Retention in care and viral suppression in pregnant/postpartum vs. nonpregnant/nonpostpartum women with HIV

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Objective: To investigate retention in care, viral suppression, and virological failure in pregnant and postpartum women with HIV compared to nonpregnant/nonpostpartum women with HIV in Denmark, and to explore factors associated with adverse HIV care outcomes.

Design: A nationwide registry-based cohort study.

Methods: All women with HIV, who delivered in Denmark from 2000 to 2019, alongside a comparison group of nonpregnant/nonpostpartum women with HIV were included from the Danish HIV Birth Cohort and the Danish HIV Cohort Study and linked to national health registries. We assessed outcomes: retention in care (two HIV RNA or $CD4^+$ measurements $\geq$90 days apart within a year), viral suppression (HIV RNA $<$200 copies/ml at the latest measurement), and virological failure (two consecutive HIV RNA measurements $>$200 copies/ml or one $>$1000 copies/ml). Incidence rate ratios evaluated group differences, and logistic regression analyzed factors linked to adverse outcomes.

Results: We included 564 pregnant and 1705 nonpregnant/nonpostpartum women with HIV. Retention in care was significantly lower during pregnancy, especially for deliveries before 2014, and in the second postpartum year. No significant differences in viral suppression were found between groups after stratification by delivery year or in women with more than 1 year since HIV diagnosis. Pregnant women had higher rates of virological failure, while postpartum women had lower rates, significant only in the second postpartum year for women delivering before 2010.

Conclusion: Based on $CD4^+$/HIV RNA measurements, retention in care was lower in pregnant and postpartum women, particularly in the second year. Reassuringly, viral suppression and virological failure rates were comparable.

AIDS 2025, **39**:1936–1945

Keywords: Danish HIV birth cohort, HIV, postpartum period, pregnancy, retention in care, sustained virologic response, women

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Received: 7 March 2025; revised: 3 June 2025; accepted: 5 June 2025.

DOI:10.1097/QAD.0000000000004275

ISSN 0269-9370

Background

Antiretroviral therapy (ART) has improved outcomes for people with HIV. For women on ART with fully suppressed HIV RNA during pregnancy, the risk of vertical HIV transmission is very low [1]. Adherence to ART in pregnancy and postpartum is essential for prevention of vertical HIV transmission and optimal maternal and child health [2]. Also, as more women in high-income settings are breastfeeding, antenatal and postpartum care is crucial to prevent postpartum vertical HIV transmission [2].

There are approximately 1900 women with HIV in Denmark, of whom the majority are immigrants, mainly from Sub-Saharan Africa [3]. Denmark is a country with a tax-based healthcare system offering free to the individual – and equal access to – medical healthcare, including ART, as well as many social support services. ART has been recommended to all pregnant women with HIV in Denmark since the late 1990s. The guidelines and management of pregnant women with HIV have changed considerably since then. Prior to 2009, ART was primarily initiated at gestational week 14 to prevent vertical HIV transmission, with discontinuation postpartum permitted in women with a $CD4^+$ cell count of at least 350 cells/μl. In 2010, the guidelines were updated to recommend initiation of treatment as soon as possible in pregnant women with HIV and a $CD4^+$ cell count less than 350 cells/μl, while women with a $CD4^+$ cell count of at least 350 cells/μl should initiate ART in pregnancy week 14. National antenatal screening for all pregnant women of HIV, Syphilis, and Hepatitis B was implemented at the same time as an opt-out program (e.g., all pregnant women are screened unless they decline) [4]. In 2014, the guidelines for pregnant women with HIV were updated once again to reflect the changes in the general treatment guidelines of "universal ART," that is, initiation of ART as soon as possible in all people with HIV, including pregnant women [5,6]. Today, the risk of vertical HIV transmission in Denmark is less than 1% [7].

The peripartum period is a vulnerable phase associated with complex medical and psychosocial issues [8–10].

Poor adherence to ART in the postpartum period can lead to viral rebound and subsequently disease progression, viral resistance, increased maternal morbidity, sexual transmission to partners, and increased risk of HIV transmission to the infant [11,12]. Declines in postnatal HIV care retention and viral suppression in women with HIV have been reported in both high [2,11,13,14] and low-income and middle-income countries [15,16].

Many studies on retention in care in pregnancy and postpartum from high-income settings originate from non-European countries [2,11–13], which differs in terms of healthcare and socioeconomic structure compared with European countries. In this Danish nationwide study, we aimed to investigate retention in care, viral suppression, and virological failure in pregnancy and postpartum in women with HIV compared to nonpregnant/nonpostpartum women with HIV. Factors associated with adverse HIV care outcome in pregnancy and postpartum were also explored.

Materials and methods

Population

All women with HIV delivering one or more child/children between January 1, 2000, and December 31, 2019, in Denmark were identified through the Danish HIV Birth Cohort (DHBC) [7]. Women were excluded if they did not have a valid personal identification number (PIN), a unique number assigned to all Danish residents at birth (or with approved immigration status).

