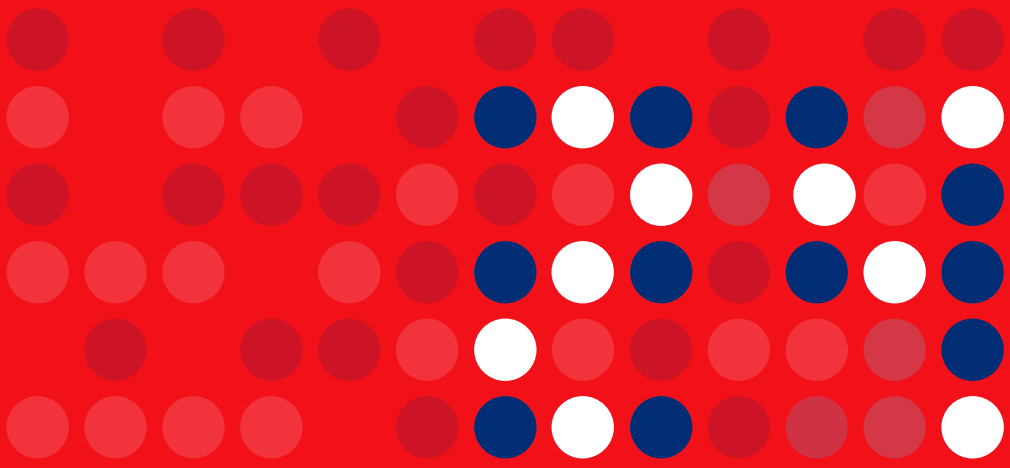
Human Immunodeficiency Virus (HIV)
Infection in the Netherlands

HIV Monitoring

HIV Monitoring Report 2024

Chapter 8: Pregnancies in women with HIV



8. Pregnancies in women with HIV

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Introduction

The most common mode of HIV acquisition for children aged 0 to 15 years worldwide is vertical transmission[1]. Vertical transmission of HIV mainly occurs perinatally during labour and delivery, or postnatally during breastfeeding. Less common is transplacental transmission in utero. Without intervention, the risk of vertical transmission varies between 15% and 45%[2,3]. Since the introduction of combination antiretroviral therapy (ART) in pregnant women, the risk of vertical transmission has been dramatically reduced to less than 1%[4,5].

Recommendations for the treatment of HIV during pregnancy have changed over time. Previously, the timing of the initiation of ART was based on the maternal CD4 cell count. As a result, a substantial proportion of women who did not need to start ART according to their CD4 cell count, started it for the first time during pregnancy, with the sole purpose of reducing maternal HIV RNA to limit the risk of vertical transmission. In many of these cases, ART was discontinued after delivery. In 2015 general treatment guidelines were revised, and ART was recommended for all individuals regardless of their CD4 cell count[6]. As a result, most women with HIV are already receiving ART at the time of conception and are advised to continue therapy during pregnancy and postpartum.

To ensure timely initiation of ART and reduce the risk of vertical transmission, it is important to ascertain a pregnant woman's HIV status. In January 2004, the Netherlands introduced standardised, opting-out HIV antibody testing for pregnant women during the first trimester of pregnancy[7]. This has resulted in a sharp decline of vertical transmission of HIV in the Netherlands, as described in further detail in *Chapter 7: Children with HIV in the Netherlands*.

This year's report focuses on women who were pregnant during the years 2016 to 2023, as this population reflects current treatment guidelines. The follow-up and therapy outcomes of all pregnant women in care during the period 1996 to 2018 were described in detail in the *2019 SHM Monitoring report*[8].

Demographics

Maternal characteristics

Geographical region of origin

Table 8.1A shows the characteristics of the 620 women with HIV with a registered one or more pregnancies when receiving care in the Netherlands between 2016 and 2023. Of these women, 450 (73%) were of non-Dutch origin and 170 (27%) were born in the Netherlands. The majority of women of non-Dutch origin were born in sub-Saharan Africa (n=276, 45%) or in the Caribbean/South America region (n=82, 13%). Ninety-two (15%) women originated from other regions, including 44 women from Central or Eastern Europe, and 23 women from South and Southeast-East Asia. The above information on country or region of origin is based on country of birth, data on migration background is not registered within SHM. However, these information is available within the environment of Statistics Netherlands (CBS). Box 8.1 gives an overview of socio-demographic and socio-economical characteristics of pregnant women in HIV care, using data from CBS if available.

Diagnosis

The majority of the 620 women (n=534, 86%) were aware of their HIV diagnosis before becoming pregnant; this proportion did not differ between women of Dutch and non-Dutch origin. In total, 86 women were newly diagnosed during their pregnancy. The proportion of women newly diagnosed varied between 3% and 11% for the years 2016-2023. These 86 women were born in:

- the Netherlands: 22/86 (13%)
- sub-Sahara Africa: 37/86 (13%)
- the Caribbean/Latin America region: 12/86 (15%)
- and other regions: 15/86 (16%)

The median time between conception and diagnosis among newly diagnosed women was 13 weeks (IQR: 10-18). Of this total, 58% received their diagnosis during the first trimester of pregnancy, 34% in their second trimester, and 8% in their third trimester. Fifty of the 86 newly diagnosed women reported an earlier negative HIV antibody test. It is not known whether these earlier tests were part of the national pregnancy screening.

For women who were newly diagnosed during the pregnancy, the median time between the date of the HIV test and first contact with one of the HIV treatment centres was 8 days (interquartile range [IQR] 6-15). The median time between the first visit to a treatment centre and receiving antiretroviral therapy was also 8 days (IQR 1-16). The moment a woman receives her HIV diagnosis from here obstetric caregiver and is referred to an HIV treatment centre is not recorded.

Clinical characteristics

Based on the first CD4 cell measurement after conception, median CD4 cell count was 548 cells/mm^3 (IQR 380-750) for all women. A lower median CD4 cell count was seen among women who were newly diagnosed with HIV (and started ART) during pregnancy (340 cells/mms, IQR 210-453). However, as CD4 cell counts during pregnancy are affected by haemodilution, which results in lower CD4 cell counts[9], CD4 cell percentages may be a more reliable parameter. These were also found to be lower than average among the group of women newly diagnosed during pregnancy (*Table 8.1A*).

