

# Missed Opportunities Among HIV-Positive Women to Control Viral Replication During Pregnancy and to Have a Vaginal Delivery

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**Introduction:** Most national guidelines for the prevention of mother-to-child transmission of HIV in Europe updated between 2001 and 2010 recommend vaginal deliveries for women with undetectable or very low viral load (VL). Our aim was to explore the

impact of these new guidelines on the rates of vaginal deliveries among HIV-positive women in Europe.

**Methods:** In a pooled analysis of data on HIV-positive pregnant women enrolled in the Swiss Mother & Child HIV Cohort Study and the European Collaborative Study 2000 to 2010, deliveries were classified as occurring pre- or postpublication of national guidelines recommending vaginal delivery.

**Results:** Overall, 2663 women with 3013 deliveries were included from 10 countries; 28% women were diagnosed with HIV during pregnancy. Combination antiretroviral therapy was used in most pregnancies (2020, 73%), starting during the first or second trimester in 78% and during the third trimester in 22%; in 25% pregnancies, the woman conceived on combination antiretroviral therapy. Overall, in 86% pregnancies, a VL < 400 copies per milliliter was achieved before delivery. The proportion of vaginal deliveries increased from 17% (414/2377) before the change in guidelines to 52% (313/600) after; elective Caesarean section rates decreased from 65% to 27%. The proportion of women with undetectable VL having a Caesarean section was 55% after implementation of new guidelines. We observed a decrease of late preterm deliveries from 16% (377/2354) before to 7% (42/599) after the change in guidelines ( $P < 0.001$ ).

**Conclusion:** There are still missed opportunities for women with HIV to fully suppress their VL and to deliver vaginally in Europe.

**Key Words:** HIV, pregnancy, mode of delivery, Europe

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## INTRODUCTION

Elective Caesarean section (CS) delivery, defined as Caesarean delivery performed before the onset of labor and before rupture of membranes (ROM), was recommended for women with HIV since 1999 following results from an observational study confirmed by a randomized trial and an international meta-analysis demonstrating evidence of its effectiveness in preventing mother-to-child transmission (MTCT) of HIV.<sup>1–3</sup> With widespread use of combined antiretroviral therapy (cART), MTCT rates have dramatically decreased, with current rates of around 1% or less reported in Europe.<sup>4–6</sup> In the context of such low transmission rates, the additional benefit of elective CS in reducing MTCT risk is

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uncertain, and the number of elective CS needed to prevent a single vertical transmission is very high. Furthermore, elective CS delivery is associated with increased costs to the health system and more importantly with increased maternal postoperative complications,<sup>7,8</sup> increased risk of morbidity in subsequent pregnancies, and deliveries including the risk of abnormal placentation such as placenta previa or accreta.<sup>9,10</sup> In HIV-positive women, elective CS was recommended at 38 completed weeks of gestation to prevent spontaneous ROM and labor, which bears an additional risk for the newborn when compared with CS performed at 39 weeks.<sup>10–12</sup>

Consequently, European national guidelines have changed over the last decade, to recommend (or allow) vaginal deliveries for HIV-positive women with either undetectable or low viral load (VL < 1000 RNA copies/mL), in the absence of an obstetric indication for elective CS.<sup>13</sup> A recent survey of European prevention of MTCT policies reported that 18 countries have national guidelines stating that HIV-positive women on successful antiretroviral therapy (ART) can deliver vaginally, with VL thresholds for vaginal delivery ranging from <1000 RNA copies per milliliter (in 5 countries) to <50 copies per milliliter (in 11 countries). The timing of the introduction of these policies varied considerably, from 1999 (in the Netherlands) to 2010 (in Sweden and Italy).<sup>13</sup>

Since these recommendations were published in Europe at a national level, the impact on obstetrical outcomes after this policy change has not been evaluated to date. There is little information about acceptance and feasibility in countries where vaginal delivery policies exist or about the actual mode of delivery after the change of guidelines according to maternal VL. Furthermore, there is some evidence that an important minority of women on cART have ongoing viral replication at the time of delivery.<sup>14</sup> Questions remain as to the reasons for missed opportunities to fully suppress HIV in these women, to minimize MTCT risk and to facilitate vaginal delivery for HIV-positive pregnant women in Europe.

