Insufficient antiretroviral therapy in pregnancy: missed opportunities for prevention of mother-to-child transmission of HIV in Europe

European Collaborative Study

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Running Head:
Missed opportunities for the PMTCT

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Background
Although mother-to-child transmission (MTCT) rates are at an all-time low in Western Europe, potentially preventable transmissions continue to occur. Duration of antenatal combination antiretroviral therapy (ART) is strongly associated with MTCT risk.

Methods
Data on pregnant HIV-infected women enrolled in the Western and Central European sites of the European Collaborative Study between January 2000 and July 2009 were analysed. The proportion of women receiving no antenatal ART or 1-13 days of treatment was investigated, and associated factors explored using logistic regression models.

Results
Of 2148 women, 142 (7%) received no antenatal ART, decreasing from 8% in 2000-03 to 5% in 2004-09 (χ^2 =8.73, p<0.01). A further 41 (2%) received 1-13 days of ART. A third (64/171) of women with "insufficient" (no or 1-13 days) antenatal ART had a late HIV diagnosis (in the third trimester or intrapartum), but half (85/171) were diagnosed pre-conception. Preterm delivery <34 weeks was associated with receipt of no and 1-13 days antenatal ART (AOR 2.9 p<0.01 and AOR 4.5 p<0.01 respectively). Injecting drug use history was associated with an increased risk of no ART (AOR 2.9 p<0.01) and severe symptomatic HIV disease with a decreased risk (AOR 0.2, p<0.01). MTCT rates were 1.1% (15/1318) among women with ≥14 days antenatal ART and 7.4% (10/136) among those with insufficient ART.

Conclusions
Over the last 10 years, around 1 in 11 women in this study received insufficient antenatal ART, accounting for 40% of mother-to-child transmissions. Half of these women were diagnosed pre-conception, suggesting disengagement from care.

Background

Rates of mother-to-child transmission (MTCT) of HIV-1 have been reduced to around 1% in Western Europe, where women have access to the full combination of measures for prevention of MTCT (PMTCT) [1-4], but some transmissions still occur [1, 4]. Voluntary antenatal HIV screening offered to all women is policy in most of these countries [5], but undiagnosed maternal HIV infection remains a reason for continued transmissions, as does seroconversion in pregnancy, non-suppressive antenatal antiretroviral therapy (ART) and adverse social circumstances in pregnancy, precluding access to optimal antenatal care [4].

An increasing number of HIV-infected pregnant women are conceiving whilst receiving ART [6, 7]. For those who are not already on treatment at conception, either because they have no clinical or immunological indications for ART or because they are diagnosed with HIV for the first time in pregnancy, antenatal ART is recommended to reduce MTCT risk [8, 9]. Decisions around timing of treatment initiation in these women must balance the possibility of adverse effects (such as preterm delivery or anaemia in the infant) [9-13] with the clinical needs of the mother and the reduction in MTCT risk associated with longer duration of antenatal ART [1, 2, 14-16]. Time to undetectable HIV viral load depends on individual baseline viral load, highly active antiretroviral therapy (HAART) regimen and treatment history, drug resistance, co-infections and ethnicity [17, 18], and virological suppression is not always achieved by delivery [1, 17, 19]. For women requiring ART for PMTCT only, British and United States guidelines recommend individualised decisions around when to start, with a move towards earlier ART initiation whilst allowing for avoidance of ART exposure during the first trimester, the period of greatest potential teratogenic risk [8, 9]. The World Health Organisation (WHO) updated its guidance in 2010, and recommends initiating ART for PMTCT from 14 weeks of gestation to ensure maximum uptake, especially in the second trimester, and to reduce the risk of intrauterine transmission [20].

Identifying factors associated with missed opportunities for PMTCT is a priority to optimise maternal health and achieve the virtual elimination of MTCT [20]. Given the importance of

antenatal ART for PMTCT, we aimed to explore factors associated with receipt of insufficient ART in a Western and Central European cohort.

