnosed with COVID-19.

	Hospitalised	Emergency room visit, but not hospitalised	Not hospitalised
n	109	37	1,162
Age, years	57.0 (51.2-65.2)	53.2 (46.6-58.7)	49.1 (40.1-56.9)
Male sex	75.9%	70.3%	81.7%
HIV transmission category			
MSM	42.6%	37.8%	67.4%
Other men	33.3%	32.4%	14.3%
Women	24.1%	29.7%	18.3%
Region of origin			
Netherlands / Europe / North America	45.0%	43.2%	59.2%
Sub-Saharan Africa	22.0%	13.5%	10.9%
Latin America / Caribbean	22.0%	16.2%	18.0%
Years known to be HIV positive	15.8 (9.9-22.5)	13.2 (9.6-19.6)	11.9 (6.9-17.2)
On ART	99.0%	100%	99.3%
HIV viral load >200 cps/mL	5 (4.7%)	3 (8.3%)	22 (1.9%)
Viral load (when detectable) in cps/mL	40,000 (6,049-62,743)	3,935 (557-43,000)	1,046 (588-52,488)
Current CD4 count, mm^3	559 (396-821)	600 (490-780)	718 (539-890)
Nadir CD4 count, mm^3	176 (60-275)	240 (74-353)	266 (140-398)
Prior AIDS diagnosis	38.0%	21.6%	18.1%

Legend: *n (%) or median (IQR), as appropriate; MSM=men who have sex with men; cps/ml=copies per millilitre; ART=antiretroviral therapy.*

Table SR2: Prevalence of comorbidities among people living with HIV who were diagnosed with COVID-19.

	Hospitalised	Emergency room presentation	Not hospitalised
Number of individuals with available data	100 of 109 (91.7%)	37 of 37 (100%)	1,122 of 1,162 (96.6%)
Obesity (BMI>30 kg/m²)	28 (28.0%)	3 (8.1%)	165 (14.7%)
Diabetes mellitus type 2	17 (17.0%)	3 (8.1%)	47 (4.2%)
Cardiovascular disease	8 (8.0%)	2 (5.4%)	22 (2.0%)
Stroke	9 (9.0%)	2 (5.4%)	19 (1.7%)
Hypertension (grade 2+ or on medication)	17 (17.0%)	4 (10.8%)	65 (5.79%)
Non-AIDS-defining malignancy	8 (8.0%)	1 (2.7%)	26 (2.3%)
Chronic kidney disease (eGFR<60 ml/min)	6 (6.0%)	2 (5.4%)	7 (0.6%)
Multimorbidity count			
0	39 (39.0%)	26 (70.3%)	833 (74.2%)
1	35 (35.0%)	9 (24.3%)	236 (21.0%)
2 or more	26 (26.0%)	2 (5.4%)	53 (4.7%)

Legend: *BMI=body mass index; eGFR=estimated glomerular filtration rate in millilitres per minute.*

Table SR2 shows the distribution of selected comorbidities among individuals diagnosed with COVID-19. All investigated comorbidities were much more prevalent among the group that was hospitalised, resulting in a higher total multimorbidity count in the hospitalised group.

Multivariable logistic regression showed that independent risk factors for hospitalisation for COVID-19 among people living with HIV were higher age, migrant status (with higher risk in individuals originating from sub-Saharan Africa or, to a lesser extent, from Latin America), obesity (BMI over 30 kg/m²), having a current CD4 count below 500 cells/mm³ (the risk was even higher when the CD4 cell count was below 200 cells/mm³), and having had a prior AIDS-defining illness (*Table SR3*). All other demographic, comorbidity, HIV-related and ART-related parameters investigated were not independently associated with a higher risk of being hospitalised following a diagnosis of COVID-19. It is noteworthy that since the moment that people living with HIV became eligible for the national SARS-CoV-2 vaccination program in April 2021, there has been a strong reduction in COVID-19-related diagnoses and hospitalisations among the population living with HIV. In May 2021, only seven hospitalisations were recorded, another one in July 2021, and there have been none since.