The aim of this study was to evaluate the impact of the change in national guidelines on rates of vaginal delivery in HIV-positive women delivering between 2000 and 2010 in 2 European MTCT cohort studies. Our specific objectives were to describe mode of delivery rates in relation to the change in national guidelines, to assess factors associated with delivery with a detectable VL, and to explore reasons for CS in women eligible for vaginal delivery after the guidelines change.

## METHODS

The European Collaborative Study (ECS) and the Swiss Mother and Child HIV Cohort Study (MoCHiV) are prospective cohort studies using similar protocols to enroll and follow-up HIV-1-positive pregnant women and their infants. The ECS, established in 1986, includes sites in Western and Eastern Europe, but the data included in this pooled analysis were limited to mother–child pairs enrolled from the 9 participating Western European countries: Belgium, Denmark, Germany, Italy, the Netherlands, Poland, Spain, Sweden, and the United Kingdom.<sup>15</sup> The MoCHiV was established in 1998 as a merger of the neonatal HIV study (initiated in 1986) and the Swiss HIV and Pregnancy Study (initiated in

1989) and is fully integrated into the adult Swiss HIV Cohort Study (SHCS).<sup>16</sup> In both studies, pregnant women are routinely offered HIV testing at participating sites, and those found to be HIV-positive invited to participate, with informed consent obtained. Ethical approval has been granted for both studies. The analysis was limited to live births between January 1, 2000, and December 31, 2010.

## Variables and Definitions

Data collected included sociodemographics, mode of HIV acquisition, type and timing of initiation of cART, maternal immunologic, virologic, and clinical characteristics, mode of delivery, and gestational age at delivery.

Baseline CD4 count and VL were defined as first measures during pregnancy. CD4 count was categorized as <200, 200–499, and ≥500 cells per microliter. VL at delivery was considered as the last measured VL before delivery between 32 and 40 weeks of gestation. Gestational age was reported to the nearest completed week based on ultrasound or last menstrual period. The first trimester was defined as 1–12 weeks of gestation, the second trimester as 13–27 weeks of gestation, and the third trimester as 28 weeks of gestation onwards. We defined a HIV diagnosis as “late” if it occurred during the third trimester or at delivery.

A CS was classified as elective if performed before the onset of contractions and ROM including CS for medical reasons. An emergency CS was classified as any CS performed after contractions had commenced or after ROM. Deliveries were classified into 2 groups: those occurring before and those occurring after the publication of the national guidelines recommending vaginal delivery for women with very low or undetectable VL (month and year of publication). Preterm delivery was defined as delivery before 37 completed gestational weeks. By gestational age, births occurring at less than 28 weeks were classified as extreme preterm, 28–31 weeks as severe preterm, 32–33 weeks as moderate preterm, and 34–36 weeks as late preterm deliveries.

VL was categorized as undetectable (<400 RNA copies/mL) and detectable (<1000 copies/mL, 1000–9999 copies/mL, 10,000–99,999 copies/mL, and ≥100,000 copies/mL). For the analyses of deliveries after the new guidelines were instituted, we used a more stringent threshold of <50 RNA copies per milliliter. Infants were classified as “uninfected” if a negative polymerase chain reaction test was reported after 1 month of age or a negative HIV antibody test after 18 months of age in nonbreastfed infants and “infected” if a positive polymerase chain reaction was reported at any time or a positive antibody test was documented after 18 months of age.

## Statistical Analyses

Multilevel logistic regression models were used to obtain unadjusted and adjusted odds ratios and their 95% confidence intervals (CI) in analyses investigating factors associated with having a detectable VL (RNA > 400 copies/mL) at the time of delivery. The following predictors were considered: maternal characteristics (age, ethnicity, and illicit drug use), HIV-related characteristics (drug class and late HIV diagnosis), and CD4 count at baseline. We considered random

effects for year of delivery, country, and repeated deliveries in the same mother.

The analysis exploring reasons for CS among women eligible for vaginal delivery after the guidelines were published excluded the following ineligible women: prior CS ( $n = 8$ ), multiple pregnancy (twin and triplet), as this was a contraindication for vaginal delivery in some countries ( $n = 1$ ), gestational age younger than 37 weeks, as this was an indication for CS for HIV-positive women in some countries ( $n = 27$ ), and zidovudine monotherapy ( $n = 1$ ).