Methods

The European Collaborative Study (ECS) on HIV-infected pregnant women and their children is an ongoing birth cohort study, in which HIV-1 infected pregnant women are enrolled and their infants prospectively followed according to a standard protocol [21]. Data were collected anonymously on standard questionnaires on maternal socio-demographic and clinical information, delivery and infant characteristics [21]. This analysis was limited to births from January 2000 to July 2009 in nine countries (Belgium, Denmark, Germany, Italy, the Netherlands, Poland, Spain, Sweden and the UK). Multiple births were excluded because of their association with preterm delivery, a factor potentially limiting duration of antenatal ART.

Definitions

Figure 1 summarises the availability of data on receipt and duration of antenatal ART. The main outcome was receipt of 'insufficient antenatal ART', defined as receipt of no ART in pregnancy or short duration of ART, initiated 1-13 days before delivery. This definition was chosen in order to focus on those with the most elevated risk of vertical transmission [22, 23]. Women receiving ART in pregnancy but with missing treatment duration (n=246) were included in the ≥14 days of ART group; 84% (191/228) were diagnosed pre-conception, 33% (48/144) had undetectable viral load at delivery, and 66% (103/155) had a CD4 count >350 cells/mm^3 at last antenatal measure.

Where HIV diagnosis was recorded one day either side of delivery (n=6), women were categorised as diagnosed intrapartum. Women diagnosed with HIV more than one day post-partum (n=3) were excluded. Gestational age was reported to the nearest completed week based on ultrasound or, in absence of ultrasound, last menstrual period. The first trimester was defined as 1-12 weeks of gestation, the second trimester as 13 to 26 weeks and the third trimester as 27 weeks of gestation onwards [24]. We defined an HIV diagnosis as "late" if it occurred during the third trimester or intrapartum. Delivery before 34 weeks gestation

(precluding 14 days of antenatal ART if started at week 32, the latest suggested by British guidelines [9]) was investigated as a factor associated with receiving no and 1-13 days antenatal ART. History of and current injecting drug use (IDU) was based on a combination of maternal self report, clinical assessment and presence of neonatal abstinence syndrome. HIV disease staging was reported according to the U.S. Centers for Disease Control and Prevention classification, with severe symptomatic HIV disease corresponding to stage C [25].

Data Analysis

Univariable comparisons were assessed with the χ^2 or Fisher's exact tests for categorical variables, and differences in clinical parameters between treatment groups with the unpaired *t* test. Logistic regression models were fitted to obtain odd ratios (OR), adjusted OR (AOR) and their 95% confidence intervals (CI) in analyses exploring factors associated with not receiving ART or receiving 1-13 days of ART, and factors associated with late HIV diagnosis among those undiagnosed at conception. Maternal factors were investigated (age at delivery, marital status, sub-Saharan African origin, IDU history, parity, severe symptomatic HIV disease) as were delivery details (year, country of delivery and gestational age). History of IDU rather than current IDU was used in the analyses, in recognition of the fact that drug use is a chronic and relapsing condition. Maternal region of birth (Sub-Saharan Africa or other), rather than ethnicity, was used in the models, as this was thought to more closely reflect immigrant status, a factor possibly affecting healthcare access. Model selection followed a forward stepwise approach, with each factor tested for its significant contribution to the model's goodness of fit using the likelihood ratio test (significance level of $p \leq 0.1$). Random effects models were fitted in all analyses to account for underlying, unobserved variation in the outcome by country of delivery [26]. All models were adjusted a priori for year of delivery to account for changes in clinical practice over time [21].

We hypothesized that different factors could be associated with receiving insufficient antenatal ART among women diagnosed with HIV pre- and post-conception [27], and therefore carried out stratified analyses in these two groups.

Statistical analyses were performed with Stata version 11.0 for Windows (StataCorp LP, College Station, Texas, USA).

