Human Immunodeficiency Virus (HIV)
Infection in the Netherlands

HIV Monitoring

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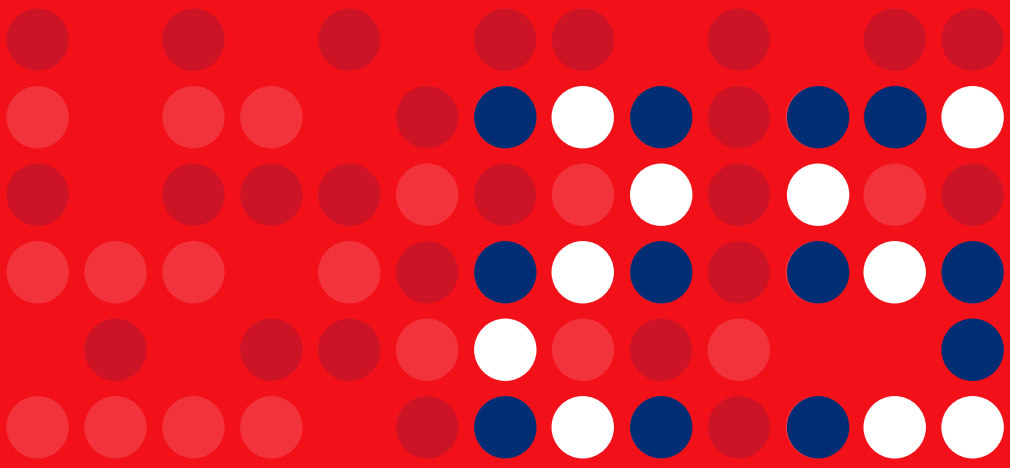
Chapter 9: Pregnancies in women with HIV



9. 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]. 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. Since 2015, ART is 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 the Netherlands, pregnant women receive opting-out HIV antibody testing during the first trimester of pregnancy[7]. In addition to the ART that a pregnant woman receives, newborns who are perinatally exposed to HIV are receiving PEP as soon as possible after birth.[39]

This year's report focuses on women who were pregnant during the years 2016 to 2024, 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 9.1A shows the characteristics of the 668 women with HIV with at least one registered pregnancy when receiving care in the Netherlands between 2016 and 2024.
These women were born in:

- the Netherlands: 178 (27%)
- sub-Saharan Africa: 298 (45%)
- the Caribbean/Latin America region: 88 (13%)
- and other regions: 104 (16%), including 53 women from Central or Eastern Europe, and 24 women from South and Southeast-East Asia.

Diagnosis

The majority of the 668 women (n=572, 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, 96 women were diagnosed during their pregnancy. The majority of the women with a diagnosis in the pregnancy were diagnosed in the national pregnancy screening program. The proportion of women newly diagnosed varied between 8% and 27% for the years 2016-2024. These 96 women were born in:

- the Netherlands: 23/178 (13%)
- sub-Saharan Africa: 44/298 (15%)
- the Caribbean/Latin America region: 13/88 (15%)
- and other regions: 16/104 (15%)

The median time between conception and diagnosis among newly diagnosed women was 13 weeks (IQR: 10-18):

- 55% received their diagnosis during the first trimester of pregnancy,
- 35% in their second trimester,
- and 9% in their third trimester.

Fifty-five of the 96 newly diagnosed women reported an earlier negative HIV antibody test, the remaining 41 women did not report ever having tested for HIV before. Within the SHM database, it is not recorded whether the 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 blood sampling for the HIV test and first contact with one of the HIV treatment centres was 9 days (interquartile range [IQR] 6-17). The median time between the first visit to a treatment centre and receiving antiretroviral therapy was also 8 days (IQR 1-15). 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 562 cells/mm^3 (IQR 380-767) for all women, 7% of the women had a first CD4 cell count after conception that was lower than 200 cells/ mm^3 and 22% of the women their first CD4 cell count after conception was <350 cells/ mm^3. A lower median CD4 cell count was seen among women who were newly diagnosed with HIV (and started ART) during pregnancy (320 cells/mms, IQR 210-455). However, as CD4 cell counts during pregnancy are lower because of haemodilution,[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 9.1A*).