Comparison group

A comparison group of women with HIV was identified through the Danish HIV Cohort Study (DHCS) [17], and included if they were between age 15 and 50 years, and not pregnant or postpartum at the time of HIV RNA/$CD4^+$ cell count measurement (defined as 1 year prior to and 2 years after child date of birth).

Data sources

Data were collected using the unique PIN to identify and track the study participants in the following registries [18].

The DHBC is a prospective, nationwide, population-based cohort study including all women with HIV giving birth to one or more children in Denmark after December 31, 1999, with consecutive ongoing enrolment [7]. Eligible women are identified and enrolled in the DHBC through the specialized clinical centers responsible for the treatment and care of pregnant women with HIV in Denmark. The DHBC collects demographic and clinical data on both the mother and child from medical records, covering pregnancy, delivery, and the early postpartum period. We extracted the following data: maternal country of origin, smoking and alcohol or illicit drug use during pregnancy, time of maternal HIV diagnosis relative to pregnancy, and time of ART initiation.

The DHCS is a population-based prospective nationwide cohort study including all people living with HIV, who have been treated at Danish HIV centers since January 1, 1995 [17]. Participants are consecutively enrolled in the DHCS, and data are updated yearly and include demographics, ART use, $CD4^+$ cell counts, and HIV RNA measurements. We extracted data on date of HIV

diagnosis, HIV RNA and CD4$^+$ cell measurements, smoking (comparison group only), and migration.

The Medical Birth Registry (MBR) contains complete information on all births in Denmark since 1973 [19]. We extracted data on maternal age at delivery, date of birth, gestational age, parity, and child sex.

National Patient Registry (NPR) and National Psychiatric Patient Registry (NPPR) contain information on all hospital contacts (inpatient, outpatient, and emergency ward visits) since 1977 and 1995, respectively [20,21]. Discharge diagnoses are classified according to the International Classification of Diseases, 10th revision (ICD-10). From these two registries, we extracted data on maternal psychiatric diagnoses (F00-F99) prior to delivery.

From the national registries at Statistics Denmark, including demographic and socioeconomic information at the population level since 1968 [18,22], we extracted data on the family's socioeconomic status defined by the adult with the highest income in the household (grouped into working, unemployed, social benefits/disability, and other) and maternal marital status.

Outcomes and definition of time periods

The following HIV care outcomes were assessed: *retention in care* (defined as two HIV RNA viral load or CD4$^+$ measurements, 90 days or more apart within a given year, as specified below), *viral suppression* (defined as HIV RNA <200 copies/ml at the latest measurement within a given year, as specified below), and *virological failure* (defined as two consecutive HIV RNA measurements >200 copies/ml or one HIV RNA measurement >1000 copies/ml within a given year, as specified below). The cutoff of HIV RNA less than 200 copies/ml was chosen to account for the variable lower limits of viral load tests in the early study period.

Time periods/observation periods were defined as follows: *pregnancy periods* were from 1 year before delivery to delivery, *first postpartum year* was from delivery to 12 months after delivery, *second postpartum periods* were from 12 to 24 months after delivery, and *comparison periods* were from January 1, to December 31, of a calendar year (Fig. 1). We only included full time periods, that is, those observation periods where individuals were available for observation for the entire year. The reason for this is that the retention in care outcome is less feasible with shorter time periods and impossible to achieve with time periods below 90 days. The same accounts to some extent for the virological failure outcome. If a woman is included in a pregnancy period in a given year, she cannot contribute to the comparison period in the same calendar year.

Statistical analysis

Categorical variables are described as counts (%), and continuous variables are described as means [95% confidence intervals (95% CIs)] or medians with the 25th to 75th interquartile ranges (IQRs). The incidence rate ratio (IRR) of events (retention in care, viral suppression, or virological failure) were calculated per observation years and reported overall, and by delivery year reflecting the changes in treatment guidelines (2000–2009, 2010–2013, and 2014–2019). We also conducted two sensitivity analyses, one excluding women not retained in care (defined by two consecutive HIV RNA measures, which may reflect data availability) and one excluding women diagnosed with HIV less than 1 year prior to HIV RNA/CD4$^+$ measurement date to account for potential differences in early disease management.

Factors associated with retention in care, viral suppression, and virological failure in pregnancy, 1 and 2 years postpartum, respectively, were assessed using univariate