Results

A total of 2148 deliveries between January 2000 and July 2009 were reported in 1940 women; 173 women had two pregnancies, 16 had three and one woman had four. Of the 2148 pregnancies, 142 (7%) were in women who received no ART, and a further 41 (2%) were in women who received less than two weeks of ART before delivery (Figure 1). Baseline maternal and pregnancy characteristics by receipt of antenatal ART are given in Table 1. Overall, in two fifths of mother-child pairs the mother was born in sub-Saharan Africa, three-quarters were married or cohabiting and around a fifth had an IDU history. Median age at delivery was 31.5 years (IQR 27.2, 35.4 years). In at least 27% (106/390) of the mother-child pairs where the mother had an IDU history there was evidence of current IDU. In just over a tenth of pregnancies the mother had severe symptomatic HIV disease, and median CD4 count (first recorded in pregnancy) was 410 cells/mm^3 (IQR 280, 580 cells/mm^3).

In almost three-quarters of pregnancies the woman was aware of her HIV infection before conception (Table 1), and in over a third of these (39%, 479/1229) the woman conceived whilst being on HAART. Among women with unknown HIV status at conception, 79% (471/596) were diagnosed by the end of the second trimester, 17% (101/596) in the third trimester and 4% (24/596) at delivery. The proportion with late HIV diagnosis (during the third trimester or at delivery) decreased over time from 24% (94/393) of those with unknown status at conception in 2000-2003, to 15% (31/203) in 2004-2009 (χ^2=6.04, p=0.014).

The proportion of pregnancies where the mother received no antenatal ART decreased from 8% (106/1355) in 2000-2003 to 5% (36/793) in 2004-2009 (χ^2=8.73, p<0.01), but no decline was seen in the proportion with 1-13 days of antenatal ART (2% (41/2006) of those with treatment) (p=0.78). Significant differences in the non-receipt of antenatal ART existed by country of delivery, from 0% (0/202) to 21% (18/87) of pregnancies (nine countries,

χ^2=72.31, p≤0.01), and also in the receipt of 1-13 days of antenatal ART, from 0% (0/13) to 6% (10/154) of pregnancies (χ^2=16.79, p=0.032).

Factors associated with receiving insufficient ART

In the group with at least 14 days of ART, 5% (99/1930) of deliveries were at less than 34 weeks gestation compared with two and four-fold this rate among the groups with no ART and 1-13 days of ART respectively (Table 1). A late HIV diagnosis was received in 3% (61/1898) of pregnancies with ≥14 days of ART, compared with 37% (64/171) of those with no or 1-13 days of ART (χ^2=323.47, p<0.01).

In half (85/171) of pregnancies with insufficient antenatal ART the woman was aware of her HIV status before conception. These women had a median CD4 count at the last antenatal measurement of 310 cells/mm^3 (IQR 240, 440 cells/mm^3) (median 25 days before delivery) compared with 450 cells/mm^3 (IQR 320, 630 cells/mm^3) among women diagnosed pre-conception and treated for at least two weeks (p<0.01). In pregnancies with pre-conception HIV diagnosis, those with no or 1-13 days of ART had a rate of severe maternal immunosuppression (CD4 count <200 cells/mm^3) twice as high as those with at least two weeks of treatment (20%, 10/49 versus 8%, 93/1149). Maternal severe symptomatic HIV disease was less frequent in pregnancies with no or 1-13 days of ART compared with those with ≥14 days of ART (7%, 8/109 vs. 14%, 197/1426, χ^2=3.67, p=0.06).

Late HIV diagnosis was strongly associated with receipt of insufficient ART, occurring in 34% (45/132) of pregnancies with no antenatal ART and 49% (19/39) of pregnancies with 1-13 days of antenatal ART, compared with 4% (80/1937) of pregnancies with ≥14 days of ART (χ^2=237.75, p<0.01 and χ^2=199.84, p<0.01 respectively). Given the overlap between late HIV diagnosis and insufficient antenatal ART, and the possibility of shared circumstances leading to the two outcomes, timing of diagnosis was omitted from multivariable models.