Mode of HIV acquisition

The self-reported mode of HIV acquisition among the 688 women was (*Table 9.1A*):

- Heterosexual contact: 587 (88%)
- Vertical transmission: 39 (6%)
- Other: 42 (6%), including exposure to contaminated blood or medical procedures (n=17), injecting drug use (n=3) and unknown mode (n=22).

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:

- 24 (4%) were known to have moved abroad, two of the women moved in their pregnancy,
- 23 were lost to follow-up (3%) and
- 7 (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 30 months (IQR: 2-55) 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 two women had a documented ART regimen reported during their last clinical visit; and
- three women had detectable HIV RNA (min. RNA = 591 copies/mL, max. = 56 234 copies/ml) during the last clinical visit.

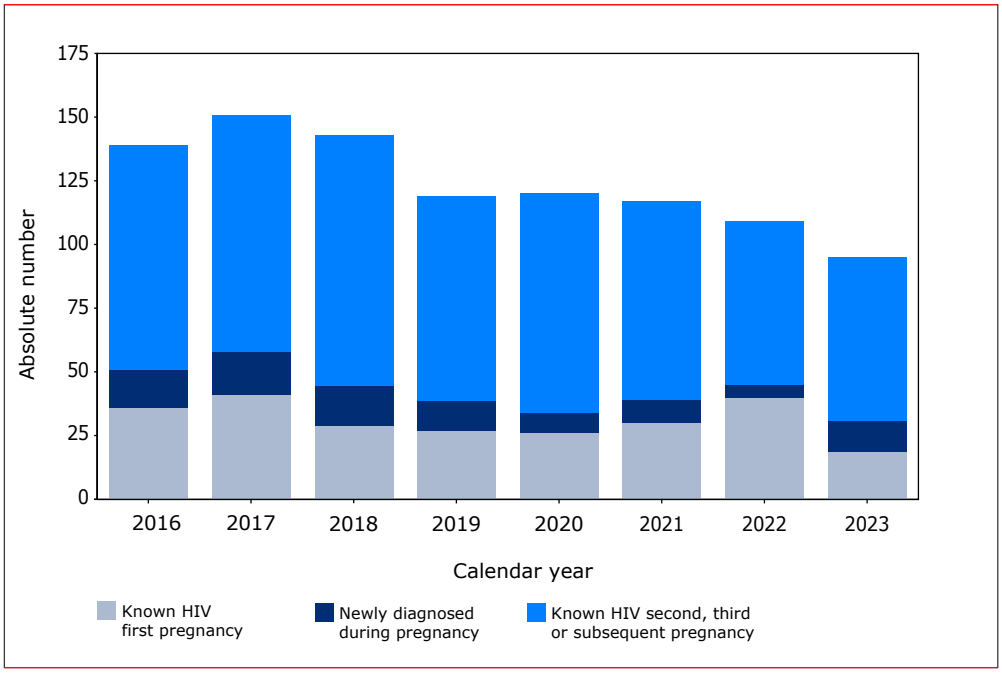
In total, 19 of the 23 pregnancies among women who became eventually lost to follow-up resulted in a live-birth, four pregnancies ended before 24 weeks. Vertical transmission or breastfeeding at the time of last clinical visit was not reported in any of these pregnancies.

Seven of the 668 women with a pregnancy between 2016 and 2024 were documented to have died during follow up, after their pregnancy. Their median age was 39 years (IQR: 32-46). Three of them delivered a child and in the other women the pregnancy was terminated by induced abortion. Two out of seven women died of aids-related causes and for four women the cause of death was a non-aids-related and one cause of death was unknown.

Number of pregnancies in women with HIV over time

In total, 1,035 pregnancies among the 668 women were reported between 2016 and 2024. 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 95 in 2023 (*Figure 9.1*). In the SHM database, the median age of all women with HIV in care is increasing from 45 years (IQR: 38-53) in 2016 to 51 years (IQR: 42-59) in 2024. The median age of women with a pregnancy was 33 (IQR:29-37) and did not change over time. 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 eight in 2020, but varied as a proportion of the total number of pregnancies per year, between 7 and 13%. Each year, approximately 80 women with HIV and a previous pregnancy, became pregnant again (*Figure 9.1*).