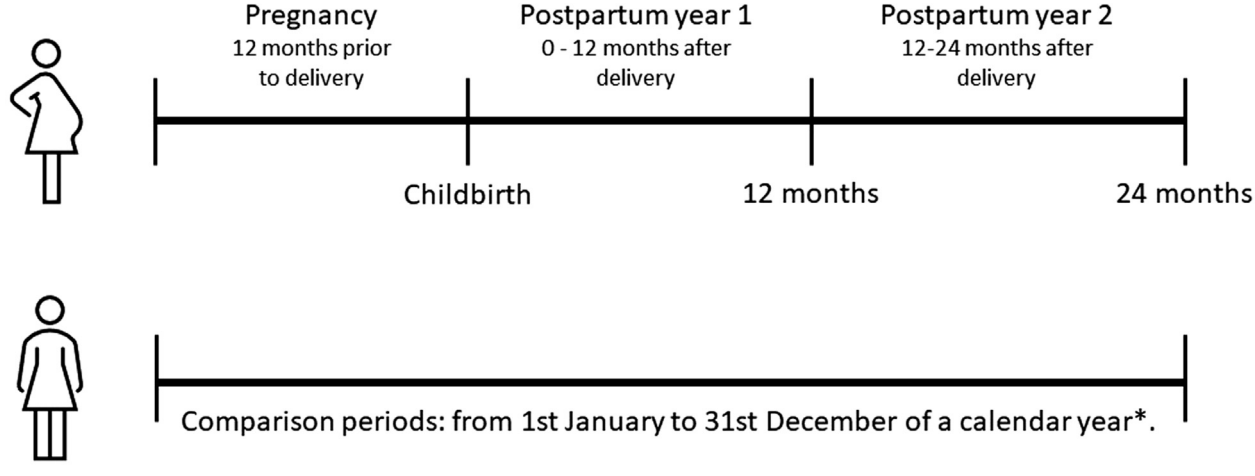

Fig. 1. Follow-up periods for pregnant/postpartum women with HIV and the comparison group of nonpregnant/nonpostpartum women with HIV. *If a woman is included in a pregnancy period in a given year, she cannot contribute to the comparison period in the same calendar year, but during the study period, a woman can participate both as pregnant and as comparison.

and multivariate logistic regression models. These analyses included only pregnant and postpartum women, and all outcomes were treated as binary outcomes irrespective of their timing. Crude odds ratios (ORs) and adjusted odd ratios (aORs) with 95% CI were reported, respectively. The following covariates were included a priori: maternal age at delivery, country of origin, year of birth, time of ART initiation, time since HIV diagnosis at delivery, and family socioeconomic group. Multicollinearity between the included covariates was assessed using variance inflation factors (VIFs). All VIFs were below less than 2, suggesting no concerning multicollinearity. Missing values were included as a separate category in both the univariate and multivariate analyses. All models included maternal unique PIN as a cluster term, to account for nonindependence of successive deliveries from the same mother. Model fit was assessed by Hosmer-Lemeshow test. Analyses were carried out using STATA 18 (STATA Corporation, College Station, Texas, USA) and *P* values of less than 0.05 were considered significant.

Results

Population

In total, 1914 women with HIV aged 15–50 years were identified in the DHCS. During the 20-year study period, there were 599 pregnancies. Of these, 35 of the mothers did not have a valid PIN and were excluded. Hence, 564 pregnant women were included in the pregnancy/postpartum group, including seven twin pregnancies. One hundred sixty-nine women were pregnant more than once during the study period. Additionally, 1705 nonpregnant/nonpostpartum women were included in the comparison group with a total of 15 596 calendar years under observation. Clinical and demographic characteristics of the study population are presented in Table 1.

Retention in care

Retention in care was lower during pregnancy and the second postpartum year compared to nonpregnant/nonpostpartum women [IRR 0.78, (95% CI: 0.69–0.86) and 0.86 (95% CI: 0.77–0.95], (Table 2 and Table S1, http://links.lww.com/QAD/D601). In a sensitivity analysis excluding women diagnosed less than 1 year, retention was lower in the second postpartum year across the whole study period [IRR 0.76 (95% CI: 0.68–0.86), Table 3].

Multivariate analysis showed that ART initiation and diagnosis during pregnancy were associated with lower odds of retention in pregnancy, while more than 5 years since diagnosis was associated with higher odds of retention (Table 4). Unemployment and no ART in pregnancy was associated with lower odds of retention one year postpartum. Delivering in 2014–2019 was associated with lower odds of retention 2 years postpartum, whereas maternal age 36–40 and second-trimester ART initiation was associated with higher odds of retention. Maternal psychiatric illness was not significantly associated with adverse HIV care outcome in pregnancy nor postpartum.

Viral suppression

Viral suppression was lower in the second postpartum year compared to the comparison group (IRR 0.89, 95% CI: 0.80–0.98), but not during pregnancy or in the first postpartum year (Table 2) or in the sensitivity analyses excluding women not in retention or diagnosed less than 1 year (Tables 3 and 5).

In the multivariate analysis, delivery in 2014–2019 increased odds of suppression, while ART initiation in the third trimester or no ART decreased it (Table 4). Factors associated with higher odds of viral suppression one year postpartum were maternal age 31–35, delivery in 2010 or later, and HIV diagnosis in the first or second trimester, while ART initiation in later trimesters or no ART during pregnancy was associated with lower odds of suppression. Maternal age 31–35 years, delivery during 2010–2019, and HIV diagnosis in early trimesters were associated with higher odds of suppression 2 years postpartum, while smoking and delayed or no ART in pregnancy was associated with lower odds of suppression.