With the exception of the above analysis, multiple births were included in all analyses the same way as single births as information regarding the delivery did not change. However, the twins and triplets were counted separately in the estimate of infection rates of the newborns.

All analyses were done using SAS v9.3 (SAS Institute, Cary, NC) and STATA v12 (STATA Corporation, College Station, TX).

## RESULTS

A total of 3013 deliveries to 2663 women between 2000 and 2010 were included; 268 women had 2 pregnancies, and 38 had 3 to 5 pregnancies during the study period. Among the 2663 pregnancies, there were 60 multiple births (59 sets of twins and 1 set of triplets).

### Maternal Characteristics

Overall, 48.1% (1240/2578) women were of black and 42.7% (1101/2578) women of white ethnicity. Most (85.7%, 1959/2286) were married or cohabiting, and median maternal age at delivery was 32 years [interquartile range (IQR): 27–36 years]; the most common mode of HIV acquisition was heterosexual contact ( $n = 2029$ , 76.2%), with 15.8% ( $n = 421$ ) reporting a history of injecting drug use. Most women (84.8%) had asymptomatic HIV disease (Centers for Disease Control and Prevention category A) and the median CD4 cell count was 452 (IQR: 319–638) at their first antenatal visit (measured at a median of 35 gestational weeks; IQR: 32–37 weeks). The proportion of severely immunosuppressed women (CD4 < 200 cells/ $\mu$ L) was 8.0%.

For the majority (2077; 72%) of pregnancies, the woman was aware of her HIV diagnosis before conception (Table 1), and in 642 pregnancies (25%), the mother conceived while receiving ART. The median interval from HIV diagnosis to conception was 5.0 (IQR: 2.5–8.5) years in those diagnosed prepregnancy. Of the 28% ( $n = 802$ ) pregnancies in which the woman received her HIV diagnosis during pregnancy, this happened during the first or second trimester in the majority of women ( $n = 650$ ; 81%). Information on antenatal ART was available for 2792 (92.7%) of mother–infant pairs; only 7.8% did not receive ART throughout pregnancy and delivery. The proportion of women receiving no antenatal ART declined significantly before and after the introduction of the new guidelines from 9.1% to 3.9%. (Table 1;  $P < 0.001$ ). Of the 1527 mother–infant pairs in which women initiated cART during pregnancy, 286 (18.7%) started ART during the first, 901 (59 %) during the second trimester, and 340 (22.3%) during the third trimester, and there was a significant decline in the

proportion starting during the third trimester before and after the new guidelines were published (Table 1;  $P < 0.001$ ). The median time of the VL measurement was 16 days (IQR: 2–35 days) before delivery. The overall proportion of pregnancies in which women achieved an undetectable VL (<400 copies/mL) at delivery was 86.0% (1550/1802) among those on cART, with the proportion increasing from 83.2% (1135/1365) before to 95.0% (415/437) after the new guidelines were in place (Fig. 1); the percentage of mother–infant pairs with a maternal delivery VL < 50 RNA copies per milliliter showed a corresponding increase from 18.3% to 40.0%.

### Viral Suppression around Delivery

A delivery VL was not available for 805 deliveries, and the analysis of factors associated with undetectable VL at delivery was, therefore, restricted to 2208 deliveries. In univariate analysis, women with a late antenatal HIV diagnosis were more than 4 times more likely to have a detectable VL around delivery (odds ratio: 4.4,  $P < 0.001$ ). Younger age, injecting drug use, lower CD4 count, and receiving monotherapy or dual therapy were other factors associated with nonsuppression of VL at delivery in univariate analyses. In the multivariable model ( $n = 2002$ ), women with late HIV diagnosis and those on mono/dual therapy were nearly 3 times more likely and women with a history of injecting drug use were 50% more likely to have a detectable VL (Table 2). Women with higher CD4 counts were significantly less likely to have nonsuppressed VL than severely immunosuppressed women, and there was a significant decrease in the odds of a detectable VL over calendar time (Table 2).