Figure 9.1: *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 (2024). Therefore, the most recent calendar year is not shown in the figure.*

Pregnancy-related characteristics

Overall, 668 women accounted for 1,035 registered pregnancies:

- 21% of the women had one registered pregnancy,
- 27% had two registered pregnancies,
- 52% of the women had three or more registered pregnancies (*Table 9.1B*).

Table 9.1A: Maternal characteristics: of pregnant women with HIV registered and monitored by stichting hiv monitoring between 2016-2024

	Total	Nether-lands	Sub-Saharan Africa	Caribbean/ South America	Other	p
Total number of women N (%)	668	178 (26.6)	298 (44.6)	88 (13.2)	104 (15.6)	
HIV diagnosis before pregnancy	572 (85.6)	155 (87.1)	254 (85.2)	75 (85.2)	88 (84.6)	0.93
Newly diagnosed during pregnancy	96 (14.4)	23 (12.9)	44 (14.8)	13 (14.8)	16 (15.4)	
Age at start of first pregnancy following HIV diagnosis Median (IQR)	33.2 (28.9. to 36.9)	31.9 (28.0 to 35.8)	33.3 (29.0 to 36.9)	34.4 (29.7 to 37.8)	34.1 (29.4 to 38.5)	0.008
HIV transmission route						
Heterosexual contact	587 (87.9)	156 (87.6)	271 (90.9)	85 (96.6)	75 (72.1)	<0.001
Vertical transmission	42 (6.3)	9 (5.1)	8 (2.7)	1 (1.1)	24 (23.1)	
Other~	39 (5.8)	13 (7.3)	19 (6.4)	2 (2.3)	5 (4.8)	
First CD4 count in pregnancy Median (IQR)	561.5 (380.0 to 766.8)	642.0 (485.0 to 837.0)	514.5 (352.5 to 727.0)	570.0 (350.0 to 758.5)	530.5 (395.0 to 811.8)	0.001
CD4 percentage Median (IQR)	32.4 (23.5 to 40.0)	37.6 (27.6 to 42.8)	29.2 (20.7 to 37.7)	28.9 (23.9 to 36.6)	32.0 (25.7 to 40.7)	0.002
First CD4 count when newly diagnosed during pregnancy Median (IQR)	320.0 (210.0 to 455.0)	355.0 (296.5 to 540.0)	260.0 (179.0 to 443.2)	306.0 (190.0 to 470.0)	360.0 (265.0 to 420.0)	0.346
CD4 percentage when newly diagnoses during pregnancy Median (IQR)	22.4 (15.8 to 26.0)	26.1 (23.0 to 32.0)	20.9 (12.6 to 23.0)	16.5 (13.0 to 21.3)	23.5 (18.6 to 24.6)	0.075

~ Mode of HIV transmission was exposure to contaminated blood or medical procedures (n=17), injecting drug use (n=3), or unknown (n=19).

Table 9.1B: Pregnancy-related characteristics of pregnant women with HIV registered and monitored by stichting hiv monitoring between 2016-2024.