Virological failure

Pregnant women had higher rates of virological failure compared to nonpregnant women (IRR 1.48, 95% CI: 1.26–1.72), particularly in those delivering after 2010 (Table 2). In the first postpartum year, failure rates were lower (IRR 0.82, 95% CI: 0.66–0.99), significantly so for women delivering in 2000–2009 (IRR 0.76, 95% CI: 0.58–0.97). Women in the second postpartum year also showed lower rates of failure (IRR 0.68, 95% CI: 0.54–0.86), but this difference became nonsignificant when stratified by birth year. Sensitivity analyses showed no differences during pregnancy, while lower failure rates were observed for women in the second postpartum year who delivered during 2000–2009 (Tables 3 and 5).

In the multivariate analysis (Table 4), delivery during 2014–2019 was associated with lower virological failure odds in pregnancy, and in the postpartum period. ART initiation or no ART in pregnancy compared to prepregnancy was associated with higher odds of failure. Smoking and being in a social benefits/disability socioeconomic group were also associated with higher failure odds in the second postpartum year, while HIV diagnosis in pregnancy was associated with lower odds of failure postpartum.

Table 1. Characteristics of women with HIV aged 15–50 years and those who became pregnant, included in the Danish HIV Cohort and delivering in year 2000–2019 in Denmark.

	All women with HIV[a] $N = 1914$	Pregnant women $n = 564$
Age[b] [mean (95% CI)]	31.41 (30.98–31.84)	32.59 (32.16–33.04)
Missing [*n* (%)]	14 (1)	
Married [*n* (%)]	691 (36)	247 (44)
Missing	394 (21)	132 (23)
Country of origin [*n* (%)]		
Denmark	627 (33)	136 (24)
African country	644 (34)	313 (56)
Asian country	227 (12)	64 (11)
Other	416 (22)	51 (9)
Family socioeconomic group [*n* (%)]		
Working	799 (42)	224 (39)
Unemployed	55 (3)	8 (2)
Social benefits/disability	504 (26)	77 (13)
Other/missing	556 (29)	255 (45)
Smoking[c] [*n* (%)]	99 (5)	74 (13)
Missing	1638 (85)	24 (4)
Illicit drug or alcohol in pregnancy [*n* (%)]		32 (6)
Missing		52 (9)
Year of HIV diagnosis [*n* (%)]		
<1995	379 (20)	41 (7)
1995–2005	713 (37)	247 (44)
2006–2015	610 (32)	241 (43)
2016–2019	198 (10)	30 (5)
Missing	14 (1)	5 (1)
Time of maternal HIV diagnosis [*n* (%)]		
Before conception		452 (80)
First trimester		60 (11)
Second trimester		30 (5)
Third trimester		15 (3)
During or <30 days of delivery		7 (1)
Time of maternal ART initiation [*n* (%)]		
Before conception		370 (66)
First trimester		54 (9)
Second trimester		109 (19)
Third trimester		22 (4)
No treatment in pregnancy		9 (2)
$CD4^+$ cell count at delivery (median [IQR])		523 [384–686]
Missing [*n* (%)]		13 (2)
HIV viral load at delivery [*n* (%)]		
<50 copies/ml		476 (84)
≥50 copies/ml		79 (14)
Missing		9 (2)
Nulliparous [*n* (%)]		220 (39)
Missing		12 (2)
Year of birth [*n* (%)]		
2000–2009		243 (43)
2010–2013		140 (25)
2014–2019		181 (32)
Child sex [*n* (%)]		
Male		278 (49)
Missing		20 (4)
Time since HIV diagnosis at delivery (median years [IQR])		5.40 [1.40–9.36]

[a]Includes all women with HIV (from the Danish HIV Cohort) at least 15 years of age in 2000 and no older than 50 years of age in 2019 and women (from the Danish HIV Birth Cohort) who at some point during the study period (year 2000–2019) become pregnant.
[b]For all women with HIV, age at HIV-diagnosis is reported, while for pregnant women with HIV, age at delivery is reported.
[c]For pregnant women with HIV smoking during pregnancy is reported.

Discussion

In this nationwide cohort study of women with HIV in Denmark, retention in care was significantly lower during pregnancy, particularly for those delivering before 2014, and in the second postpartum year, compared to nonpregnant/nonpostpartum women. However, no significant differences in viral suppression were found between the groups after stratifying by delivery year or in sensitivity analyses. Pregnant women had higher rates of virological failure, while postpartum women had lower rates, though this was only significant in the second postpartum year for women delivering before 2010.

Table 2. Crude incidence rate ratios of HIV care outcome in pregnant/postpartum women with HIV compared to nonpregnant/nonpostpartum women with HIV.