Mode of HIV acquisition

Among the 620 women, heterosexual contact was the most common self-reported mode of HIV acquisition (88%). Nine women reported mode of exposure to contaminated blood, while, for three women of non-Dutch origin, the reported most likely mode of transmission was injecting drug use. Thirty-nine pregnant women acquired HIV through vertical transmission themselves. For the remaining 21 women, the mode of acquisition was unknown (*Table 8.1A*).

Population no longer in care

Based on SHM data, a total of 43 (7%) women were no longer in care in the Netherlands; of these:

- 17 (3%) were known to have moved abroad,
- 21 were lost to follow-up (3%) and
- 5 (1%) women were documented to have died during follow up.

No significant differences were observed between women of Dutch and non-Dutch origin in terms of those lost to follow-up. Of the women lost to follow-up, all except one women were lost to follow-up after their pregnancy ended; with a median time between delivery and last clinical visit of 19 months (IQR: 2-61) and 19 women had at least one clinical visit after the pregnancy Of the women who were lost to follow-up:

- seven women started ART during their pregnancy, all were newly diagnosed with HIV;
- all but one woman had a documented ART regimen reported during their last clinical visit; and
- three women had detectable HIV RNA results (min RNA= 591 and max= 34,144 copies/ml) during the last clinical visit.

In total, 16 of the 21 pregnancies among women who became eventually lost to follow-up resulted in a live-birth, two in an abortion and three in a miscarriage before 24 weeks. Vertical transmission or breastfeeding at the time of last clinical visit was not reported in any of the pregnancies.

Five of the 620 women with a pregnancy between 2016 and 2023 were documented to have died during follow up, after their pregnancy. Their median age was 39 years (IQR: 32-44). Three of the five women delivered a child and in two cases the pregnancy was ended by induced abortion. Two out of five women died of aids related causes and for two women the cause of death was a non-aids related malignancy.

***Box 8.1:** Identifying socio-demographic and socio-economic characteristics of pregnant women with HIV, using data from Statistic Netherlands*

Background

Perinatal transmission of HIV has reduced since ART became available for pregnant women. However, timely initiation of ART is important. Therefore, pregnant women in the Netherlands are screened for HIV through the Dutch national pregnancy screening program. The HIV prevalence observed in this program has been stable over the last few years at 0.05%[1]. We identified socio-demographic and economic characteristics of pregnant women with HIV and compared these with characteristics of pregnant women without HIV.

Methods

Data from SHM provide some information on socio-demographic characteristics of pregnant women with HIV (e.g. age and gender at birth). However SHM is unable to provide other societal characteristics of pregnant women such as socio-economic status or education level. To fill in these gaps in knowledge, SHM analyzed non-public data from Statistics Netherlands (CBS). CBS is an independent organization that collects, processes and publish statistical data on Dutch residents (*Chapter 3*). Data of women registered by SHM and who were pregnant

during the years 2016-2023 were combined with data from CBS. These data were analyzed within a secure CBS environment. Socio-demographic and economic characteristics of women diagnosed in the pregnancy were compared to a random selection of 1% of women without HIV who declared pregnancy-related health costs in 2020. To minimize the risk of data leading to the identification of an individual, results including less than 10 observations were not reported. Results are based on calculations by SHM using non-public microdata from Statistics Netherlands and Vektis C.V.

Results

529 (85%) out of the of 620 pregnant women with HIV registered and monitored by SHM between 2016-2023 could be combined with available CBS data in the same year as the onset of the pregnancy.

Pregnant women with HIV and time of HIV diagnosis.

Of the women with HIV who were pregnant between 2016 and 2023, 458 were diagnosed with HIV before their pregnancy in the observation period, whilst 71 women were diagnosed HIV during the pregnancy.

Compared to already diagnosed women, newly diagnosed women were more often (*Figure Box 8.1*):

- aged below 25 years (24% vs 10%),
- had a second generation migration background (18% vs 13%),
- lived in a household without children (32% vs 16%) and
- lived in a middle or low urbanized region (27% vs 22%)

Newly diagnosed women during the pregnancy

To identify socio-demographic and economic characteristics of women who were newly diagnosed with HIV during the pregnancy, socio-economical characteristics of the 71 newly diagnosed pregnant women were compared with 2,987 pregnant women without HIV.

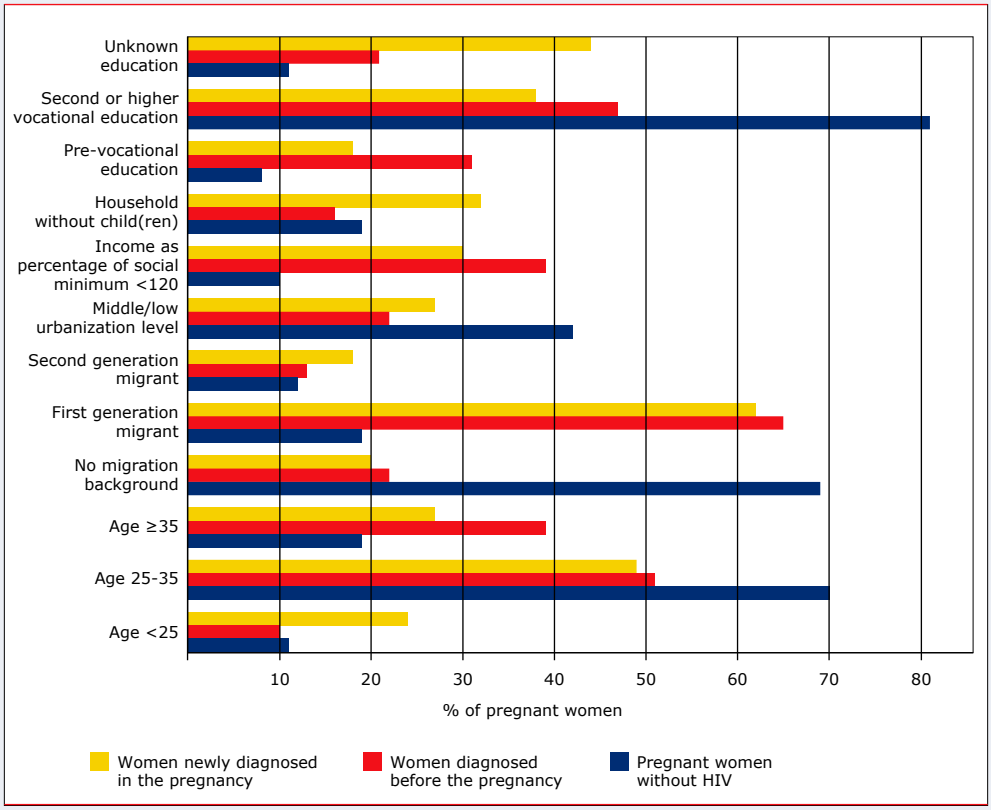
Compared to the general population of pregnant women without HIV, newly diagnosed women(*Figure Box 8.1*):

- more often had a first or second generation migration background (62% and 18% vs 19% and 12%)
- more often had an income below 120% of the social minimum (30% vs 10%)
- more often lived in a household without children (32% vs 19%) and
- less often lived in a middle or low urbanized region (27% vs 42%).