In logistic regression analyses, preterm delivery at <34 weeks of gestation was the only factor associated with receipt of 1-13 days of ART (AOR 4.37 vs. delivery ≥34 weeks, 95% CI 1.95-

9.78 $p<0.01$, adjusting for year and country of delivery). Factors associated with not receiving ART are shown in Table 2. In both univariable and multivariable analyses, IDU history, maternal clinical HIV stage and preterm delivery <34 gestational weeks were associated with not receiving ART. A quarter (24/106) of pregnancies with current maternal IDU had no antenatal ART compared with 8% (20/249) of those in ex-IDUs ($\chi^2=13.89$, $p<0.01$).

Although univariable analysis suggested that maternal sub-Saharan African origin was associated with a decreased probability of non-receipt of ART (OR 0.51 for not receiving ART among African vs. non-African women, 95% CI 0.35-0.75, $p<0.01$), this association was accounted for by IDU history, a factor almost exclusive to white women (377 of 383 pregnancies with maternal IDU history were in white women).

Where the mother had a history of IDU, HIV diagnosis was more likely to have occurred pre-conception than where there was no maternal history of IDU (89% vs. 68% of pregnancies, $\chi^2=67.17$, $p<0.01$). However, where HIV diagnosis occurred after conception, women with an IDU history were more likely to be diagnosed late (35% (14/40) vs. 20% (108/536) of pregnancies with no maternal IDU history, $\chi^2=4.92$, $p=0.027$). No other maternal characteristics were associated with late HIV diagnosis among those diagnosed antenatally.

In the model limited to 1473 mother-child pairs with HIV diagnosis before conception, insufficient ART was received in 85 (6%). Absence of a cohabiting partner and IDU history were associated with not receiving antenatal ART (Table 3), but these factors were not significantly associated with short duration of ART. Delivery at <34 weeks was associated with short duration of ART only (Table 3).

Among 596 mother-child pairs with HIV diagnosis after conception, there was insufficient antenatal ART in 86 (14%). History of IDU was associated with not receiving ART but not with short duration of ART (Table 4). Preterm delivery <34 weeks was associated with both no ART and short duration of treatment.

Vertical transmission

The vertical transmission rate was 1.7% (95% CI 1.1-2.5%) overall and was significantly higher in pregnancies with insufficient ART: 5.8% (95% CI 2.2-12.2%) among pregnancies with no ART and 12.1% (95% CI 3.4-28.2) in those with 1-13 days of ART, compared with 1.1% (95% CI 0.6-1.9) among those with longer duration of ART (p<0.01 for both). Of the 25 HIV-infected infants, 40% (10/25) were born to the 9% of women who received insufficient antenatal ART.

Missing data

Pregnancies with insufficient ART were significantly more likely than those with sufficient ART to have missing data on maternal marital status, HIV disease symptoms and IDU (p<0.02 for each variable), probably because these pregnancies were more likely to be unmonitored or in women with a late HIV diagnosis, and therefore to have less complete antenatal care records.

Discussion

Over the last ten years in this cohort of HIV-infected women giving birth in Western and Central Europe, 7% of pregnancies were in women who received no antenatal ART, despite diagnosis before delivery in the majority of cases. The proportion without antenatal ART declined between 2000-2003 and 2004-2009. Among those pregnancies where antenatal ART was received, duration of treatment was less than two weeks in 2%, and this proportion stayed constant over time. Although less than 10% of pregnancies were in women who received insufficient antenatal ART, these pregnancies accounted for 40% of all vertical transmissions and thus represent important missed opportunities for PMTCT. In over a third of pregnancies with insufficient antenatal ART the woman was diagnosed late in pregnancy, but half the women knew their HIV status at conception and a significant proportion of these women required treatment for their own health.

The women who received insufficient antenatal ART in this cohort were a heterogeneous group. Factors imposing a time limit on possible duration of antenatal ART (i.e. late antenatal HIV diagnosis and preterm delivery) were associated with not receiving ART and particularly with

short duration (1-13 days) of ART. Women who received no antenatal ART were more likely to have characteristics suggesting marginalisation, such as being single and having an IDU history. They were also significantly less likely to have severe symptomatic HIV disease, which may have contributed to a lack of health-seeking behaviour, or perceived lack of need for treatment.