### Mode of Delivery

Of 3013 deliveries, the information on mode of delivery was available in 98.8% (2977/3013). After the guidelines recommending vaginal delivery for women with undetectable VL were instituted, there was a significant increase in the proportion of women delivering vaginally to 52.2% compared with 17.4% before the recommendations were made (Table 1;  $P < 0.002$ ). In the 316 vaginal deliveries after guidelines, forceps were used in 2 (0.6%) and vacuum in 15 (4.8%) deliveries. Among the 611 births after the guidelines, 45% of those to women with VL < 50 copies per milliliter and 57% of those to women with VL 50 to 399 were vaginal (Fig. 2). Overall, the proportion of emergency CS increased slightly with a rate of 17.2% before and 20.8% after the guidelines (Table 1). Among all emergency CSs, the proportion occurring in women with undetectable VL was 20% (Fig. 3).

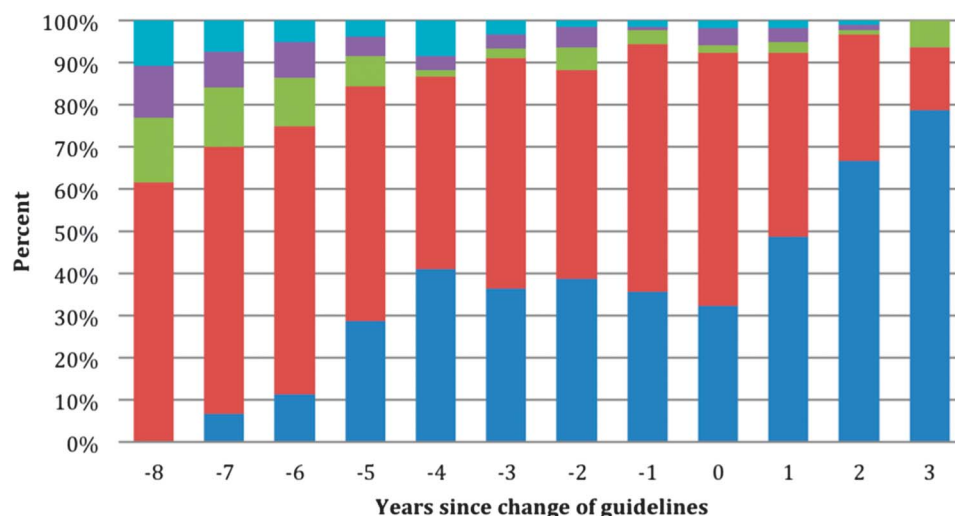
Looking at trends in the years following guidelines change, there was a steady increase in the proportion of vaginal deliveries, and very few vaginal deliveries occurred among women with detectable VL (Fig. 3). However, CS was the mode of delivery in 104 of 188 (55.3%) of women with fully suppressed VL at delivery (Fig. 2). In 37 of 104 women, there was a contraindication for vaginal delivery (8 previous CS, 27 < 37 weeks, 1 multiple pregnancy, 1 zidovudine monotherapy). The reason for CS was documented in 63 of the remaining 67 patients with undetectable VL. In 35% of cases (22/63), these women could have had a vaginal