Conclusions

Compared to pregnant women with a known HIV status, women who were newly diagnosed during a pregnancy in or after 2016 were younger and more often had a second generation migration background. When compared to the general population of pregnant women, women who were newly diagnosed with HIV in the pregnancy, more often lived in a household without children, and had a lower income. These data provide more insight into sub-populations of women with potentially higher HIV prevalence, which may help in developing prevention and screening strategies. Women newly diagnosed with HIV in the pregnancy more often had a migration background, including women with a second generation migration background. These are women who are born in the Netherlands and who had at least one parent who was born abroad. However, one fifth of newly diagnosed women did not have a migration background. This finding confirms the need of the universal pregnancy screening for HIV.

Figure Box 8.1: Socio-demographic and socio-economical description of women with HIV and a documented pregnancy between 2016 and 2023.



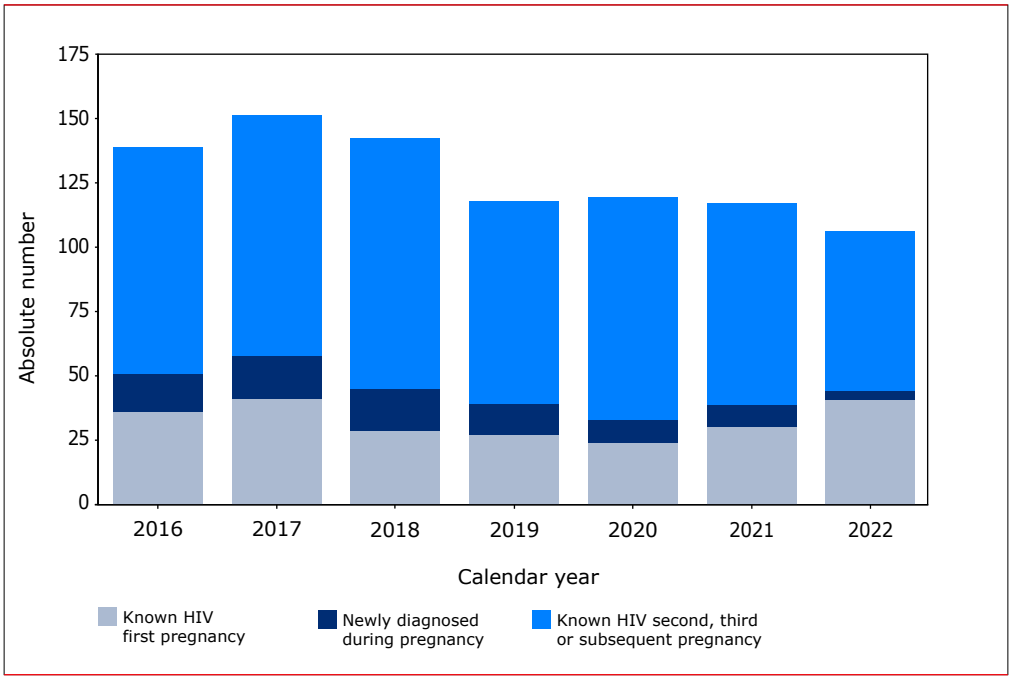
Reference

1. Procesmonitor PSIE 2022. RIVM/TNO 2024 C.P.B. van der Ploeg (TNO), J.A.M. Odijk (RIVM), M. van Lent (RIVM)

Number of pregnancies in women with HIV over time

In total, 940 pregnancies among the 620 women were reported between 2016 and 2023. The absolute annual number of pregnancies in women with HIV in care in the Netherlands is following a downward trend from 151 in 2017 to 106 in 2022 (*Figure 8.1.*)The median age of women in care was 45 years (IQR: 38-25) in 2016 and 49 years (IQR: 41-58) in 2022. The downward trend in the absolute number of pregnancies is possibly reflecting the increasing age of women in care. The number of women newly diagnosed with HIV during pregnancy varied between 17 in 2017 and three in 2022, but varied as a proportion of the total number of pregnancies per year, between 3-11%. The number of second, third or subsequent pregnancies in women who had already received an HIV diagnosis was approximately 80 per year (*Figure 8.1*).

Figure 8.1: *Absolute number of first and subsequent pregnancies per year, stratified by whether HIV status was already known before pregnancy, or newly diagnosed during pregnancy. Note: there is backlog in data collection of pregnancy related data for pregnancies starting in the most recent year in the SHM database (2023). Therefore, the most recent calendar year is not shown in the figure.*



Pregnancy-related characteristics

Overall, 620 women accounted for 940 registered pregnancies: 22% of the women had one registered pregnancy, 27% had two registered pregnancies, and 52% of the women had three or more registered pregnancies (*Table 8.1B*).

***Table 8.1A:** Maternal characteristics: of pregnant women with HIV registered and monitored by stichting hiv monitoring between 2016-2023*