	RETENTION IN CARE					
	Pregnant women vs. comparison group		Postpartum year 1 vs. comparison group		Postpartum year 2 vs. comparison group	
	IRR (95% CI)	*P*	IRR (95% CI)	*P*	IRR (95% CI)	*P*
Total	0.78 (0.69–0.86)	<0.001	0.99 (0.90–1.09)	0.91	0.86 (0.77–0.95)	<0.01
2000–2009	0.72 (0.61–0.84)	<0.001	0.95 (0.82–1.09)	0.51	0.87 (0.74–1.02)	0.96
2010–2013	0.75 (0.60–0.92)	<0.01	1.04 (0.86–1.24)	0.63	0.92 (0.75–1.12)	0.42
2014–2019	0.88 (0.73–1.05)	0.15	1.01 (0.84–1.20)	0.89	0.78 (0.62–0.97)	0.02
	VIRAL SUPPRESSION					
	Pregnant women vs. comparison group		Postpartum year 1 vs. comparison group		Postpartum year 2 vs. comparison group	
	IRR (95% CI)	*P*	IRR (95% CI)	*P*	IRR (95% CI)	*P*
Total	1.00 (0.91–1.13)	0.92	0.94 (0.85–1.04)	0.22	0.89 (0.80–0.98)	0.02
2000–2009	1.09 (0.94–1.26)	0.23	0.95 (0.81–1.11)	0.52	0.90 (0.76–1.05)	0.18
2010–2013	0.93 (0.77–1.12)	0.45	0.94 (0.76–1.13)	0.51	0.92 (0.76–1.12)	0.41
2014–2019	0.95 (0.81–1.12)	0.56	0.93 (0.78–1.05)	0.43	0.89 (0.73–1.07)	0.21
	VIROLOGICAL FAILURE					
	Pregnant women vs. comparison group		Postpartum year 1 vs. comparison group		Postpartum year 2 vs. comparison group	
	IRR (95% CI)	*P*	IRR (95% CI)	*P*	IRR (95% CI)	*P*
Total	1.48 (1.26–1.72)	<0.001	0.82 (0.66–0.99)	0.04	0.68 (0.54–0.86)	<0.001
2000–2009	1.19 (0.96–1.45)	0.10	0.76 (0.58–0.97)	0.02	0.66 (0.36–1.11)	0.11
2010–2013	2.07 (1.49–2.79)	<0.001	0.94 (0.58–1.46)	0.82	0.64 (0.35–1.08)	0.08
2014–2019	2.45 (1.69–3.46)	<0.001	0.92 (0.47–1.63)	0.82	0.55 (0.20–1.21)	0.13

Several studies from various settings have reported low postpartum retention in care [2,11–14,23–26]. In contrast to our findings, most show low postpartum viral suppression rates, often below 50% [2,11–13,27]. Differences in study periods, populations, and definition of retention outcome complicate direct comparisons across studies, and none of these studies, all conducted before 2015, included comparison groups. Only one study compared postpartum women to nonpostpartum women and found a higher risk of virological failure (defined as a single measure of HIV RNA >200 copies/ml) among postpartum women in the UK [28]. Similar to our study, ART initiation and HIV diagnosis during pregnancy were consistently associated with adverse HIV care outcomes. This finding is supported by other studies [2,13,26,29], including a recent analysis from the Swiss HIV Cohort showing that ART initiation during pregnancy was associated with less likelihood of postpartum engagement and retention in women, who were virally suppressed at delivery [23].

Lower retention rates during the second postpartum year may be due to the heightened stress during this period [30,31]. Many women attempt to balance work, family, and social life, and attending clinic visits may be difficult to prioritize [31,32]. Additionally, changes in clinical practice, such as reduced frequency of HIV RNA measurements for individuals with stable viral suppression, could result in fewer clinic visits and contribute to lower retention rates. The lower odds of retention observed for women delivering between 2014 and 2019 may reflect this shift in clinical practice. Also, no difference in postpartum virological failure was observed in the later study period. Overall, more recent deliveries were linked to better HIV care outcomes during both pregnancy and the postpartum period, likely reflecting advancements in the availability, tolerability, and efficacy of contemporary ART over time. A finding also observed in the Swiss HIV Cohort [23]. These improvements in HIV care outcomes are especially important in the context of breastfeeding, where enhanced postpartum follow-up may help ensure safer breastfeeding practices. The higher virological failure rate observed in pregnant women may be due to recent HIV diagnoses. When excluding women diagnosed less than a year before pregnancy or those not retained in care, there was no significant difference in virological failure during pregnancy. Contrary to earlier studies [12,26,28], we found lower rates of failure in postpartum women, particularly in the second postpartum year and the early

Table 3. Sensitivity analysis of crude incidence rate ratios of HIV care outcome in pregnant/postpartum women with HIV compared to nonpregnant/nonpostpartum women with HIV limited to women with HIV diagnosis ≥1 year of measurement date.