	Total	Nether-lands	Sub-Saharan Africa	Caribbean/ South America	Other	p
Total number of pregnancies N (%)	1,035	276 (26.7)	474 (45.8)	129 (12.5)	156 (15.1)	
Total number of pregnancies ever after 2016						
3	540 (52.2)	127 (46.0)	277 (58.4)	65 (50.4)	71 (45.5)	0.006
2	276 (26.7)	88 (31.9)	101 (21.3)	40 (31.0)	47 (30.1)	
1	219 (21.2)	61 (22.1)	96 (20.3)	24 (18.6)	38 (24.4)	
Pregnancy outcome						
Delivery after at least 24 weeks	683 (66.0)	186 (67.4)	308 (65.0)	82 (63.6)	107 (68.6)	0.507
Miscarriage or stillbirth, <24 weeks	218 (21.1)	51 (18.5)	109 (23.0)	24 (18.6)	34 (21.8)	
Induced abortion, <24 weeks	131 (12.7)	38 (13.8)	55 (11.6)	23 (17.8)	15 (9.6)	
Unknown	3 (0.3)	1 (0.4)	2 (0.4)			
Mode of delivery						
Vaginal	466 (45.0)	142 (51.4)	196 (41.4)	52 (40.3)	76 (48.7)	0.162
Caesarean, secondary	109 (10.5)	18 (6.5)	57 (12.0)	18 (14.0)	16 (10.3)	
Caesarean, elective	101 (9.8)	25 (9.1)	49 (10.3)	12 (9.3)	15 (9.6)	
Pregnancy duration was <24 weeks	353 (34.1)	90 (32.6)	167 (35.2)	47 (36.4)	49 (31.4)	
Unknown	6 (0.6)	1 (0.4)	5 (1.1)			
Pregnancy duration						
≥37 weeks	599 (57.9)	154 (55.8)	278 (58.6)	71 (55.0)	96 (61.5)	0.183
32-37 weeks	68 (6.6)	27 (9.8)	21 (4.4)	11 (8.5)	9 (5.8)	
24-32 weeks	15 (1.4)	5 (1.8)	8 (1.7)		2 (1.3)	
<24 weeks	353 (34.1)	90 (32.6)	167 (35.2)	47 (36.4)	49 (31.4)	
Birth weight (grams) Median (IQR)	3,102.5 (2,766.2 to 3,483.8)	3,117.5 (2,646.2 to 3,417.0)	3,125.0 (2,809.5 to 3,520.0)	3,061.5 (2,776.2 to 3,485.0)	3,075.0 (2,790.0 to 3,485.0)	0.462
Perinatal death	5 (0.5)	2 (0.7)	3 (0.6)			

Table 9.1C: ART initiation among pregnant women with HIV registered and monitored by stichting hiv monitoring between 2016-2024.

	Total	Nether-lands	Sub-Saharan Africa	Caribbean/ South America	Other	p
Total number of births N (%)	683	186 (27.2)	308 (45.1)	82 (12.0)	107 (15.7)	
Antiretroviral therapy started						
Before pregnancy	576 (84.3)	162 (87.1)	254 (82.5)	69 (84.1)	91 (85.0)	0.587
During pregnancy	107 (15.7)	24 (12.9)	54 (17.5)	13 (15.9)	16 (15.0)	
Latest available plasma HIV RNA level prior to delivery						
<50 copies/ml	660 (96.6)	182 (97.9)	294 (95.5)	80 (97.6)	104 (97.2)	0.460
50-500 copies/ml	15 (2.2)	3 (1.6)	9 (2.9)	2 (2.4)	1 (0.9)	
>500 copies/ml	4 (0.6)		4 (1.3)			
Unknown	4 (0.6)	1 (0.5)	1 (0.3)		2 (1.9)	
Time between delivery and latest HIV RNA measurement (weeks)						
Median (IQR)	2.4 (1.0 to 4.3)	2.5 (1.0 to 4.5)	2.4 (0.9 to 4.0)	2.6 (1.3 to 4.4)	2.6 (0.9 to 4.3)	0.777

Pregnancy outcome

The 1,035 pregnancies resulted in 683 (66%) births ≥24 weeks (including both live and stillbirths), including 13 twin pregnancies. A total of 349 (34%) pregnancies ended in miscarriage or still birth <24 weeks or abortion; 218 (21%) were miscarriages or still births<24 weeks and 131 (13%) were abortions. For the remaining three (<1%) pregnancies, the outcome is unknown due to missing data(*Table 9.1B*).

Pregnancy duration, preterm birth and perinatal death

A total of 683 pregnancies lasted at least 24 weeks and are therefore counted as a birth (*Table 9.1B*):

- 599 (88%) of the pregnancies lasted at least 37 weeks,
- 83 (12%) pregnancies resulted in preterm birth (defined as a pregnancy duration of 24-37 weeks). It is worth noting that 35/83 preterm births had a pregnancy duration of 36 weeks.
- 1 live birth had an unknown pregnancy duration.

The prevalence of preterm birth is higher compared to that in the general population (7%)[29].

Perinatal death, including antepartum death, occurred in five (<1%) births. Congenital disorders were registered for 18 infants.

Mode of delivery

If viral suppression during pregnancy is 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 63% of women of Latin America or Caribbean origin. Sixteen percent of newborns were delivered by an elective Caesarean section and another 15% by a secondary Caesarean section (*Table 9.1B*).