	Total	Nether-lands	Sub-Saharan Africa	Caribbean/ South America	Other	p
Total number of women N (%)	620	170 (27.4)	276 (44.5)	82 (13.2)	92 (14.8)	
HIV diagnosis before pregnancy	534 (86.1)	148 (87.1)	239 (86.6)	70 (85.4)	77 (83.7)	0.880
Newly diagnosed during pregnancy	86 (13.9)	22 (12.9)	37 (13.4)	12 (14.6)	15 (16.3)	
Age at start of first pregnancy following HIV diagnosis Median (IQR)	33.3 (29.2 to 37.0)	31.9 (28.1 to 35.9)	33.6 (29.4 to 37.0)	34.4 (29.9 to 38.1)	34.1 (29.7 to 38.6)	0.011
HIV transmission route						
Heterosexual contact	548 (88.4)	151 (88.8)	252 (91.3)	79 (96.3)	66 (71.7)	<0.001
Vertical transmission	39 (6.3)	9 (5.3)	6 (2.2)	1 (1.2)	23 (25.0)	
Other~	33 (5.3)	10 (5.9)	18 (6.5)	2 (2.4)	3 (3.3)	
First CD4 count in pregnancy Median (IQR)	547.0 (380.0 to 750.0)	611.0 (447.0 to 830.0)	498.5 (360.8 to 712.5)	590.0 (362.5 to 764.2)	500.0 (371.2 to 750.0)	0.021
CD4 percentage Median (IQR)	32.2 (23.4 to 39.1)	36.9 (28.2 to 40.6)	28.8 (21.8 to 36.8)	35.0 (21.8 to 39.8)	32.3 (26.1 to 38.0)	0.018
First CD4 count when newly diagnosed during pregnancy Median (IQR)	340.0 (210.0 to 453.0)	355.0 (293.0 to 520.0)	270.0 (165.8 to 432.8)	408.0 (219.0 to 470.0)	320.0 (265.0 to 390.0)	0.375
CD4 percentage when newly diagnoses during pregnancy Median (IQR)	22.4 (15.8 to 26.0)	27.8 (24.5 to 33.3)	20.9 (13.2 to 23.0)	16.5 (13.8 to 21.9)	21.1 (19.3 to 22.8)	0.081

~ *Mode of HIV transmission was exposure to contaminated blood (n=9), injecting drug use (n=3), unknown (n=21).*

Table 8.1B: Pregnancy-related characteristics of pregnant women with HIV registered and monitored by stichting hiv monitoring between 2016-2023

	Total	Nether-lands	Sub-Saharan Africa	Caribbean/ South America	Other	p
Total number of pregnancies N (%)	940	252 (26.8)	430 (45.7)	119 (12.7)	139 (14.8)	
Total number of pregnancies ever after 2016						
3	487 (51.8)	114 (45.2)	248 (57.7)	61 (51.3)	64 (46.0)	0.039
2	249 (26.5)	75 (29.8)	96 (22.3)	34 (28.6)	44 (31.7)	
1	204 (21.7)	63 (25.0)	86 (20.0)	24 (20.2)	31 (22.3)	
Pregnancy outcome						
Delivery after at least 24 weeks	617 (65.6)	168 (66.7)	278 (64.7)	73 (61.3)	98 (70.5)	0.276
Miscarriage or stillbirth, <24 weeks	201 (21.4)	48 (19.0)	100 (23.3)	23 (19.3)	30 (21.6)	
Induced abortion, <24 weeks	119 (12.7)	35 (13.9)	50 (11.6)	23 (19.3)	11 (7.9)	
Unknown	3 (0.3)	1 (0.4)	2 (0.5)			
Mode of delivery						
Vaginal	421 (44.8)	128 (50.8)	179 (41.6)	45 (37.8)	69 (49.6)	0.134
Caesarean, secondary	95 (10.1)	24 (9.5)	46 (10.7)	12 (10.1)	13 (9.4)	
Caesarean, elective	94 (10.0)	15 (6.0)	47 (10.9)	16 (13.4)	16 (11.5)	
Pregnancy duration was <24 weeks	324 (34.5)	84 (33.3)	153 (35.6)	46 (38.7)	41 (29.5)	
Unknown	7 (1)	1 (<1)	6 (1)	0	0	
Pregnancy duration						
>=37 weeks	542 (57.7)	141 (56.0)	249 (57.9)	64 (53.8)	88 (63.3)	0.235
32-37 weeks	61 (6.5)	24 (9.5)	20 (4.7)	9 (7.6)	8 (5.8)	
24-32 weeks	13 (1.4)	3 (1.2)	8 (1.9)	0	2 (1.4)	
<24 weeks	324 (34.5)	84 (33.3)	153 (35.6)	46 (38.7)	41 (29.5)	
Unknown	1|(<1)	0	1|(<1)	0	0	
Birth weight (grams) Median (IQR)	3100.0 (2770.0 to 3470.0)	3117.5 (2693.8 to 3411.0)	3100.0 (2790.0 to 3515.0)	3038.0 (2780.0 to 3470.0)	3115.0 (2822.5 to 3523.0)	0.639
Perinatal death	5 (0.5)	2 (0.8)	3 (0.7)	0	0	0.587

Table 8.1C: ART initiation among pregnant women with HIV registered and monitored by stichting hiv monitoring between 2016–2023

	Total	Nether-lands	Sub-Saharan Africa	Caribbean/ South America	Other	p
Total N (%)	617	168 (27.2)	278 (45.1)	73 (11.8)	98 (15.9)	
Antiretroviral therapy started						
Before pregnancy	521 (84.4)	145 (86.3)	232 (83.5)	61 (83.6)	83 (84.7)	0.724
During pregnancy	96 (15.6)	23 (13.6)	46 (16.5)	12 (16.4)	15 (15.3)	
No antiretroviral therapy during pregnancy	0	0	0	0	0	0.011
Latest available plasma HIV RNA level prior to delivery						
<50 copies/ml	586 (95.0)	163 (97.0)	257 (92.4)	71 (97.3)	95 (96.9)	0.286
50–500 copies/ml	17 (2.8)	4 (2.4)	10 (3.6)	2 (2.7)	1 (1.0)	
>500 copies/ml	4 (0.6)	0	4 (1.4)	0	0	
Unknown	10 (1.6)	1 (0.6)	7 (2.5)	0	2 (2.0)	
Time between delivery and latest HIV RNA measurement (weeks)						
Median (IQR)	2.6 (1.0 to 4.3)	2.6 (1.1 to 4.4)	2.6 (0.9 to 4.1)	2.9 (1.4 to 4.4)	2.6 (0.8 to 4.2)	0.857

Pregnancy outcome

The 940 pregnancies resulted in 617 (65%) births ≥24 weeks (including both live and stillbirths), including 10 twin pregnancies. A total of 320 (34%) pregnancies ended in miscarriage or still birth <24 weeks or abortion; 201 (21%) were miscarriages or still births<24 weeks and 119 (13%) were abortions. For the remaining three (<1%) pregnancies, the outcome is unknown due to missing data.