Delivery at <34 weeks gestation was associated with an almost three-fold increased risk of no antenatal ART and over four-fold increased risk of receiving 1-13 days antenatal ART, and was a particularly important risk factor for insufficient ART among women diagnosed antenatally. Preterm delivery is an important practical barrier to women receiving sufficient antenatal prophylaxis before delivery [4], is associated with detectable viral load at delivery [28] and is a risk factor for intrapartum MTCT, further raising this risk by precluding elective caesarean section [29, 30]. Antenatal HAART has been shown to be associated with preterm delivery in several studies including the ECS [10, 31-33], but initiation of HAART before or early in pregnancy is also associated with a lower MTCT risk than initiation later in pregnancy [14]. Although evidence on optimal timing of initiation of antenatal ART is lacking, WHO recommendations suggest starting ART for PMTCT as soon as antenatal care allows [34]. This approach is particularly relevant for women most at risk of preterm delivery [4], given the value of additional weeks of antenatal ART in reducing MTCT risk [2].

In this study, the proportion of pregnancies without any antenatal ART (6%) was higher than the 2-3% reported previously in Western Europe [6, 7, 15, 19]. The observed improvement in coverage over time coincides with the scale-up of treatment across Europe [14], improvements in the uptake of screening [35] and an increase in the proportion of HIV-infected pregnant women with known status at conception [6, 15, 19]. African immigrants (two-fifths of the cohort), were no more likely to be diagnosed late or to lack ART, despite potential problems accessing care after immigration. However, late diagnosis was an important factor overall among women lacking ART, suggesting a lack of antenatal care and health literacy – the capacity to understand and act on health information [36].

In around half of the pregnancies without antenatal ART the mother was aware of her HIV status before pregnancy, similar to findings from the French Perinatal Cohort [27]. Despite previous contact with healthcare services these women did not benefit from PMTCT interventions, indicating an important missed opportunity for prevention. Information on refusal of antenatal ART was not collected in our study, but in the French study, around a third of women not receiving ART had declined treatment [27]. Lack of continuity between antenatal and general HIV care may contribute to delays in women accessing PMTCT interventions; having a routine healthcare provider has previously been shown to reduce delays in seeking HIV care after a diagnosis [37]. History of IDU and lack of a partner are factors associated with poor social support and treatment delay [38, 39]. Our results highlight the need for practical support and outreach for women at risk of disengaging from ongoing HIV care before a pregnancy occurs, throughout pregnancy and beyond delivery, to optimise the woman's own health as well as uptake of and adherence to PMTCT interventions [27].

The association between history of IDU and not receiving ART has previously been reported in pregnant [40] and non-pregnant [41, 42] populations, as has the association between IDU and both lack of antenatal care and late HIV diagnosis [40]. Opioid substitution therapy for pregnant IDUs improves compliance with antenatal care [43] and could form an important component of PMTCT care, together with outreach services.

In this study we lacked information on socioeconomic characteristics (including income, employment and housing), which may be associated with access to PMTCT interventions and care. Women with missed opportunities for PMTCT linked to marginalisation may therefore be incompletely characterised. Differences between countries in HIV epidemiology, screening policies and guidelines [5] may limit the generalisability of these results to specific countries. The association between missing data on variables of interest and receipt of insufficient antenatal ART suggest an underestimate of the size of association between these and the outcome. Our outcome measure of <14 days of ART was designed to capture women most at risk of vertical transmission but did not necessarily capture all at risk women, since there is no precise duration of ART considered sufficient to minimise MTCT risk. Finally, we lacked

information on reasons for non-receipt of ART (including woman's refusal and toxicity), and were therefore unable to fully describe the factors leading to lack of treatment.

In conclusion, there remain missed opportunities for PMTCT and for optimising the health of childbearing women with HIV infection in Europe. An emphasis on earlier antenatal HIV diagnosis and earlier initiation of ART will help reduce transmissions resulting from insufficient ART in pregnancy, but additional interventions may be needed for those at risk of disengagement from care.