	RETENTION IN CARE					
	Pregnant women vs comparison group		Postpartum year 1 vs. comparison group		Postpartum year 2 vs. comparison group	
	IRR (95% CI)	*P*	IRR (95% CI)	*P*	IRR (95% CI)	*P*
Total	0.92 (0.83–1.03)	0.18	0.92 (0.83–1.01)	0.09	0.76 (0.68–0.86)	<0.001
2000–2009	0.88 (0.74–1.05)	0.15	0.91 (0.78–1.06)	0.24	0.81 (0.69–0.96)	0.01
2010–2013	0.91 (0.73–1.14)	0.42	0.93 (0.76–1.13)	0.47	0.75 (0.59–0.92)	<0.01
2014–2019	1.00 (0.83–1.21)	0.97	0.91 (0.74–1.09)	0.29	0.69 (0.54–0.87)	<0.01
	VIRAL SUPPRESSION					
	Pregnant women vs. comparison group		Postpartum year 1 vs. comparison group		Postpartum year 2 vs. comparison group	
	IRR (95% CI)	*P*	IRR (95% CI)	*P*	IRR (95% CI)	*P*
Total	1.04 (0.94–1.16)	0.40	0.97 (0.88–1.07)	0.50	0.91 (0.82–1.00)	0.06
2000–2009	1.16 (0.99–1.36)	0.07	0.99 (0.84–1.16)	0.92	0.93 (0.73–1.08)	0.34
2010–2013	0.96 (0.78–1.18)	0.73	0.87 (0.71–1.05)	0.14	0.91 (0.75–1.10)	0.33
2014–2019	0.97 (0.81–1.15)	0.71	0.94 (0.79–1.11)	0.46	0.89 (0.73–1.08)	0.24
	VIROLOGICAL FAILURE					
	Pregnant women vs. comparison group		Postpartum year 1 vs. comparison group		Postpartum year 2 vs. comparison group	
	IRR (95% CI)	*P*	IRR (95% CI)	*P*	IRR (95% CI)	*P*
Total	0.98 (0.78–1.20)	0.83	0.77 (0.61–0.95)	0.01	0.69 (0.54–0.88)	<0.01
2000–2009	0.86 (0.65. 1.14)	0.30	0.72 (0.54–0.96)	0.01	0.69 (0.51–0.90)	<0.01
2010–2013	1.43 (0.91–2.16)	0.10	0.78 (0.44–1.27)	0.33	0.67 (0.36–1.13)	0.12
2014–2019	1.13 (0.59–1.95)	0.65	0.97 (0.50–1.72)	0.96	0.58 (0.21–1.27)	0.16

study period. One possible reason is that while some women may have stopped treatment after childbirth in the early 2000 s, those who began ART during pregnancy were likely to continue it postpartum. In contrast, nonpregnant women's treatment initiation depended on their $CD4^+$ cell count, explaining the differing failure rates.

Our finding that women in the second postpartum year have both significantly lower odds of suppression and lower odds of failure seems counterintuitive. This difference may be attributed to the definitions of the two outcomes: suppression is determined by a single measurement of HIV RNA less than 200 copies/ml within a year, while failure is identified either by two consecutive measurements exceeding 200 copies/ml or by a single measurement over 1000 copies/ml within the same timeframe. Virological failure in relation to our definition requires sustained nonadherence, and postpartum women may experience temporary dips in adherence, without long-term impacts [33].

Several modifiable factors associated with postpartum adverse HIV care outcome have been identified [29,34]. Perinatal depression has been associated with postnatal adverse HIV care outcome in some studies [30,35], but not in others [23,36]. Our study used ICD-10 diagnoses for psychiatric illness, potentially underestimating associations with adverse outcomes by not including milder cases or those treated outside hospitals. Additionally, smoking during pregnancy and receiving social benefits/disability were associated with higher odds of failure and decreased odds of suppression, a finding supported by others [23,37]. This underscores the need for smoking cessation programs and enhanced support for socioeconomically vulnerable women during pregnancy. Moreover, while country of origin was not associated with HIV care outcomes in our analysis, structural and cultural factors remain important considerations for care engagement. Evidence on effective postpartum strategies is limited, however, multidisciplinary care coordination across the pregnancy–postpartum period and peer support interventions have shown potential to improve HIV care outcomes during this time [29,32].

Strengths and limitations

A main strength of this study is its nationwide, population-based design. The use of registries ensured uniform, unbiased individual-level data, with limited loss to follow-up. While we could not distinguish between

Table 4. Factors associated with retention in care, viral suppression, and virological failure in pregnancy and postpartum in women with HIV delivering one or more children in year 2000–2019 in Denmark.