**TABLE 1.** Demographics of Study Cohort

Variable	Total	Before Guidelines	After Guidelines
Deliveries, N (%)	3013 (100)	2402 (79.7)	611 (20.3)
Country (n = 3013), n (%)			
Belgium	595 (19.8)	317 (14.5)	220 (36.0)
Denmark	47 (1.6)	47 (2.0)	0 (0)
Germany	169 (5.6)	169 (7.0)	0 (0)
Italy	618 (20.5)	618 (25.7)	0 (0)
Netherlands	211 (7.0)	0 (0)	211 (34.5)
Poland	89 (3.0)	89 (3.7)	0 (0)
Spain	325 (10.8)	310 (12.9)	15 (2.5)
Sweden	240 (8.0)	240 (10.0)	0 (0)
Switzerland	435 (14.4)	303 (12.6)	132 (21.6)
United Kingdom	284 (9.4)	251 (10.5)	33 (5.4)
Parity—Nulliparous (n = 2318)	1159 (38.5)	948 (39.5)	211 (34.5)
HIV diagnosis (n = 2879), n (%)			
Preconception	2077 (72.1)	1672 (72.7)	405 (70.1)
First or second trimester	650 (22.6)	495 (21.5)	155 (26.8)
Third trimester	133 (4.6)	115 (5.0)	18 (3.1)
At delivery	19 (0.7)	19 (0.8)	0 (0)
Start of antenatal ART during pregnancy (n = 1527), n (%)			
First or second trimester	1187 (77.7)	894 (74.7)	293 (88.8)
Third trimester	340 (22.7)	303 (25.3)	37 (11.2)
ART type at delivery (n = 2767), n (%)			
Mono/dual therapy	287 (10.4)	277 (12.7)	10 (1.7)
cART	2020 (73.0)	1493 (68.6)	527 (89.2)
Unknown	95 (3.4)	76 (3.5)	19 (3.2)
None	365 (13.2)	330 (15.2)	35 (5.9)
CDC stage (n = 2311), n (%)			
A	1960 (84.8)	1521 (84.0)	439 (87.6)
B	165 (7.1)	129 (7.1)	36 (7.2)
C	186 (8.1)	160 (8.8)	26 (5.2)
Viral load *(copies/mL) (n = 2208), n (%)			
<50	507 (23.0)	318 (18.3)	189 (40.0)
50–399	1264 (57.3)	1008 (58.1)	256 (54.2)
400–999	142 (6.4)	131 (7.6)	11 (2.3)
1000–9999	186 (8.4)	175 (10.1)	11 (2.3)
≥10,000	109 (4.9)	104 (6.0)	5 (1.1)
CD4 cell count (n = 2524), n (%)			
<200	202 (8.0)	171 (8.9)	31 (5.2)
200–499	1229 (48.7)	978 (50.6)	251 (42.4)
≥500	1093 (43.3)	783 (40.5)	310 (52.4)
Gestational age at delivery (completed wk) (n = 2953), n (%)			
<32	104 (3.5)	89 (3.8)	15 (2.5)
32–33	88 (3.0)	70 (3.0)	18 (3.0)
34–36	419 (14.2)	377 (16.0)	42 (7.0)
Full term (≥37 wk)	2342 (79.3)	1818 (77.2)	524 (87.5)
Mode of delivery (n = 2977), n (%)			
Elective CS	1717 (57.7)	1555 (65.4)	162 (27.0)
Emergency CS	533 (17.9)	408 (17.2)	125 (20.8)
Vaginal	727 (24.4)	414 (17.4)	313 (52.2)

\*Measurement closest to delivery during the third trimester.  
 CDC, Centers for Disease Control and Prevention.



**FIGURE 1.** Viral load at delivery before and after the new guidelines.

■ RNA<50 ■ RNA 50-399 ■ RNA 400-999 ■ RNA 1000-9999 ■ RNA≥10000

delivery, as for 19 cases, the reason given for CS was maternal HIV infection, and in 3 cases, it was ROM.

## Infant Outcomes

Median gestational age at delivery was 38 weeks (IQR: 37–39 weeks); 20.7% deliveries were premature (Table 1), with 1.0% ( $n = 29$ ) of all deliveries being extremely premature (<28 weeks), 2.5% ( $n = 74$ ) severely premature (28–31 weeks), and 3.0% ( $n = 88$ ) moderately premature (32–33 weeks). Late preterm deliveries (34–36 weeks) accounted for 14.2% of all deliveries overall (Table 1), with a significant decrease after the introduction of the new guidelines from 16.0% (377/2354) to 7.0% (42/599) ( $\chi^2 = 6.26$ ,  $P < 0.001$ ). Of the late preterm deliveries ( $n = 419$ ), 55.7% ( $n = 209$ ) of those taking place before the guidelines were performed as elective CS versus 28.6% ( $n = 12$ ) afterward. Median birth weight was 2.9 kg (IQR: 2.5–3.2 kg). Overall, the HIV mother to child transmission rate was 1.6% (36/2329; 95% CI: 1.1 to 2.1), with a rate of 1.7% (34/1991; 95% CI: 1.2 to 2.4) before and 0.6% (2/338; 95% CI: 0.07 to 2.1) after guidelines.

## DISCUSSION

Our findings quantify the impact of a policy change for mode of delivery options among HIV-positive pregnant women in the largest European cohort across Europe described to date. As expected, we observed an increasing proportion of women with undetectable VL at delivery (63% to 78%) and increasing rates of vaginal deliveries from 17% before to 52% after the updated guidelines. Of note, rates of vaginal deliveries were increasing before the updated guidelines were published indicating that formulation of new guidelines was driven by clinical practice.