Table 1: Maternal and delivery characteristics, by receipt of antenatal ART

	All births (*n*=2148) *n* (%)	**No antenatal ART (*n*=142) *n* (%)**	**1-13 days of antenatal ART (*n*=41) *n* (%)**
Maternal characteristics			
Marital status (n=1930)			
Married or cohabiting	1434 (74%)	79 (69%)	21 (62%)
Single	496 (26%)	36 (31%)	13 (38%)
Ethnic group (n=2101)			
White	1019 (49%)	87 (63%)	18 (45%)
Black	985 (47%)	44 (32%)	22 (55%)
Other	97 (5%)	7 (5%)	0
Sub-Saharan African origin (n=2089)			
No	1225 (59%)	101 (73%)	18 (45%)
Yes	864 (41%)	38 (27%)	22 (55%)
Parity at enrolment (n=2033)			
0	868 (43%)	54 (41%)	16 (40%)
1	670 (33%)	40 (30%)	17 (43%)
2 or more	495 (24%)	38 (29%)	7 (18%)
History of IDU (n=2091)			
No	1701 (81%)	84 (64%)	36 (88%)
Yes	390 (19%)	48 (36%)	5 (12%)
Timing of HIV diagnosis (n=2069)			
Pre-conception	1473 (71%)	69 (52%)	16 (41%)
1^{st} / 2^{nd} trimester	471 (23%)	18 (14%)	4 (10%)
3^{rd} trimester / delivery	125 (6%)	45 (34%)	19 (49%)
HIV disease symptoms (n=1535)			
Asymptomatic / non-severe HIV symptoms	1330 (87%)	72 (95%)	29 (88%)
Severe symptomatic HIV disease	205 (13%)	4 (5%)	4 (12%)
CD4 count - first in pregnancy (cells/mm^3) (n=1722)			
<200	218 (13%)	10 (14%)	6 (18%)
200-349	441 (26%)	21 (30%)	12 (36%)
≥350	1063 (62%)	38 (55%)	15 (45%)
Delivery			
Time period (n=2148)			
2000-2003	1355 (63%)	106 (75%)	25 (61%)
2004-2009	793 (37%)	36 (25%)	16 (39%)
Mode (n=2044)			
Vaginal or emergency caesarean section	747 (37%)	64 (48%)	19 (49%)
Elective caesarean section	1297 (63%)	70 (52%)	20 (51%)
Gestation weeks (n=2109)			
<34	123 (6%)	16 (12%)	8 (20%)
34-36	330 (16%)	23 (17%)	7 (17%)
≥37	1656 (79%)	99 (72%)	26 (63%)

Table 2: Factors associated with receiving no antenatal ART (*n*=2148)

Covariate	Proportion (*n*) not receiving ART	Crude Odds Ratio (95% CI)	*p*-value	*Adjusted odds ratio (95% CI)	*p*-value
History of IDU					
No	4.9% (84/1701)	1.00		1.00	
Yes	12.3% (48/390)	2.70 (1.86-3.92)	<0.01	2.91 (1.55-5.44)	<0.01
HIV Symptoms					
Asymptomatic / non-severe symptoms	5.4% (72/1330)	1.00		1.00	
Severe symptomatic HIV disease	2.0% (4/205)	0.35 (0.13-0.96)	0.042	0.23 (0.08-0.67)	<0.01
Preterm delivery <34 weeks gestation					
No	6.1% (122/1986)	1.00		1.00	
Yes	13.0% (16/123)	2.28 (1.31-3.99)	<0.01	2.93 (1.40-6.10)	<0.01
Year of delivery					
2000-2003	7.8% (106/1355)	1.00		1.00	
2004-2009	4.5% (36/793)	0.56 (0.38-0.83)	<0.01	0.69 (0.39-1.23)	0.208

* All AORs are estimated accounting for country of delivery (random effects) and adjusted for year of delivery

Table 3: Factors associated with receiving no and 1-13 days antenatal ART, among women diagnosed pre-conception
*All AORs are estimated accounting for country of delivery (random effects) and adjusted for year of delivery