		Retention in care			Viral suppression			Virological failure		
		Pregnancy	1 year postpartum	2 years postpartum	Pregnancy	1 year postpartum	Postpartum 2 years	Pregnancy	1 year postpartum	2 years postpartum
	n	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
Maternal age at delivery										
<30 years	164	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
31–35 years	216	1.32 (0.81–2.17)	1.07 (0.62–1.83)	1.46 (0.90–2.37)	1.12 (0.62–2.03)	**2.21 (1.26–3.85)**	**2.02 (1.18–3.46)**	0.98 (0.57–1.69)	**0.51 (0.29–0.92)**	**0.45 (0.24–0.86)**
36–40 years	147	**2.12 (1.16–3.88)**	1.61 (0.81–3.19)	**2.58 (1.41–4.72)**	0.76 (0.36–1.62)	2.05 (0.98–4.33)	1.65 (0.84–3.24)	0.79 (0.42–1.51)	0.72 (0.33– 1.55)	0.49 (0.19–1.28)
>40 years	43	1.09 (0.45–2.63)	0.81 (0.31–2.10)	1.74 (0.70–4.36)	0.96 (0.33–2.84)	1.81 (0.61–5.34)	2.06 (0.72–5.92)	1.32 (0.52–3.35)	0.49 (0.16–1.55)	0.24 (0.05–1.13)
Smoking during pregnancy	74	1.19 (0.60–2.37)	1.41 (0.67–2.98)	0.92 (0.48–1.75)	0.64 (0.31–1.31)	**0.49 (0.27–0.90)**	**0.53 (0.29–0.95)**	1.51 (0.81–2.81)	1.64 (0.84–3.20)	**2.02 (1.03–3.94)**
Nulliparous	220	1.54 (1.00–2.39)	0.92 (0.55–1.54)	0.71 (0.46–1.10)	0.63 (0.36–1.11)	0.81 (0.50–1.31)	0.84 (0.53–1.33)	0.69 (0.45–1.08)	**1.88 (1.15–3.06)**	1.27 (0.74–2.17)
Year of birth										
2000–2009	243	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
2010–2013	140	0.78 (0.47–1.31)	1.66 (0.82–2.96)	0.94 (0.57–1.54)	1.26 (0.71–2.25)	**2.29 (1.28–4.10)**	**2.07 (1.18–3.61)**	0.77 (0.44–1.33)	**0.52 (0.30–0.92)**	**0.37 (0.19–0.70)**
2014–2019	181	1.07 (0.64–1.80)	0.83 (0.47–1.47)	**0.51 (0.30–0.85)**	**2.48 (1.24–4.96)**	**3.01 (1.58–5.71)**	**2.44 (1.35–4.43)**	**0.40 (0.23–0.70)**	**0.25 (0.13–0.49)**	**0.18 (0.07–0.44)**
Time of ART initiation										
Before conception	370	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
First trimester	54	**0.28 (0.15–0.53)**	0.99 (0.42–2.33)	1.28 (0.63–2.59)	1.40 (0.55–3.59)	0.61 (0.28–1.34)	0.60 (0.46–1.62)	**9.52 (4.51–20.08)**	1.68 (0.70–4.02)	**3.24 (1.35–7.79)**
Second trimester	109	**0.22 (0.13–0.38)**	0.90 (0.44–1.84)	**2.20 (1.16–4.17)**	1.09 (0.52–2.31)	**0.35 (0.20–0.64)**	**0.43 (0.24–0.79)**	**12.26 (6.91–21.78)**	**2.63 (1.35–5.14)**	**2.35 (1.15–4.81)**
Third trimester/no treatment in pregnancy	31	**0.03 (0.01–0.13)**	**0.30 (0.11–0.82)**	0.57 (0.23–1.49)	**0.11 (0.04–0.27)**	**0.24 (0.10–0.57)**	**0.29 (0.12–0.69)**	1.77 (0.67–4.66)	**3.49 (1.37–8.91)**	**4.36 (1.63–11.62)**
Time of maternal HIV diagnosis										
Before conception	452	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
First trimester	60	**0.17 (0.07–0.40)**	2.98 (0.91–9.83)	**2.77 (1.03–7.43)**	1.48 (0.45–4.82)	**2.48 (1.07–5.73)**	2.49 (1.09–5.65)	1.94 (0.86–4.40)	**0.28 (0.11–0.75)**	0.63 (0.24–1.67)
Second trimester	30	**0.05 (0.01–0.23)**	1.43 (0.43–4.77)	2.35 (0.69–7.96)	0.75 (0.19–2.91)	**5.46 (1.83–16.22)**	**7.36 (2.28–23.71)**	1.82 (0.63–5.29)	**0.14 (0.04–0.52)**	**0.16 (0.03–0.81)**
Third trimester/during or <30 days of delivery	22	**0.08 (0.01–0.77)**	1.28 (0.13–12.58)	0.84 (0.15–4.94)	0.36 (0.08–1.54)	0.94 (0.17–5.24)	1.16 (0.21–6.29)	0.84 (0.24–2.98)	2.19 (0.33–14.37)	0.28 (0.08–0.99)
Family socioeconomic group										
Working	224	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Unemployed/social benefits/disability	85	0.61 (0.33–1.15)	**0.51 (0.27–0.97)**	0.62 (0.33–1.13)	0.98 (0.47–2.10)	0.62 (0.31–1.25)	0.60 (0.32–1.14)	1.83 (0.95–3.5)	1.48 (0.75–2.91)	**2.63 (1.26–5.49)**
Other/missing	255	0.75 (0.47–1.18)	0.88 (0.50–1.53)	0.88 (0.54–1.43)	0.83 (0.46–1.51)	0.80 (0.43–1.48)	0.76 (0.43–1.34)	1.15 (0.69–1.91)	1.13 (0.65–1.96)	1.08 (0.52–2.26)
Time since HIV diagnosis										
Less than 5 years	266	Ref	Ref		Ref	Ref	Ref	Ref	Ref	Ref
5–10 years	175	**1.78 (1.09–2.92)**	0.76 (0.40–1.45)	0.96 (0.56–1.65)	1.70 (0.88–3.30)	1.07 (0.55–2.08)	0.87 (0.46–1.62)	0.80 (0.46–1.39)	1.28 (0.64–2.59)	1.11 (0.51–2.43)
>10 years	129	**3.40 (1.71–6.78)**	1.07 (0.47–2.42)	1.04 (0.51–2.09)	1.61 (0.69–3.73)	1.19 (0.54–2.64)	1.19 (0.54–2.63)	0.50 (0.24–1.06)	0.75 (0.30–1.92)	0.85 (0.28–2.51)