The median duration of hospitalisation was six (interquartile range [IQR] 3-14) days. Individuals who were admitted to the ICU remained hospitalised for a median of 25 (IQR 9-40) days; the median duration of hospitalisation was 28 (IQR 14-51) days in those who survived.

In total, 19 (1.4%) of the 1,308 people living with HIV diagnosed with SARS-CoV-2 were reported to have died as a direct result of COVID-19. The observed mortality rates in the various age groups were: 0% (n=0) in 304 aged 18-39 years, 0.3% (n=1) in 342 aged 40-49 years, 0.7% (n=3) in 417 aged 50-59 years, 2.8% (n=5) in 182 aged 60-69 years, 12.0% (n=6) in 50 aged 70-79 years, and 50% (n=4) in eight aged 80 years and over. For five individuals, age was unknown. Of the 19 individuals that died, 12 (of a total of 109, 11.0%) had been hospitalised for COVID-19 (five of whom had been admitted to the ICU [out of a total of 18, 27.8%]), two had visited the emergency room (out of a total of 37, 5.4%), and five had not been hospitalised (out of a total of 1,162, 0.4%). Of the seven individuals who had not been hospitalised and had died, five were known to be living in a nursing home prior to their COVID-19 diagnosis. Of the remaining two individuals who had not been hospitalised, but who died of COVID-19, one individual was a stroke survivor with three additional major comorbidities, and one individual was a 60-year-old woman from sub-Saharan Africa, with no known comorbidities, a good treatment response on ART, a current CD4 between 200 and 250, and a nadir CD4 cell count below 100.

Table SR3: *Independent predictors of hospitalisation among people living with HIV who were diagnosed with COVID-19.*

Risk factor	OR (95% CI)	P-value
Age (per 10 years increase)	1.9 (1.1-2.3)	<0.0001
Region of origin		
Europe / North America	1	
Sub-Saharan Africa	2.9 (1.6-5.4)	0.0007
Latin America	1.7 (0.9-2.9)	0.086
Obese (BMI>30)	2.2 (1.3-3.7)	0.0018
Current CD4 count, cells/mm^3		
0-199	5.9 (2.4-14.7)	0.0001
200-499	1.9 (1.1-3.0)	0.013
500+	1	
Prior AIDS diagnosis	1.9 (1.2-3.0)	0.0061

Legend: *BMI=body mass index.*

Table SR4 shows the demographics, HIV-related characteristics, and comorbidities of those who died from COVID-19, compared to those who survived. As expected, there were very substantial differences.

Because of the low number of COVID-19-related deaths, statistical power to formally explore risk factors using regression analysis is low. Exploratory multivariable logistic regression models showed that independent risk factors for COVID-19-related mortality were higher age, having a sub-Saharan African or Latin American origin, having a higher number of concomitantly diagnosed comorbidities, having a current CD4 count below 500/mm^3 (with the risk being even higher when the CD4 cell count was below 200/mm^3), and having a detectable plasma HIV-1 viral load of more than 200 cps/ml *(Table SR5*). However, because of low statistical power, these findings should be interpreted with caution; the observed associations are based on very few observations and hence the model's estimates are likely inflated. SARS-CoV-2 vaccinations among people living with HIV not only resulted in a drop in COVID-19-related hospitalisations, but a similar strong reduction in COVID-19-related deaths. The last COVID-19-related death was recorded in April 2021.