	No ART (vs. any ART) (*n*=1473)			1-13 days of ART (vs. ≥14 days of ART) (*n*=1404)		
	Proportion (*n*) not receiving ART	Crude Odds Ratio (95% CI)	*Adjusted Odds Ratio (95% CI)	Proportion (*n*) receiving 1-13 days of ART	Crude Odds Ratio (95% CI)	*Adjusted Odds Ratio (95% CI)
Marital status						
Married / cohabiting	4.0% (41/1019)	1.00	1.00	0.7% (7/978)	1.00	
Single	7.6% (24/314)	1.97 (1.17-3.32) *p*=0.01	1.88 (1.06-3.33) *p*=0.030	1.7% (5/290)	2.43 (0.77-7.73) *p*=0.131	
History of IDU						
No	3.1% (35/1121)	1.00	1.00	1.2% (13/1086)	1.00	
Yes	10.2% (33/325)	3.50 (2.14-5.74) *p*<0.01	2.00 (1.06-3.77) *p*=0.033	1.0% (3/292)	0.86 (0.24-3.03) *p*=0.810	
Preterm delivery <34 weeks gestation						
No	4.4% (60/1377)	1.00		1.0% (13/1317)	1.00	1.00
Yes	9.4% (9/96)	2.27 (1.09-4.73) *p*=0.028		3.5% (3/87)	3.58 (1.00-12.82) *p*=0.05	3.62 (1.01-12.98) *p*=0.048
Year of delivery						
2000-2003	5.9% (54/911)	1.00	1.00	1.1% (9/857)	1.00	1.00
2004-2009	2.7% (15/562)	0.44 (0.24-0.78) *p*<0.01	0.58 (0.31-1.09), *p*=0.088	1.3% (7/547)	1.22 (0.45-3.30) *p*=0.693	1.25 (0.46-3.40) *p*=0.656

Table 4: Factors associated with receiving no and 1-13 days of ART, among women diagnosed after conception
*All AORs are estimated accounting for country of delivery (random effects) and adjusted for year of delivery

	No ART (vs. any ART) (*n*=596)			1-13 days of ART (vs. ≥14 days of ART) (*n*=533)		
	Proportion (*n*) not receiving ART	Crude Odds Ratio (95% CI)	*Adjusted Odds Ratio (95% CI)	Proportion (*n*) receiving 1-13 days of ART	Crude Odds Ratio (95% CI)	*Adjusted Odds Ratio (95% CI)
Marital status						
Married / cohabiting	9.6% (36/374)	1.00		4.1% (14/338)	1.00	
Single	6.1% (10/163)	0.61 (0.30-1.27) *p*=0.188		4.6% (7/153)	1.11 (0.44-2.81) *p*=0.826	
History of IDU						
No	8.4% (45/536)	1.00	1.00	4.5% (22/491)	1.00	
Yes	27.5% (11/40)	4.14 (1.94-8.83) *p*<0.01	2.46 (1.04-5.86) *p*=0.041	3.5% (1/29)	0.76 (0.10-5.86) *p*=0.793	
Preterm delivery <34 weeks gestation						
No	10.0% (57/571)	1.00	1.00	3.5% (18/514)	1.00	1.00
Yes	24.0% (6/25)	2.85 (1.09-7.42) *p*=0.032	5.27 (1.74-16.03) *p*<0.01	26.3% (5/19)	9.84 (3.20-30.29) *p*<0.01	11.15 (3.31-37.55) *p*<0.01
Year of delivery						
2000-2003	10.9% (43/393)	1.00	1.00	4.3% (15/350)	1.00	1.00
2004-2009	9.9% (20/203)	0.89 (0.51-1.56) *p*=0.682	0.77 (0.39-1.51) *p*=0.441	4.4% (8/183)	1.02 (0.42-2.45) *p*=0.963	0.85 (0.33-2.18) *p*=0.733