In terms of mode of delivery, 96% of the women who delivered vaginally had an HIV RNA below 50 copies/ml. This figure was 93% 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 secondary Caesarean section were obstetric indications such as foetal distress and failure to progress in the second stage of labour.

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

Therapy uptake

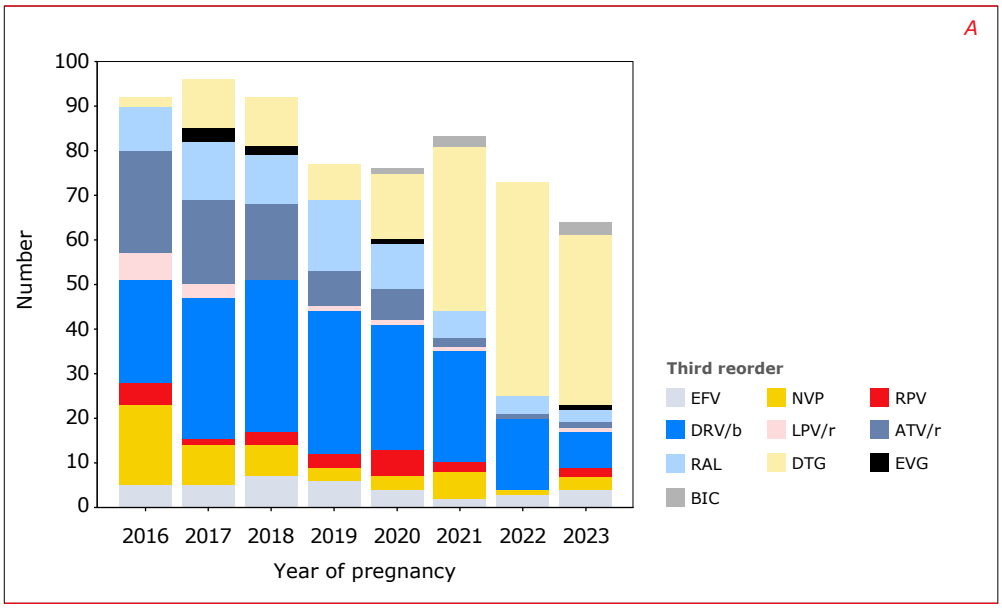
From 2016 onwards, during the 683 pregnancies lasting at least 24 weeks, all women received ART during the pregnancy:

- in 576 (84%) pregnancies, ART was initiated before pregnancy
- in 107 (16%) pregnancies, ART was started during pregnancy (Table 9.1C). Including 20 women who were diagnosed before their pregnancy. In total, two women discontinued treatment before delivery.

For 681 out of the 683 pregnancies, information on ART regimens during delivery was available. *Figure 9.2A* 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 2023.

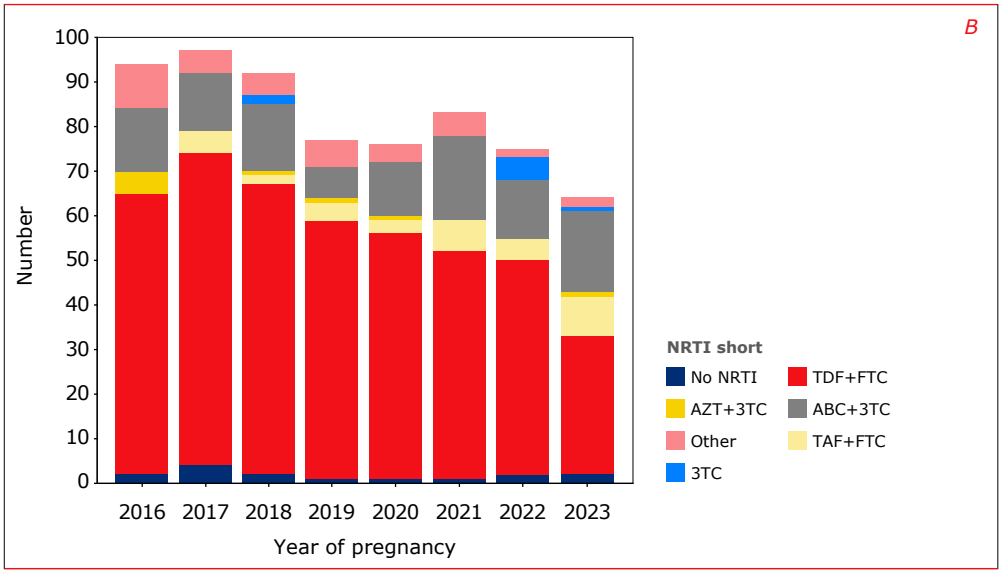
- Integrase inhibitors (INSTI) use increased from 4% in 2016 to 64% in 2023.
- Use of NNRTIs decreased from 30% in 2016 to 14% in 2023
- Use of PIs decreased from 56% to 16%(*Figure 6.2C*).
- In 18 pregnancies a two-drug regimen was used, which were combination of NRTI+INSTI or PI+INSTI.