In the context of the new guidelines and in the absence of an obstetric indication for elective CS, decisions about mode of delivery largely depend on maternal VL. We found that 14% of the women receiving ART did not achieve an unde-

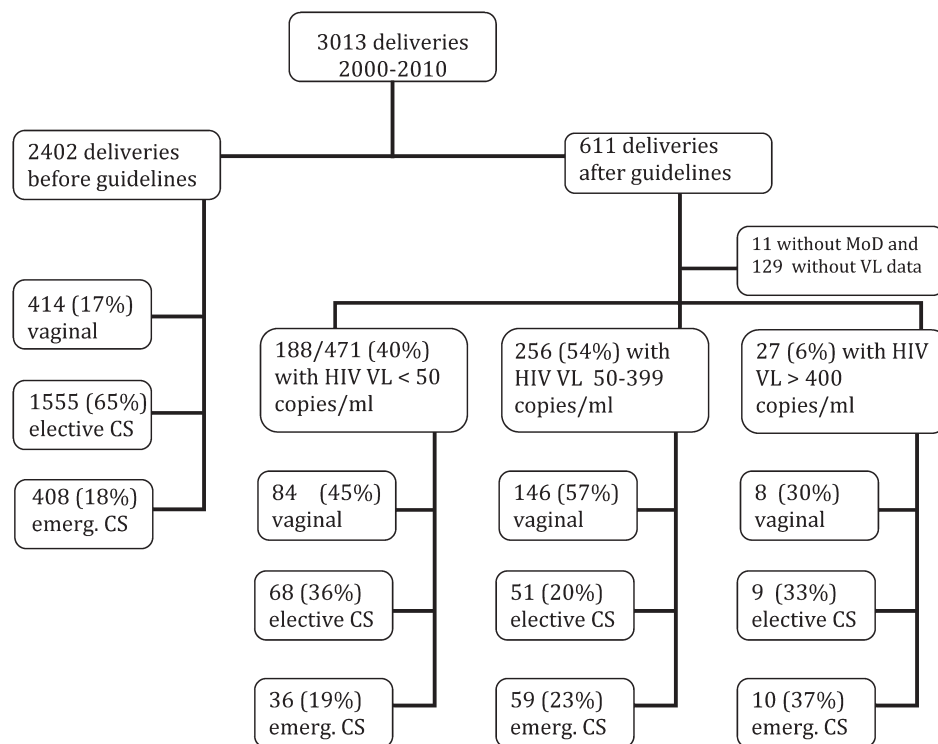
tectable VL (>400 copies/mL) at the time of delivery, and overall, 7% women did not receive any antenatal ART. There is a substantial proportion of women with ongoing viral replication at delivery, which is supported by comparable findings of a Brazilian cohort with 43%,<sup>17</sup> a U.S. cohort with 32%,<sup>18</sup> and a Canadian cohort with 16%<sup>19</sup> of women with a detectable

**TABLE 2.** Random Effects Logistic Regression Model for Factors Associated With Having a Detectable VL (>400) at Delivery

	OR	P	AOR*	95% CI	P
Ethnic group					
White	1	—	1	—	—
Black	0.68	0.001	0.68	0.51 to 0.89	0.006
Other	0.63	0.033	0.67	0.41 to 1.10	0.111
Late HIV diagnosis					
No	1	—	1	—	—
Yes	<b>4.40</b>	<b>&lt;0.001</b>	<b>2.88</b>	<b>1.74 to 4.44</b>	<b>&lt;0.001</b>
Maternal age					
For 5-year increase	<b>0.86</b>	<b>&lt;0.001</b>	<b>0.87</b>	<b>0.80 to 0.96</b>	<b>0.005</b>
Injecting drug use					
No	1	—	1	—	—
Yes	<b>1.69</b>	<b>&lt;0.001</b>	<b>1.49</b>	<b>1.08 to 2.05</b>	<b>0.015</b>
ART class					
cART	1	—	1	—	—
Mono/dual therapy	2.73	<b>&lt;0.001</b>	<b>2.90</b>	<b>2.05 to 4.09</b>	<b>&lt;0.001</b>
CD4 cell count					
<200	1	—	1	—	—
200–499	0.44	<b>&lt;0.001</b>	<b>0.43</b>	<b>0.30 to 0.63</b>	<b>&lt;0.001</b>
≥500	0.30	<b>&lt;0.001</b>	<b>0.25</b>	<b>0.17 to 0.36</b>	<b>&lt;0.001</b>
Year of delivery	0.78	<b>&lt;0.001</b>	<b>0.82</b>	<b>0.73 to 0.93</b>	<b>0.04</b>

\*Model is also adjusted for country as a random effect.