Pregnancy duration, preterm birth and perinatal death

A total of 617 pregnancies lasted at least 24 weeks and are therefore counted as a birth. The duration of these pregnancies is known in 616 cases. Overall, 542 of 617(88%) pregnancies lasted at least 37 weeks, whereas 74 (12%) pregnancies resulted in preterm birth (defined as a pregnancy duration of 24-37 weeks). The prevalence of preterm birth is higher compared to that in the general population (7%)[29]. It is worth noting that 44% of the preterm births had a pregnancy duration of 36 weeks.

Perinatal death, including antepartum death, occurred in five (1%) births. Congenital disorders were registered for 15 infants.

Mode of delivery

If viral suppression during pregnancy can be achieved with ART, vaginal delivery is recommended for women with HIV[10,11]. However, in the presence of detectable HIV RNA levels at, or near the time of delivery, elective Caesarean section is recommended to minimise the risk of vertical transmission. The European AIDS Clinical Society (EACS) guidelines state that elective Caesarean section should be carried out if HIV RNA concentration is above 50 copies/ml in weeks 34-36 of pregnancy[12], whereas Dutch guidelines allow a vaginal delivery with HIV RNA below 500 copies/ml and declining viral loads[13]. In such cases intravenous zidovudine is given during labour.

Overall, 68% of newborns were delivered vaginally; 76% of the women of Dutch origin delivered vaginally, compared to 64% of women of SSA origin or 61% of women of Latin America or Caribbean origin. Fifteen percent of newborns were delivered by an elective Caesarean section and another 16% by a secondary Caesarean section.

In terms of mode of delivery, 98% of the women who delivered vaginally had an HIV RNA below 50 copies/ml. This figure was 94% for women who delivered by elective Caesarean section, and 91% for those with a secondary (unplanned) Caesarean section ($p<0.0001$). Among women who delivered by secondary Caesarean section, the HIV RNA was between 53 and 550 copies/ml. The most common reported reasons for Caesarean section were foetal distress and failure to progress in the second stage of labour.

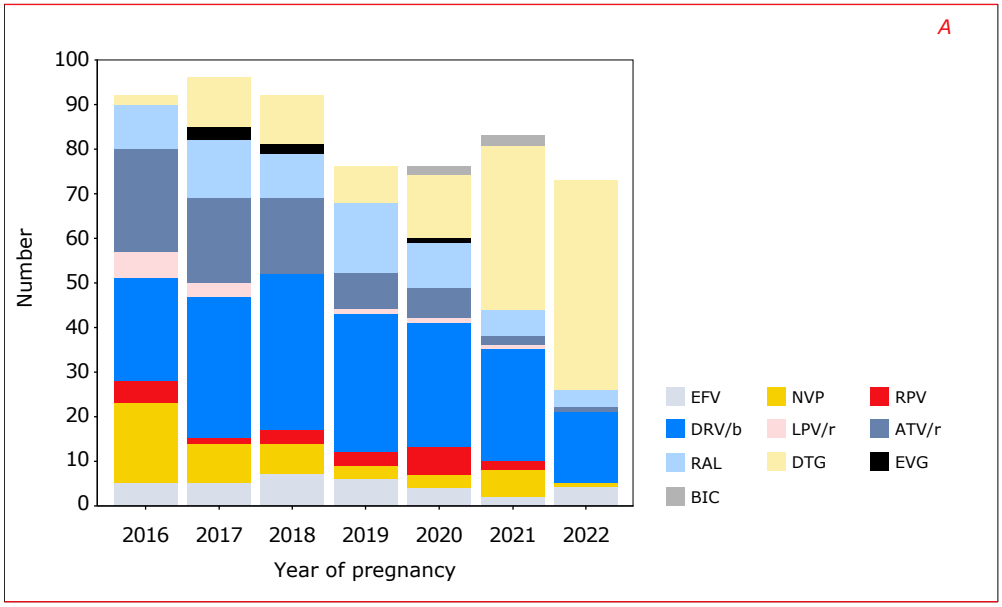
A therapy (ART) uptake and therapy response in pregnant women

Therapy uptake

From 2016 onwards, during the 617 pregnancies lasting at least 24 weeks, all women received ART: in 521 (84%) pregnancies, women were already on ART at the time of conception, while in 96 (16%) pregnancies, ART was started during pregnancy (*Table 8.1C*).

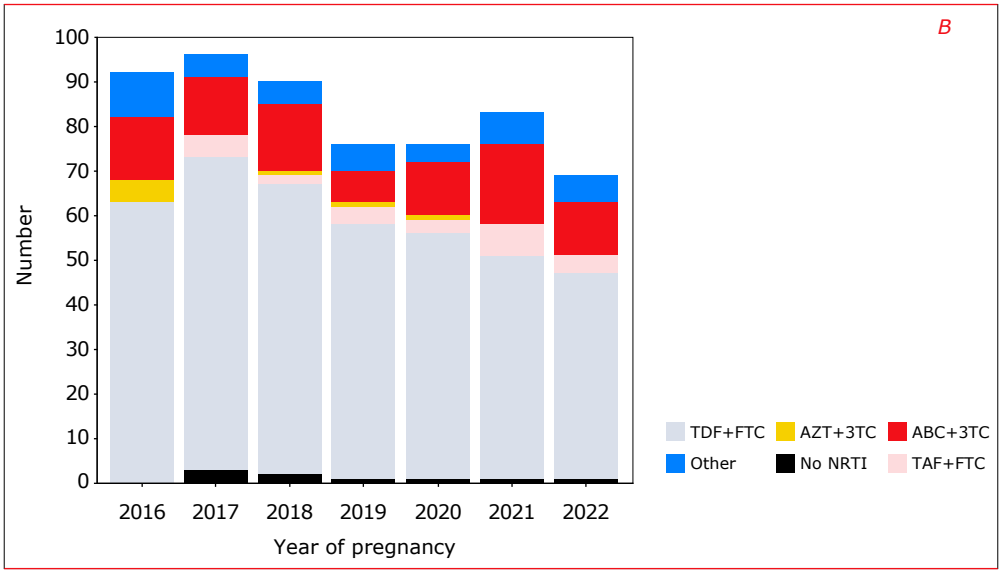
For 613 out of the 617 pregnancies, information on ART regimens was available. *Figure 8.2A* shows the most commonly used third-drug additions to the nucleoside analogue reverse transcriptase inhibitor (NRTI) backbone as part of ART in pregnant women and during delivery between 2016 and 2022. The use of integrase inhibitors (INSTI) in pregnancy increased from 4% in 2016 to 55% in 2022. This increase coincides with a decrease in the use of NNRTI-containing regimens from 30% in 2016 to 7% in 2022 and a decrease in the use of PI from 55% to 23%(*Figure 8.2C*). In 13 pregnancies a two-drug regimen was used, which were combinations of NRTI+INSTI or PI+INSTI.