Figure 9.2A: *The most commonly used third-drug additions to the nucleoside analogue reverse transcriptase inhibitor (NRTI) backbone used as part of ART regimens during 500 pregnancies in 2016–23 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 9.2B: *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 (2024). 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 9.2C: Antiretroviral class use stratified by calendar year period regimens during pregnancies in 2016–2023, 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 (2024). Therefore, the most recent calendar year is not shown in the figure.

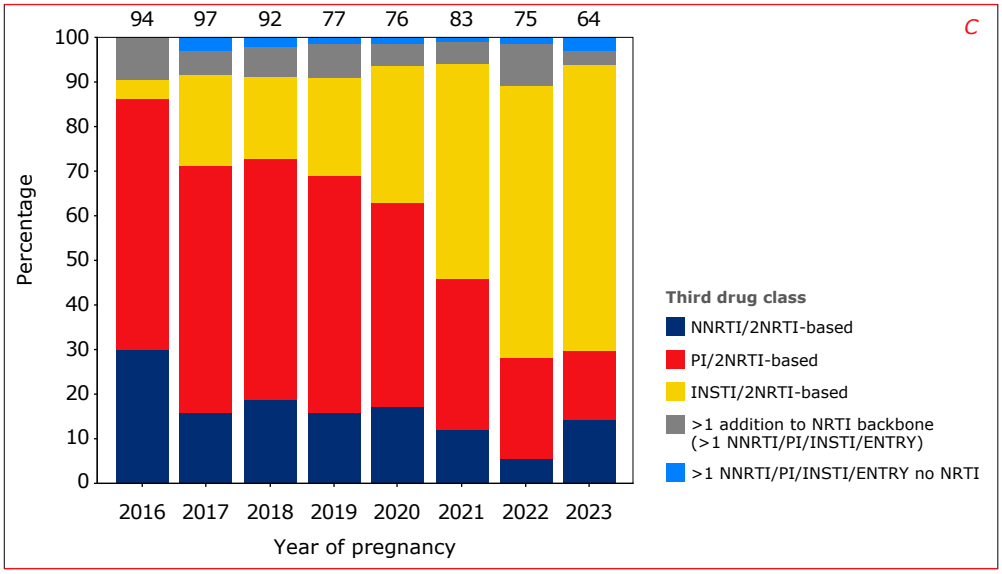


Figure 9.2B provides an overview of the components of the NRTI backbone used during pregnancy between 2016 and 2023. The most commonly prescribed backbones were the combination of:

- Tenofovir disoproxil fumarate and emtricitabine (TDF+FTC) (66%).
- Abacavir and lamivudine (ABC+3TC) (17%).
- Tenofovir alafenamide and emtricitabine (TAF+FTC) (6%)

A switch in ART regimen was reported during 234 pregnancies. While no reason was documented in 22 cases, the most common documented reason for switching in the remaining pregnancies was pregnancy-related (n=142). In 30% of all pregnancy-related switches a cobicistat-boosted regimen was replaced. Other common pregnancy-related switches included a switch from an integrase-containing regimen to a protease inhibitor (darunavir or atazanavir) or 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 2024. All women had an HIV RNA level below 50 copies/ml at the time of delivery.