OR, odds ratio; AOR, adjusted OR. Bold text represents statistically significant results.

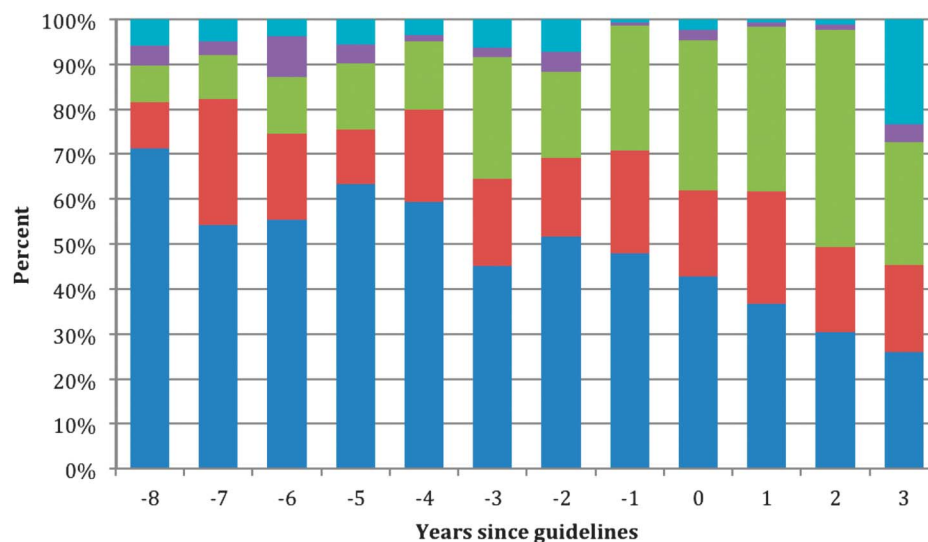


**FIGURE 2.** Flow chart of included deliveries according to timing in relation to guideline publication with postguideline deliveries stratified by delivery VL.

Abbreviations: CS - caesarean section; MoD - mode of delivery; VL - viral load

HIV VL at delivery. Comparisons between studies are complicated by variable definitions of undetectable VL according to different assays used. We found an association between having a detectable VL at delivery and late HIV diagnosis, younger maternal age, and history of injecting drug use. In the American study, younger age and illicit drug use and lower CD4 cell

count at start of therapy were significantly associated with having a detectable HIV VL at the time of giving birth, whereas as in our study, the type of ART used was not significant.<sup>18</sup> The association with younger age may be explained by worse adherence to ART in younger age groups. In an Italian study, the probability of having a detectable VL (19%) at delivery was



**FIGURE 3.** Mode of delivery before and after publication of the new guidelines stratified by delivery VL.

■ Elective CS ■ Emergency CS ■ Vaginal with VL<400  
 ■ Vaginal with VL≥400 ■ Vaginal with unknown VL

associated with lower CD4 cell count at enrollment and treatment modification during pregnancy (adjusted odds ratio: 1.66, 95% CI: 1.07 to 2.57,  $P = 0.024$ ).<sup>20</sup> In contrast, a former report of the ECS showed 27% of women with a detectable VL at delivery with shorter time to achieving an undetectable VL, associated with African origin and baseline VL but not with baseline CD4 cell counts.<sup>21</sup> However, in this analysis, white women were more likely to have a detectable VL; this may reflect residual confounding, as our analysis did not include baseline VL or adherence.