Figure 8.2A: *The most commonly used third-drug additions to the nucleoside analogue reverse transcriptase inhibitor (NRTI) backbone used as part of ART regimens during pregnancies in 2016-2022 with an minimum duration 24 weeks.*



Note: *there is backlog in data collection of pregnancy related data for pregnancies starting in the most recent year. Therefore, the most recent calendar year is not shown in the figure.*

Figure 8.2B: *The nucleoside reverse transcriptase (NRTI) backbone used as part of ART regimens during pregnancies in 2016-2022 with an minimum duration 24 weeks.*



Note: *there is backlog in data collection of pregnancy related data for pregnancies starting in the most recent year in the SHM database (2023). Therefore, the most recent calendar year is not shown in the figure.*

Legend: *3TC = lamivudine; /b = boosted (cobicistat or ritonavir); /r = ritonavir-boosted; /c = cobicistat-boosted; ABC = abacavir; ATV = atazanavir; AZT = zidovudine; DRV = darunavir; DTG = dolutegravir; BIC = bictegravir; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; IDV = indinavir; LPV = lopinavir; NFV = nelfinavir; NVP = nevirapine; RAL = raltegravir; RPV = rilpivirine; SQV = saquinavir; TDF = tenofovirdisoproxil fumarate; TAF = tenofovir alafenamide; NRTI = nucleoside analogue reverse transcriptase inhibitor.*

Figure 8.2C: Antiretroviral class use stratified by calendar year period regimens during pregnancies in 2016–2022, with an minimum duration 24 weeks. Note: there is backlog in data collection of pregnancy related data for pregnancies starting in the most recent year in the SHM database (2023). Therefore, the most recent calendar year is not shown in the figure.

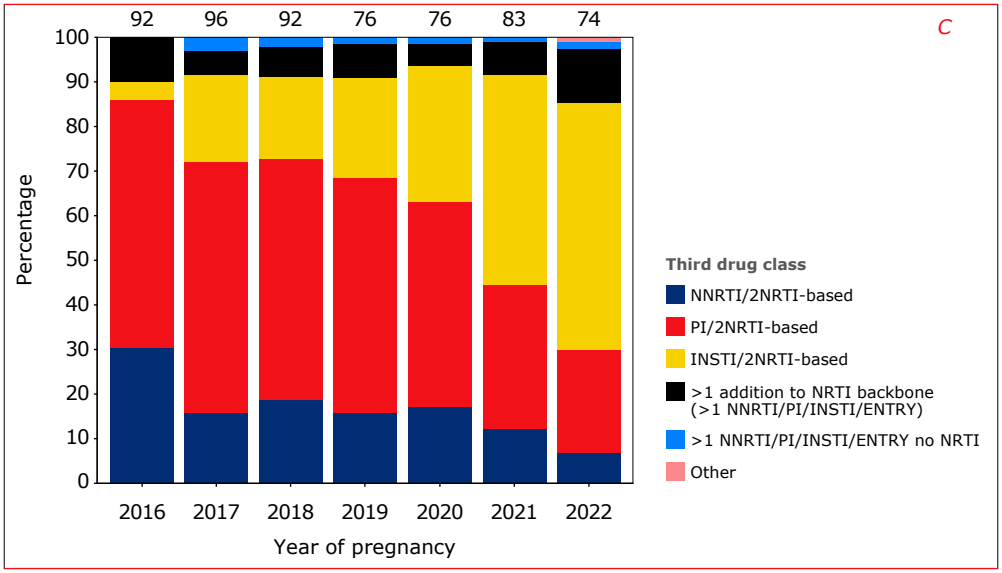


Figure 8.2B provides an overview of the components of the NRTI backbone used during pregnancy between 2016 and 2022. The most commonly prescribed backbone was the combination of tenofovir disoproxil fumarate and emtricitabine (TDF+FTC) (69%), followed by a combination of abacavir and lamivudine (ABC+3TC) (16%).

A switch in ART regimen was reported during 191 pregnancies. While no reason was documented in 5 cases, the most common documented reason for switching in the remaining pregnancies was pregnancy-related (n=128). In 40% of the pregnancy-related switches a cobicistat-boosted regimen was discontinued. Other common pregnancy-related switches included ART that was switched from an integrase-containing regimen to a protease inhibitor (darunavir or atazanavir). Other common switches were within the class of integrase inhibitors, particularly from dolutegravir or elvitegravir to raltegravir. After switching, 2% of the women used a regimen which included a non-preferred antiretroviral (ARV) agent, except in the special circumstances outlined in the most recent guidelines[14].

Due to reduced serum levels of cobicistat during the second and third trimesters of pregnancy, and hence also reduced levels of darunavir and elvitegravir when boosted with cobicistat, regimens containing cobicistat were no longer recommended during pregnancy from 2018 onwards[15]. In the Netherlands, cobicistat at the time of delivery was used in four pregnancies between 2018 and 2022. All women had an HIV RNA level below 50 copies/ml at the time of delivery.

Therapy response

Figure 8.3 shows the percentage of women on ART and their latest available plasma HIV RNA level prior to delivery. HIV RNA levels were categorised as below 50 copies/ml, 50-500 copies/ml, and above 500 copies/ml.[a]

In 97% of the overall births, the mothers had an HIV RNA level below 50 copies/ml at the time of delivery, and 3% had an HIV RNA level above 50 copies/ml. The proportion of women with an HIV RNA below 50 copies/ml at the time of delivery was above 95% in all years, with exception of 2017.

In total, 20 women had HIV RNA levels above 50 copies/ml (50-500 copies/ml: n=16, >500 copies/ml: n=4, median RNA=128 copies/ml; minimum=53, maximum= 15500) prior to delivery.

a Dutch guidelines allow a vaginal delivery with HIV RNA below 500 copies/ml and declining viral loads[13] or with a undetectable HIV RNA <50 or <20 copies/ml, depending on the used assay. Elite controller or long-term non-progressor refers to an individual with HIV who is able to control HIV without ART and maintain a CD4 cell count in normal range.