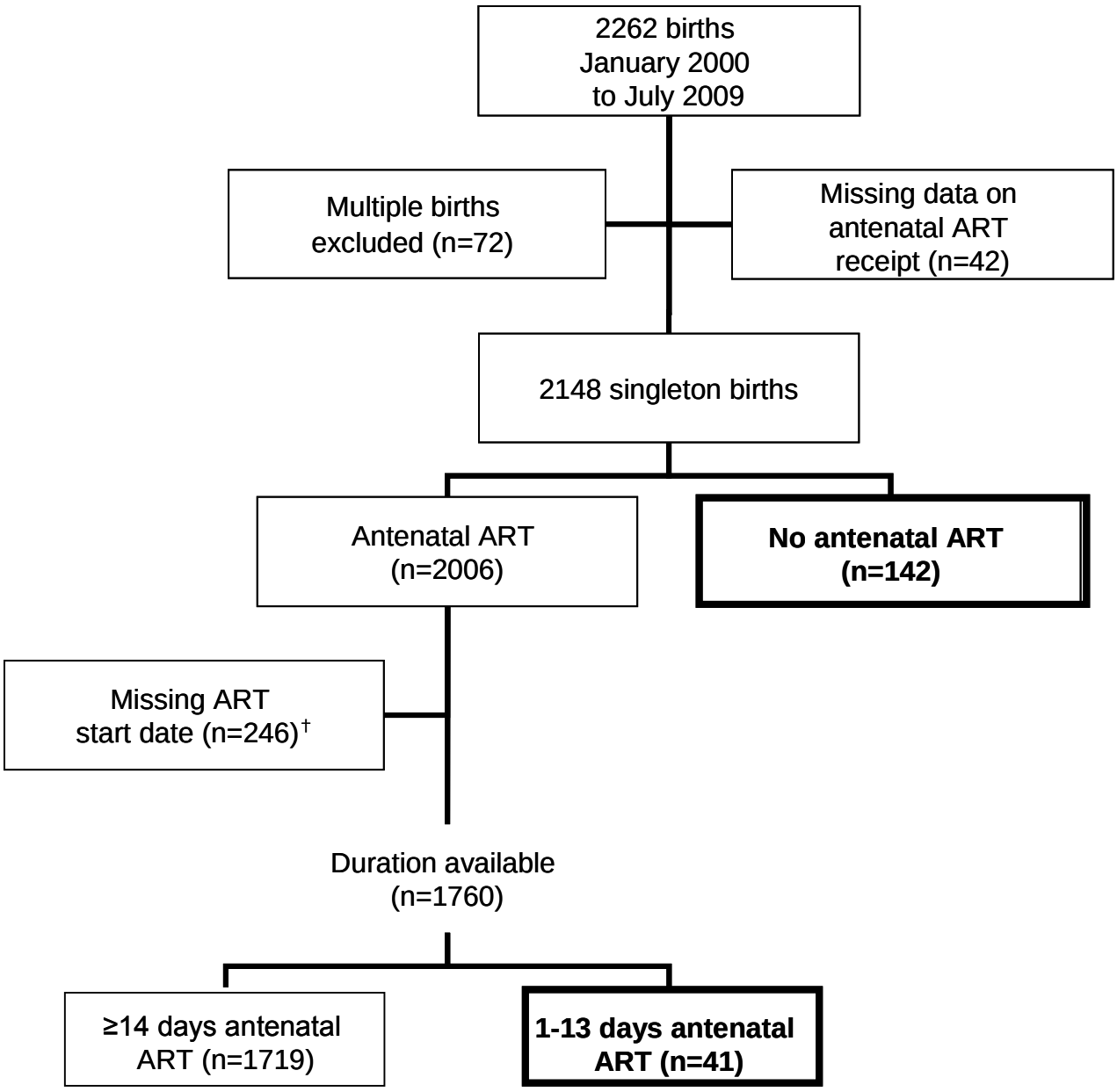

Figure 1: Availability of data on outcome of "insufficient" (<14 days) antenatal antiretroviral therapy (ART)
†Women with missing ART start date are included in the ≥14 days antenatal ART group in all analyses

European Collaborative Study Group

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The authors declare no competing interests.

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