Therapy response

Figure 9.3 shows the percentage of women on ART and their latest available plasma HIV RNA level prior to delivery. In 80% of the deliveries this HIV RNA measurement was within 4 weeks prior to delivery. HIV RNA levels were categorised as below 50 copies/ml, 50-500 copies/ml, and above 500 copies/ml.[a]

- Overall 97% of the mothers had an HIV RNA below 50 copies/ml, 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.

In total, 19 women had HIV RNA levels above 50 copies/ml (50-500 copies/ml: n=15, >500 copies/ml: n=4, median RNA=153 copies/ml; minimum=53, maximum=15,500) prior to delivery(*Table 9.2*).

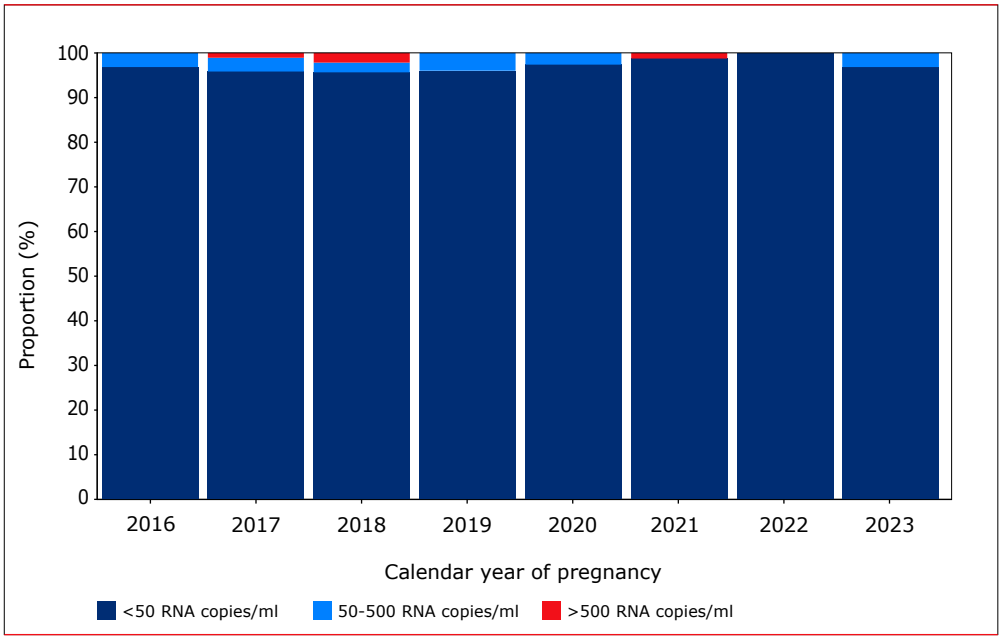
a Dutch guidelines allow a vaginal delivery with HIV RNA below 500 copies/ml and declining viral loads[13] or with a undetectable HIV RNA <50 or <20 copies/ml, depending on the used assay.

Table 9.2: Overview of characteristics of 19 women with a detectable HIV RNA level prior to delivery.

Women with detectable HIV RNA	19	
Age (median, IQR)	32 (27–36)	
Newly diagnosed during pregnancy	7 (37)	6 women were diagnosed after the first trimester.
ART initiated during pregnancy	7 (37)	
ARV at time of detectable HIV RNA*		
INSTI-containing	11 (57)	
NNRTI-containing	2 (11)	
PI-containing	6 (32)	
Mode of delivery		RNA (minimum; maximum)
Caesarean section	13 (69)	53, 15,500 copies/ml
Vaginal	4 (21)	70, 1,003 copies/ml
Unknown	2 (10)	
Zidovudine during delivery		
Yes	14 (74)	
No	4 (21)	
Unknown	2 (10)	
Evaluation of drug resistance	14 /19	• Pre-treatment drug resistance data was available to 9 women: 2/9 NRTI-associated resistance mutations were found • Drug resistance data after ART initiation was available for 8 women: 5 sequences harboured resistance to at least one NNRTI; and for 3 also resistance to at least one NRTI. • In 3 women the resistance mutation was measured during the pregnancy.

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

Figure 9.3: 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 (2024). Therefore, the most recent calendar year is not shown in the figure.