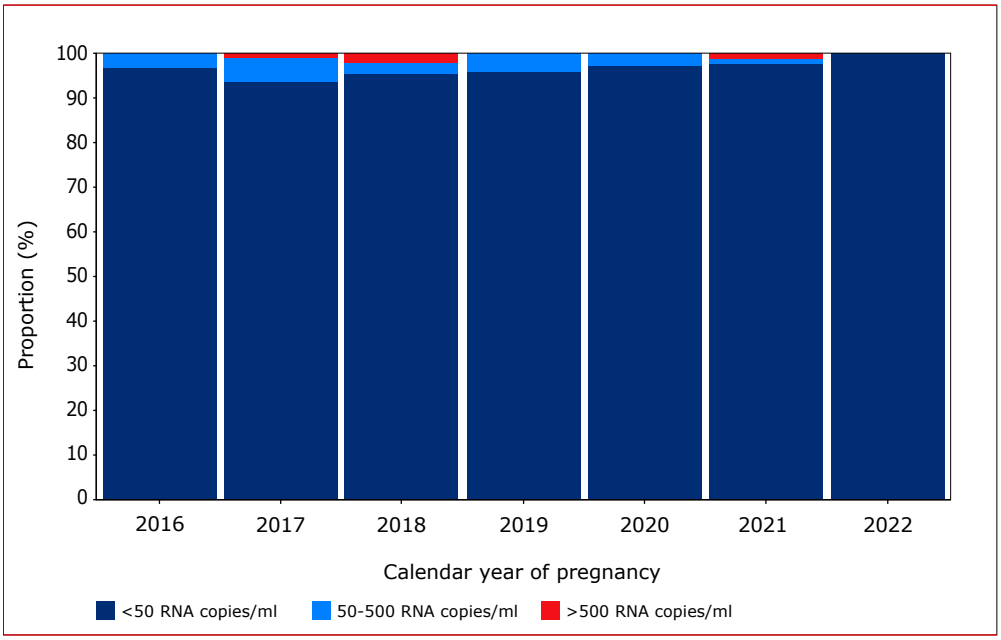
Table 8.2: Overview of characteristics of women with a detectable HIV RNA level prior to delivery.

Women with detectable HIV RNA	20 (n,%)	
Newly diagnosed during pregnancy	8 (40)	6 women were diagnosed after the first trimester.
ART initiated during pregnancy	8 (40)	
ARV at time of detectable HIV RNA*		
INSTI-containing	9 (45)	
NNRTI-containing	2 (10)	
PI-containing	8 (40)	
Unknown regimen	1 (5)	
Mode of delivery		RNA (minimum; maximum)
Caesarean section	13 (65)	53, 15500 copies/ml
Vaginal	6 (30)	70, 1003 copies/ml
Unknown	1 (5)	
Zidovudine during delivery		
Yes	13 (65)	
No	6 (30)	
Unknown	1 (5)	
Evaluation of drugs resistance	14	4/14 women with a sequence were found to have high-level drug-resistance to at least one NNTRI; 3/4 had a sequence within 4 months after the start of ART and for 1 woman resistance was evaluated for the first time more than 4 months after ART was initiated and was evaluated in the pregnancy.

**None of the women used a two-drug regimen at time of detectable HIV RNA*

At time of database closure, no vertical transmission was reported among the infants born to mothers who had HIV RNA levels above 50 copies/ml at the time of delivery.

Figure 8.3: Distribution of women using ART with their latest HIV RNA levels prior to delivery: <50 copies/ml, 50-500 copies/ml, or >500 copies/ml for pregnancies with a minimum duration of 24 weeks.



Note: there is backlog in data collection of pregnancy related data for pregnancies starting in the most recent year in the SHM database (2023). Therefore, the most recent calendar year is not shown in the figure.

Vertical transmission rate in the Netherlands

Between 2016 and 2023, 617 births were registered in the Netherlands among mothers who knew they had HIV prior to conception, or were first diagnosed during pregnancy. All mothers received ART during their pregnancy. Vertical transmission in the Netherlands has become extremely rare and this resulted in a very low vertical transmission rate in pregnant women on ART in the Netherlands, which is in line with low reported vertical transmission rates in other western European countries[16,17,18,19]. To avoid inadvertently identification of individuals in cases of rare events (which we defined as <5), we will not report the rate of vertical transmission.

Postpartum follow up

Postpartum follow up was defined as the first 12 months after delivery and was considered for all pregnancies with a minimum duration of 24 weeks. Here we describe therapy and virological suppression rates during the postpartum period, as well as breastfeeding rates.

Therapy

Of the 617 pregnancies lasting 24 weeks or longer, 81 were excluded from this analysis: 57 because of insufficient follow up between delivery and the time of database closure; and 24 because the women were no longer in care (one had moved abroad and nine were reported as lost to care during the postpartum period).

For the remaining 536 pregnancies in 436 women, ART was initiated before conception or during pregnancy in 80% and 20% of cases, respectively. The majority of women used an integrase inhibitor-containing regimen during the postpartum period (47%). The use of integrase inhibitor increased from 24% in 2016, to 58% in 2020 and 61% in 2023.

In 34 of these 536 pregnancies, ART was discontinued postpartum:

- The most common documented reason was a decision by the patient (n=21).
- In two cases the documented reason was elite controller or long-term non-progressor.[b]
- In 3 cases the documented reason was toxicity.
- And in 8 cases the documented reason was end of pregnancy.

In 15 out of the 34 cases, therapy was restarted after a median of five weeks (IQR 3-11). In the remaining 19 cases, ART was not restarted postpartum, however 12 women did start again after the postpartum period had ended. Six women did not have a documented restart of ART at the time of database closure.

Virological outcome

Detectable viremia postpartum was defined as at least one HIV RNA measurement above 50 copies/ml during the postpartum period. On the basis of this definition:

- Detectable HIV RNA >50 copies/ml was observed in 14% of the 536 pregnancies analysed. When taking into account >200 copies/ml, 9% of the pregnancies had a detectable HIV RNA.

b Elite controller or long-term non-progressor refers to an individual with HIV who is able to control HIV without ART and maintain a CD4 cell count in normal range.