Table SR4: *Characteristics of individuals diagnosed with COVID-19 who died from COVID-19 compared to those who survived.*

	Survived	Died of COVID-19
Number of individuals	1,289	19
Age, years	49.9 (40.5-57.5)	70.1 (64.9-78.5)
Male sex	80.9%	79.0%
HIV transmission category		
MSM	64.9%	42.1%
Other men	16.0%	36.8%
Women	19.1%	21.1%
Region of origin		
Netherlands / Europe / North America	57.8%	42.1%
Sub-Saharan Africa	11.9%	15.8%
Latin America / Caribbean	18.0%	36.8%
Years known HIV-positive	12.2 (7.1-17.6)	18.7 (13.6-23.5)
On ART	99.3%	100%
HIV viral load <200 cps/mL	97.7%	94.7%
Current CD4 cell count, cells/mm^3	708 (525-889)	391 (250-719)
Nadir CD4 cell count, cells/mm^3	260 (130-390)	119 (62-200)
Prior AIDS diagnosis	19.5%	36.8%
Comorbidities		
Number of individuals with available data	1,242 of 1,289	18 of 19
Obesity (BMI>30)	15.6%	16.7%
Diabetes mellitus	5.0%	27.8%
Cardiovascular disease	2.3%	16.7%
Stroke	1.9%	33.3%
Hypertension (grade 2+ or on medication)	6.1%	55.6%
Non-AIDS-defining malignancy	2.6%	16.7%
Chronic kidney disease (eGFR<60 ml/min)	0.8%	27.8%
Multimorbidity count		
0	72.1%	16.7%
1	22.4%	16.7%
2	4.8%	38.9%
3	0.7%	11.1%
4 or more	0.1%	16.7%

Legend: *n (%) or median (IQR), as appropriate; MSM=men who have sex with men; cps/ml=copies per millilitre; ART=antiretroviral therapy; BMI=body mass index; eGFR=estimated glomerular filtration rate in millilitres per minute.*

Table SR5: Independent predictors of mortality among people living with HIV who were diagnosed with COVID-19.

Risk factor	OR (95% CI)	P-value
Age (per 10 years increase)	8.9 (3.7-21.0)	<0.0001
Region of origin		
European / North America	1	
Sub-Saharan Africa	6.1 (0.8-22.9)	0.078
Latin America	4.8 (1.0-22.9)	0.048
Number of concomitantly diagnosed comorbidities (per 1 comorbidity increase)	2.9 (1.5-5.6)	0.0017
Current CD4 count (cells/mm^3)		
0-199	12.2 (1.4-105.4)	0.023
200-499	7.3 (1.7-32.3)	0.0080
500+	1	
HIV-1 viral load >200 copies/mL	11.0 (1.9-64.3)	0.0077

Impact of the COVID-19 pandemic on HIV care in the Netherlands

The COVID-19 pandemic has had an unprecedented impact on healthcare systems in virtually every country in the world, including on the delivery of care in HIV treatment centres in the Netherlands. Many members of HIV treatment teams were, and are still actively engaged in frontline COVID-19 care. Serious restrictions were put in place on access to standard HIV care at times when hospitals were experiencing peak hospitalisation rates for COVID-19.

In 2020, there were approximately 411 newly-diagnosed HIV infections, a figure that was lower than expected based on numbers in previous years. This may be the result of disrupted testing services, due to the partial lockdown in response to COVID-19 in 2020, but it could also be, in part, the result of a backlog in notifying SHM of new HIV diagnoses. Aside from this, the impact of COVID-19-related restrictions on the HIV epidemic appears to have been limited. For instance, of those diagnosed in 2020, 30% received their first HIV-positive test result at a sexual health centre, 29% at a hospital, and 35% at a general practice. These proportions are the same as those reported for 2019.

At times, HIV care providers were required to severely restrict the number of non-emergency routine visits to HIV outpatient clinics. Nevertheless, 91.9% of individuals in care had a documented contact with their HIV care provider in 2020 (either via a physical consultation, telemedicine or contact by email), compared to 89.7% in 2019. There were only slight decreases in the percentage of individuals still in care receiving plasma HIV RNA and CD4 cell count testing. The percentage

tested at least once for plasma HIV RNA was 98.9% in 2019 and 96.7% in 2020, and the percentage tested at least once for CD4 cell count was 80.6% in 2019 and 74.8% in 2020. These percentages are compared across centres in *Chapter 7*.