In a French cohort, the elective CS rate in HIV-positive women decreased between 1997 and 2004 from 56% to 41% and in a national study in the United Kingdom and Ireland, the elective CS rate declined from 66% in 1999 to 50% in 2006. The likelihood of having an elective CS varies according to the geographic location, as does the background rate of elective CS in the population.<sup>22</sup> However, the rates of emergency CS are stable in the French cohort at 29%,<sup>5</sup> whereas in the United Kingdom and Ireland and in this cohort, the rate of emergency CS marginally increased from 17% in 1999% to 23% in 2006 and from 17.2% to 20.8%, respectively. Indeed, we had expected higher rates of emergency CS associated with the new guidelines, given that more pregnancies not delivered by elective CS were potentially at risk of non-HIV-related obstetric complications, but this was not confirmed by our data.

Of concern, in this cohort, despite viral suppression, the rates of vaginal deliveries were lower than expected. Nearly half of women with an undetectable VL after the change of guidelines had a CS and 35% of these were performed because of maternal HIV or ROM. This might be attributable to the fact that implementation of a vaginal delivery policy was difficult after the era of recommended elective CS. In addition, the theoretical risk of HIV transmission associated with obstetrical interventions such as fetal pH measurement, episiotomy, instrumental deliveries,<sup>23,24</sup> and with duration of ruptured membranes,<sup>25</sup> described in the era before ART was broadly available, may have favored the CS choice. Maternal request is another important factor influencing mode of delivery decisions. The CS rate based on mother's demand can be quite substantial and varies between countries.<sup>22,26</sup> Our results suggest that the policy for vaginal delivery among women with undetectable or very low VL is only slowly becoming established within practice over time.

Two smaller European studies have shown that only 57% and 65%, respectively, of HIV-positive women with undetectable VL at delivery and planned vaginal delivery were ultimately able to deliver this way.<sup>26,27</sup> In a Canadian cohort, reasons for the high elective CS rate were multiparity, maternal request, and origin from resource-poor countries with different approaches for prevention of MTCT.<sup>19</sup> Livingston et al<sup>28</sup> found the following reasons for elective CS in women who could have had a vaginal delivery based on their suppressed VL: fear of HIV transmission in 39.3%, history of previous CS in 29.8%, request of mother in 5.8%, and hypertension and preeclampsia in 4.6%. For emergency CS in women with fully suppressed viral replication, the same study found a nonreassuring fetal heart rate to be the most common reason (21.8%).<sup>28</sup> Azria et al<sup>29</sup> reported that CS for failure to progress in labor was performed in HIV-

positive women an average of 1 hour earlier compared with uninfected controls, indicating that maternal HIV infection even with suppressed VL influenced the mode of delivery. All these studies highlight the issue that mode of delivery continues to be influenced to some extent by HIV status irrespective of viral suppression.

The preterm delivery rate in our study was high at around 20%. The former recommendations were to perform elective CS before ROM or onset of labor to prevent increased MTCT risk. This might have had an impact on the decision to perform CS in the late preterm period, for example 36 weeks. It is noteworthy that neonates at 36 weeks remain at higher risk of morbidity compared with those born at 37–40 weeks of gestation regarding respiratory distress, jaundice, and hypoglycaemia.<sup>11,30</sup> A positive finding of this study confirmed a significant reduction of elective CS in the late preterm period after the new guidelines. We anticipate this trend to continue over time. Furthermore, our results indicate the need to consider how a reduction of the CS rates in women with undetectable VL in the future could be achieved.

This analysis represents the first study describing rates of mode of delivery in HIV-positive women across Europe taking into account varying national MTCT policies and health care structures. We are aware that our findings are limited by the observational nature of our data, the missing information about planned mode of delivery, and differences between countries in decision-making processes. Lack of detailed and/or comprehensive data on drug adherence on baseline VL and missing information on exact duration of ART precluded use of these variables in our analyses. Our dataset does not include information of all Western European countries (eg, no French data), as not all countries participate in the ECS.

## CONCLUSION

Rates of vaginal delivery in HIV-positive pregnant women are increasing in Europe for women with suppressed VL. Despite this, there is evidence of missed opportunities for viral suppression and for having a vaginal delivery in women with suppressed HIV VL. Barriers to HIV testing before or during early pregnancy and to commencing an effective ART sufficiently early in pregnancy need to be addressed. Furthermore, future research is needed to address how to promote earlier engagement in care among HIV-positive pregnant women, and retention in HIV care postnatally, to achieve viral suppression and the opportunity for vaginal delivery for HIV positive pregnant women in both their index and subsequent pregnancies.

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