The following variables were not significantly associated with any of the HIV care outcomes: maternal country of birth, alcohol/drug use in pregnancy, and maternal psychiatric use (data not shown). aOR, adjusted odds ratio. Adjusted for maternal age at delivery, country of origin, year of birth, time of ART initiation, time since HIV diagnosis at delivery, and family socioeconomic group. Significant results are highlighted in bold.

Table 5. Sensitivity analysis of crude incidence rate ratios of HIV care outcome in pregnant/postpartum women with HIV compared to nonpregnant/nonpostpartum women with HIV limited to women who were in retention.

	VIRAL SUPPRESSION					
	Pregnant women vs. comparison group		Postpartum year 1 vs. comparison group		Postpartum year 2 vs. comparison group	
	IRR (95% CI)	*P*	IRR (95% CI)	*P*	IRR (95% CI)	*P*
Total	1.04 (0.93–1.16)	0.46	0.95 (0.86–1.06)	0.38	0.91 (0.81–1.02)	0.11
2000–2009	1.11 (0.93–1.33)	0.21	0.96 (0.81–1.14)	0.67	0.93 (0.78–1.12)	0.46
2010–2013	0.98 (0.78–1.22)	0.89	0.94 (0.76–1.14)	0.52	0.88 (0.71–1.09)	0.26
2014–2019	0.95 (0.78–1.14)	0.57	0.92 (0.76–1.11)	0.41	0.89 (0.70–1.13)	0.34
	VIROLOGICAL FAILURE					
	Pregnant women vs. comparison group		Postpartum year 1 vs. comparison group		Postpartum year 2 vs. comparison group	
	IRR (95% CI)	*P*	IRR (95% CI)	*P*	IRR (95% CI)	*P*
Total	0.99 (0.77–1.26)	0.95	0.87 (0.69–1.10)	0.25	0.72 (0.54–0.95)	0.02
2000–2009	0.88 (0.63–1.20)	0.42	0.79 (0.59–1.06)	0.11	0.67 (0.47–0.92)	0.01
2010–2013	1.42 (0.81–2.36)	0.17	0.89 (0.49–1.53)	0.72	0.76 (0.36–1.41)	0.40
2014–2019	1.41 (0.73–2.52)	0.25	1.28 (0.63–2.33)	0.41	0.72 (0.19–1.86)	0.55

loss to clinic (but retained in HIV care elsewhere) versus loss to care (i.e., access to ART and care), the implications are likely minimal, as the DHBC collects data on all individuals in HIV care across Denmark, and in the comparison group we only included women with a full year of follow-up. Our analysis relied solely on $CD4^+$/HIV RNA measurements, which may underestimate clinical appointments since it excludes those without blood tests. Additionally, changes in the recommended frequency of HIV RNA measurements for individuals with stable viral suppression could misclassify some as not retained in care [38].

Conclusion

Based on number of $CD4^+$/HIV RNA measurements, retention in care among women with HIV was lower in pregnancy and postpartum, particularly in the second postpartum year, compared to nonpregnant/nonpostpartum periods. Reassuring, there was no difference in viral suppression or virological failure observed between the groups. HIV diagnosis in pregnancy and ART initiation in pregnancy were consistently associated with adverse HIV care outcomes, highlighting the importance of early HIV diagnosis and prompt treatment initiation before or early in pregnancy. Future qualitative studies are essential to explore in greater detail the underlying reasons for adverse HIV care outcomes.

Acknowledgements

All authors contributed to study design, data collection, data interpretation, writing the report, and approved the final version. E.M. had full access to the data and did the statistical analysis together with L.O. E.M. wrote the first draft of the article, and together with N.W. had the original concept for the study.

This work was supported by the Aase and Ejner Danielsens Foundation. The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Ethics

The project was approved by the Danish Data Protection Agency (P-2020-257). According to Danish law, approval from the National Committee on Health Research Ethics was not required as no biomedical intervention was performed.

The study data are protected according to Danish and European Union data protection guidelines and are therefore not readily available due to legal restrictions.

Conflicts of interest

E.M. reports unrestricted grants from the Novo Nordisk Foundation and Gilead Sciences, outside of the submitted work, and personal fees from Gilead, Bristol Myers Squibb, and GlaxoSmithKline, outside of the submitted work: honorarium paid to her institution. T.L.K. reports personal fees and grants from ViiV/GlaxoSmithKline, MSD, Gilead, CLS Behring, Baxalta, and Vertex, outside of the submitted work. The remaining authors declare no conflicts of interest.

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