Since the start of the COVID-19 pandemic, there has been a large shift from standard-of-care, six-monthly visits at the HIV outpatient clinics to telemedicine using phone and video calls. The percentage of patients who had a physical consultation with an HIV specialist decreased from 93.4% in 2019 to 45.2% in 2020. The percentage of patients who had a physical consultation with another specialist, consultant, or nurse consultant/specialist similarly decreased from 32.5% in 2019 to 19.0% in 2020. In contrast, the percentage of patients who had a non-physical consultation with any type of healthcare professional increased from 12.5% in 2019 to 63.8% in 2020. Most of these consultations occurred over the telephone or via email (94.4%) and a few occurred virtually using video consultation (1.6%) or other means (5.1%). The differences in how each centre transitioned from physical to non-physical consultations can be found in *Chapter 7*.

In *Chapter 2*, we observed that despite restrictions on routine HIV care, there was a further decrease in the time between HIV diagnosis and the start of cART (*Figures 2.1A* and *2.1B*). The median CD4 count at cART initiation was 344 cells/mm^3 (IQR 160-560), which is consistent with the observed trend in the preceding years. Of all adults in HIV care and on cART, 2.9% had no HIV-1 viral load measurement available in 2020. Of the individuals with an available measurement, 97.6% had an HIV-1 viral load below 200 copies/mL, which is not dissimilar to previous years' figures (*Table 2.2*). We observed a decrease in the number of treatment changes in 2020, compared to previous years. Between 2015 and 2019, the proportion of all patients on cART who made at least one change to their cART regimen fluctuated between 22.2% and 26.6% per calendar year; in 2020, this proportion decreased substantially to 16.4%. The distribution of the recorded reasons for switching cART were very similar to those reported for preceding years.

In *Chapter 3*, we describe HIV-related and non-HIV-related morbidity and (all-cause) mortality. Only 12 COVID-19-related deaths were recorded in 2020 (and, to date, nine COVID-19-related deaths in 2021). The observed all-cause mortality rate in people living with HIV in the period 2017-19 was stable between 8.4 and 8.5 deaths per 1,000 person years of follow up, but, in 2020, this increased slightly to 9.0 deaths per 1,000 person years of follow up (*Figure 3.1*). However, it should be noted that because of the increased average age of the population living with HIV in the Netherlands, the difference between the observed all-cause mortality rate, and the expected age-matched and gender-matched mortality rate, continued to decrease, also in 2020, in accordance with long-term trends.

The observed time trends in the incidence of major non-AIDS-defining comorbidities (diabetes mellitus, chronic kidney disease, non-AIDS-defining malignancies, myocardial infarction, stroke, and anal cancer) were not significantly different in 2020 compared to preceding years (*Figures 3.3A-G*).

Discussion

We recorded 1,308 COVID-19 events in people living with HIV in the Netherlands in the period prior to 6 September 2021. In total, 109 (8.3%) individuals were hospitalised, with 18/109 (1.4%) requiring ICU admission. These rates are likely inflated as, at the beginning of the pandemic, SARS-CoV-2 PCR testing was only available for severely ill individuals presenting at a hospital. Furthermore, not every symptomatic individual will have presented for SARS-CoV-2 testing, and probably a substantial proportion of SARS-CoV-2-infected individuals will have had asymptomatic disease. Because of these limitations, the observed rate of severe COVID-19 disease (i.e., hospitalisation and death), represents an upper bound. Not until well-designed seroprevalence studies have been conducted will we be able to reliably estimate what proportion of people living with HIV who acquire a SARS-CoV-2 infection go on to develop severe COVID-19 disease.