Vertical transmission rate in the Netherlands

Between 2016 and 2024, 683 births were registered in the Netherlands among mothers known to live with HIV prior to conception or first diagnosed during pregnancy. All mothers received ART during their pregnancy and in 97% of the pregnancies the HIV RNA was below 50 copies/ml. 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 683 pregnancies lasting 24 weeks or longer, 71 were excluded from this analysis: 48 because of insufficient follow up between delivery and the time of database closure; and 23 because the women were no longer in care (3 had moved abroad and nine were reported as lost to care during the postpartum period).

For the remaining 612 pregnancies in 486 women, ART was initiated before conception or during pregnancy in 81% and 19% of cases, respectively. The majority of women used an integrase inhibitor-containing regimen during the postpartum period (51%). The use of integrase inhibitor increased from 24% in 2016, to 57% in 2020 and 88% in 2024.

In 39 (6%) of these 612 pregnancies, ART was discontinued postpartum:

- The most common documented reason was a patient decision (n=26).
- In two cases the documented reason was elite controller or long-term non-progressor[b].
- In 3 cases the documented reason was experienced ART toxicity.
- In 8 cases the documented reason was end of pregnancy and in one case the reason was not reported.

In 16 out of the 39 cases, therapy was restarted after a median of 4.6 weeks (IQR 2-10). In the remaining 23 cases, ART was not restarted postpartum, however 15 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 82(13%) of the 612 pregnancies analysed. When taking into account >200 copies/ml as a detection margin, 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 573/612 (94%) women with documented continued use of ART postpartum:
- 63 (12%) had at least one episode of an HIV RNA level above 50 copies/ml (median HIV RNA=257 copies/ml, minimum=52 and maximum=85,900 copies/ml)
- 35 (6%) had a HIV RNA level above 200 copies/ml,
- 25 had more than one episode of an HIV RNA level above 50 copies/ml during the postpartum period.
- 14 of the 63 women with an HIV RNA above 50 copies/ml were newly diagnosed with HIV during the pregnancy.
- 49/63 women were diagnosed and treated before conception, of whom 67% (n=33) had earlier episodes of detectable HIV RNA levels more than 6 months after the start of initial ART.

In the 39/612 (6%) women who discontinued the use of ART postpartum:
- One woman did not had HIV RNA measurements;
- 19 (49%) had at least one episode of an HIV RNA level above 50 copies/ml (median HIV RNA=19,800 copies/ml, minimum 617 and maximum 450,000 copies/ml).
- 19 women remained virally suppressed during the postpartum period:
  - 11 women eventually restarted ART;
  - 1 woman who became virally unsuppressed after the postpartum period;
  - 5 women with 7 pregnancies continued to report high CD4 cell counts and HIV RNA levels <50 copies/ml in the absence of ART;

Breastfeeding

In the Netherlands, pregnant women with sustained virological suppression are informed about the possibility of breastfeeding. The final decision about the baby feeding is a result of a shared decision by the patient and health care professional. Breastfeeding in such cases is recommended for a maximum of six months.

Data about the baby feeding were available for 540 of the 612 pregnancies, and breastfeeding was reported in 49 pregnancies (the duration of breastfeeding was not documented). It is noteworthy that all women had documented use of ART and that all women had HIV RNA levels below 50 copies/ml during or below the detection limit of the used assay during the first 6 months of the postpartum period. The median number of HIV RNA measurements during the first 6 months after delivery among the 49 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 of HIV in the Netherlands has become very rare in pregnant women using ART during the period 2016 to 2024, resulting in a very low perinatal HIV infection rate. 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 was more often the case in 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 all pregnant women, and close monitoring is especially needed in women who were newly diagnosed with HIV after conception and those with a history of virological failure.

Although most women were aware of living with HIV prior to their pregnancy, 14% were newly diagnosed during pregnancy. Based on SHM data, 24% of them originated from the Netherlands and 76% 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 of 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 its continuation postpartum. We observed an increasing proportion of women who received integrase inhibitors during pregnancy as well as during the postpartum period. However, therapy compliance after delivery requires close attention. 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]. The aetiology of preterm delivery is complex and multifactorial, it is unclear whether ART use or other demographic or 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, it has become standard of care that ART is used at conception and not interrupted after 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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