For the subset of women with documented continued use of ART postpartum:

- 55 (11%) had an HIV RNA level above 50 copies/ml (median HIV RNA=257 copies/ml, minimum=52 and maximum=85900 copies/ml)
- and 31 (6%) had a HIV RNA level above 200 copies/ml,
- 23 of whom had more than one episode of an HIV RNA level above 50 copies/ml during the postpartum period.
- Twelve of the 55 women with an HIV RNA above 50 copies/ml were newly diagnosed with HIV during the pregnancy, whilst 43 women were diagnosed before the onset of the pregnancy and had also already started ART. Seventy-four percent (n=32) had earlier episodes of detectable HIV RNA levels more than 6 months after the start of ART.

In the 34 women who discontinued the use of ART postpartum:

- 19 (56%) experienced viral rebound (median HIV RNA=19,800 copies/ml, minimum 617 and maximum 450000 copies/ml).
- 13 women had an undetectable HIV RNA level during the post-partum period, including 8 women who did not restart ART after discontinuing therapy during the postpartum period;
  - Three of these 8 women continued to report high CD4 cell counts and low HIV RNA levels in the absence of ART;
  - Three experienced a viral rebound after the postpartum period;
  - Five cases remained virally suppressed (two of whom eventually restarted ART).

Breastfeeding

The option of breastfeeding for women with sustained virological suppression is discussed based on shared decision-making in the Netherlands. Breastfeeding in such cases is recommended for a maximum of six months.

Breastfeeding data were available for 470 of the 536 pregnancies, and was reported in 39 pregnancies (the duration of breastfeeding was not documented). It is noteworthy that all women had documented use of ART and that all except one women had HIV RNA levels below 50 copies/ml during the first 6 months of the postpartum period. In one case the measured HIV RNA was below 75 copies/ml and the subsequent HIV RNA measurement was also undetectable, it is not registered if the mother was breastfeeding at time of these HIV RNA measurements. The median number of HIV RNA measurements during the first 6 months after delivery among the 39 pregnancies with reported breastfeeding was 2 HIV RNA measurements (IQR 1-4 measurements). No cases of vertical transmission were documented.

Summary and conclusions

All women with a registered pregnancy since 2016 have received ART during their pregnancy. More than 97% had an HIV RNA level below 50 copies/ml around the time of delivery and 99% had an HIV RNA level below 500 copies/ml. Vertical transmission in the Netherlands has become very rare, resulting in a very low vertical transmission rate in pregnant women using ART during the period 2016 to 2023. This finding is comparable to the low figures reported in other western European countries[16,17,18,19].

A small proportion of women had detectable HIV RNA levels near the time of delivery. This included women who were newly diagnosed with HIV and thus started ART during the pregnancy, and women who were already using ART at conception but had earlier episodes of detectable HIV RNA levels. To maintain a low rate of vertical transmission of HIV, it is important to provide multidisciplinary care for – and close monitoring of – women newly diagnosed with HIV after conception, as well as those with a history of virological failure.

Although most women were aware of their HIV status prior to their pregnancy, 14% were newly diagnosed during pregnancy. Based on SHM data, 27% of the women originated from the Netherlands and 73% were of non-Dutch origin. Interestingly, a substantial number of women who were newly diagnosed in their pregnancy had an earlier recorded negative HIV test. Unfortunately data on the reason for these earlier tests is not collected. Hence it is not known whether these tests were part of the national pregnancy screening brought about by an earlier pregnancy, or because of other underlying reasons for testing.
In most of newly diagnosed women, the diagnosis was a result of the national pregnancy screening for HIV, syphilis and hepatitis B (PSIE)[21]. This screening is offered to all women in the first trimester of pregnancy. However, our data showed that some women received their HIV diagnosis during the second or third trimester of pregnancy, which could complicate the timely start of ART. It should be pointed out that in the general population timely screening within PSIE is only achieved in 75% of all women[22]. This may be a result of late booking of the first antenatal clinical visit. However, PSIE reports a decline in timely screening since the introduction of the non-invasive prenatal testing (NIPT)[21]. This test was allowed after 11 weeks of pregnancy and may result in taking a single blood sample to test for HIV, HBV and syphilis as well as the NIPT test, at the same time.
Due to technical improvements, the NIPT is offered from 10 weeks pregnancy onwards as from April 2023 as part of the national pre- and neonatal screening programme[20].

Finally, ART has been recommended for all individuals regardless of CD4 cell count since 2015, including postpartum. We observed an increasing proportion of women who received integrase inhibitors during pregnancy as well as during the postpartum period. From 2016 onwards, 11% of women who continued to use ART postpartum had at least one episode of viraemia. In earlier studies, adherence to therapy has been reported to deteriorate during the postpartum period[23,24,25,26,27,28].

The proportions of preterm births and Caesarean sections among women with HIV were higher than those observed in the general population (12% and 31% compared to 7% and 17%[29]). Other studies have found a high prevalence of caesarean sections in women with undetectable HIV RNA levels[30], compared to the general population[31] or a higher rate of premature delivery[40]. However as invasive perinatal procedures, such as foetal blood sampling or the placement of a foetal scalp electrode, are contraindicated in women with HIV[13] the threshold to perform a Caesarean section is generally lower. It is not clear whether this lower threshold contributed to the higher number of Caesarean sections observed. In addition, premature delivery has been linked to ART use, especially in the first 12 weeks of pregnancy[32,33,34]. As the aetiology of preterm delivery is complex and multifactorial, it is unclear whether this or other, for example socio-economic factors, can explain the high proportion of preterm births[35]. The association between various ARVs and adverse pregnancy outcomes, including low birthweight, has been evaluated in different studies, with conflicting results[36].

Recommendations

As a result of changes in the guidelines concerning treatment of HIV in 2015, ART is more likely to be used at conception and continued post-delivery. This is expected to result in a greater number of women with undetectable HIV RNA levels earlier in their pregnancy and around the time of delivery.

Women with HIV who start ART during pregnancy require a high degree of support; not only during the pregnancy itself to ensure suppressed HIV RNA levels at the time of delivery, but also post-partum to maintain adherence to ART, especially if they wish to breastfeed. As an alternative to formula feeding, some care providers now discuss the option of breastfeeding (for a maximum period of six months) with women who have sustained undetectable viremia and no issues with therapy or visit adherence, based on shared decision-making. This is not (yet) common practice throughout the Netherlands, but is expected to become more common in the next few years. Women who decide to exclusively breastfeed should be closely monitored clinically and virologically, along with their infants[37,38]. In the Netherlands, this monitoring is described in the HIV exposure follow up protocol for newborns[39].

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