The observed mortality rates in people living with HIV diagnosed with COVID-19 were very low in those aged below 50 years. In the older age strata, the mortality rates quickly increased. In those hospitalised for COVID-19, the observed mortality rate was 11.0%, in those admitted to the ICU, it was 27.8%. However, in all age groups, mortality strongly clustered in individuals who either had multiple general risk factors (i.e., comorbidities), or those with poorer responses on ART (i.e., a low current or nadir CD4 count, a prior AIDS-defining condition, or a plasma HIV-1 viral load above 200 cps/mL). Furthermore, migrants born in sub-Saharan Africa or Latin America (including the Caribbean) appeared to be at increased risk of hospitalisation and death independent of age, comorbidities and HIV-related parameters. However, because of the very limited number of events, there is still the possibility of residual confounding.

As these estimated mortality rates are based on an incomplete dataset, they should be interpreted with caution. Hospitalisations and deaths because of COVID-19 are generally more quickly communicated to SHM than mild cases, and most asymptomatic cases of SARS-CoV-2 infection will have gone completely undiagnosed, probably resulting in an overestimation of the mortality rate in the group that was not hospitalised. The observed mortality rate of 0.4% in the group that was not hospitalised was further inflated by the fact that four of

the five reported COVID-19-related deaths in this group occurred in individuals in poor health living in nursing homes, and in one individual that was living at home but suffered from serious disability as the result of a prior stroke.

Migrants appear to be at increased risk of severe and fatal COVID-19 disease. In the general population, several migrant and ethnic groups are currently substantially less likely to be vaccinated. It should be noted that virtually all observed COVID-19-related mortality occurred before people living with HIV became eligible for the national SARS-CoV-2 vaccination programme, and hence a lower vaccination rate cannot explain the increased risk of mortality in migrants. However, HIV care providers should prioritise pro-actively addressing misinformation, misunderstandings, genuine concerns, and other barriers to COVID vaccination in these high-risk groups.

As comorbidities are important risk factors for severe COVID-19, and are more prevalent in people living with HIV than in the general population, vaccination is also a vitally important strategy for lowering the burden of severe COVID-19 disease in these high-risk individuals. It is expected that the high vaccination rate in the Dutch population living with HIV will prevent large numbers contracting SARS-CoV-2 and being hospitalised. However, the unvaccinated will remain at risk of severe COVID-19. It is currently unknown what proportion of people living with HIV may have an insufficient immune response to the currently-available SARS-CoV-2 vaccines, but several formal studies are underway to document the rate of and risk factors for SARS-CoV-2 vaccine failure in people living with HIV.

The COVID-19 pandemic has had an unprecedented impact on the delivery of HIV health care in the HIV treatment centres in the Netherlands. We observed no obvious deviations from the long-term trends in the number of newly-diagnosed people living with HIV, or in the time between diagnosis and entry into care and start of cART. However, only continued monitoring will make it clear whether, in the coming year(s), there will be a larger than expected number of people diagnosed with HIV, and whether a higher proportion of them will be late presenters with severely-decreased CD4 cell counts at the moment of entering HIV care.

There was a large increase in the proportion of consultations by (video) phone and emails in 2020. Laboratory monitoring was performed less often in 2020 than in preceding years, however, the vast majority of people living with HIV had an HIV-1 viral load measurement at least once during 2020. The proportion of people living with HIV on ART with a plasma HIV-1 viral load below 200 copies/mL in 2020 was very similar to preceding years, indicating that, for the majority on cART, there do not seem to have been major disruptions in their access to and ability to use cART.

There was also no significant increase in the all-cause mortality rate in 2020, compared to preceding years. There were likewise no changes in the long-term trends in the incidence of major non-HIV-related comorbidities in 2020. This suggests that there has been no significant underdiagnosis of these events in people living with HIV in 2020. However, only continued monitoring of the outcomes will show whether, in the coming year(s), the incidence (and disease stage at diagnosis) of these outcomes will increase.

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