The mother-to-child HIV transmission epidemic in Europe: evolving in the East and established in the West

European Collaborative Study*

Objectives: To carry out an epidemiological analysis of the emerging epidemic in an Eastern European country and to compare the approach to prevention of mother-to-child transmission (MTCT) with that in Western Europe.

Design: Prospective cohort study established in 1985 in Western Europe and extended to Ukraine in 2000.

Methods: Data on 5967 HIV-infected pregnant women and their infants (1251 from Ukraine and 4716 from Western/Central Europe) was analysed. Factors associated with transmission were identified with logistic regression.

Results: HIV-infection among pregnant women enrolled in Western European centres has shifted from being largely injecting drug use (IDU)-related to heterosexually-acquired; in Ukraine IDU also gradually declined with women increasingly identified without specific risk factors. In Ukraine in 2000–2004 most (80%) women received single dose nevirapine (sdNVP) and/or short-course zidovudine prophylaxis [MTCT rate 4.2%; 95% confidence interval (CI), 1.8–8.0 for sdNVP with short-course zidovudine]; 2% ($n = 27$) received antenatal HAART and 33% ($n = 418$) delivered by elective caesarean section (CS); in Western European centres 72% of women received HAART (MTCT rate 1.0%; 95% CI, 0.4–1.9) and 66% delivered by elective CS during the same period.

Conclusions: Our findings indicate distinct differences in the epidemics in pregnant women across Europe. The evolution of the MTCT epidemic in Ukraine does not appear to be following the same pattern as that in Western Europe in the 1980s and 1990s. Although uptake of preventive MTCT prophylaxis has been rapid in both Western Europe and Ukraine, substantial challenges remain in the more resource-constrained setting in Eastern Europe.

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Introduction

An estimated 580 000 HIV-infected people live in Western Europe and 1.3 million in Eastern Europe and Central Asia [1]. The HIV epidemic in Western Europe was established in the early 1980s, mostly among homosexual men and injecting drug users (IDUs). Today, heterosexual transmission prevails, accounting for 58% of new infections in 2003, largely associated with origin from sub-Saharan Africa [2,3]. It was not until the mid- to late-1990s that the HIV epidemic fully emerged in Eastern Europe, where two countries (the Russian

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Federation and Ukraine) bear the brunt of the epidemic [2,4,5], and although initially focused among IDUs, new HIV infections among non-IDU heterosexuals are now rapidly increasing [2]. HIV seroprevalence in Central Europe is substantially lower than that elsewhere in Europe, with most HIV diagnoses concentrated in Romania and Poland [5].

Use of antenatal HAART, elective caesarean section (CS) delivery and no breastfeeding is highly effective in reducing mother-to-child transmission (MTCT) of HIV [6–8]. Prevention of MTCT (PMTCT) programmes have resulted in only around 250 vertically-acquired HIV infections in Western Europe annually, despite increasing numbers of HIV-infected women [9]. In Eastern Europe, there is a higher prevalence of HIV infection (1.0 versus 0.3% in the West), more infected women of childbearing age (34% of total HIV-infected population versus 26% in the West) and health care systems have only limited capacity to cope with the worsening HIV epidemic [1,10]. In Ukraine, 2115 infants were born to women with identified HIV-infection in 2004, a 40% increase since 2003 (Dr N Zhilka, personal communication, 2005). The approach to PMTCT in Ukraine currently follows models used in other resource-limited settings: single dose nevirapine (sdNVP) to mothers intrapartum and to the neonate and/or short course antenatal zidovudine (ZDV) prophylaxis, with formula feeding [11–13]. Similar approaches are being used in other Eastern European countries with high HIV prevalence and/or incidence [14].

The European Collaborative Study (ECS) is an ongoing cohort study which started nearly 20 years ago in Western Europe and extended to Ukraine in 2000. This provided the opportunity for an epidemiological analysis of the situation in Ukraine, comparison with Western Europe and assessment of whether the experience in the West has relevance for the younger epidemic in the East.

Methods

HIV-1 infected pregnant women were enrolled and their infants prospectively observed in accordance with standard protocols [6,15]. Pregnant women are screened for HIV infection within standard antenatal care, with all but one centre having a universal antenatal HIV screening policy [16] and those infected invited to enrol; pregnant women identified as HIV-infected from before pregnancy were also invited to participate. Informed consent was obtained before enrolment, according to local guidelines and ethics approval was granted. The ECS was set up in 1985. Centres from Spain, Italy, the United Kingdom, Germany and Belgium have participated since the study started, with centres from Sweden (1986), the Netherlands (1987), Poland (1989), Denmark (1995) and Ukraine (2000) joining subsequently.

Information collected included maternal CD4 cell count (since 1992), most likely maternal mode of HIV acquisition and antiretroviral prophylaxis/treatment. In the Ukraine centres, CD4 cell counts were available for a small, selected group only [$n = 71$, of which 69 were receiving antiretroviral therapy (ART), two-thirds from one centre]. Delivery and infant characteristics recorded included mode of delivery, sex, birthweight, gestational age and infection status. Maternal CD4 cell counts nearest the time of delivery were used here.

Infants with persistence of antibody beyond 18 months of age and/or a positive virological marker of infection on two separate blood samples regardless of age were included as infected [6,15]. If a child from a Western/Central European centre was HIV antibody-negative and no virus or antigen had ever been detected, (s)he was classified as uninfected, regardless of age. In the centres in Ukraine, due to a lack of virological diagnostic laboratory facilities, dried blood spot filter papers were collected and sent to Amsterdam for testing (Retina^{TM} Rainbow HIV-1 RNA assay; Primagen, Amsterdam, The Netherlands). As diagnosis of HIV infection based on clinical symptoms may occur earlier than exclusion of infection in settings with limited access to virological tests [17], only children born 18 months or more before the time of the analysis were included in the estimation of MTCT rates in the Ukraine centres to reduce likelihood of bias; definition of HIV infection here was based on the development of AIDS and HIV-associated mortality ($n = 12$), persistence of antibody beyond 18 months ($n = 24$) or detectable virus in two or more blood samples taken on different occasions ($n = 6$).

Elective CS was defined as delivery before rupture of membranes and onset of labour, premature delivery as occurring before 37 weeks of gestation, with gestational age confirmed by ultrasound and reported to the nearest completed week, and IDU in pregnancy according to self-report, clinical report or neonatal drug withdrawal symptoms. Women with CD4 cell counts < 200 cells/μl were classified as severely immunosuppressed. Multiple births (32 twin pairs, one triplet) were treated as separate mother–child pairs.

Univariable comparisons for categorized variables were tested with the χ^2 test or χ^2 test for trend. Univariable and multivariable logistic regression analysis was used to obtain odds ratios (OR), adjusted odds ratios (AOR) and 95% confidence intervals (95% CI). All probability values were two-tailed. Data entry was carried out using MS Access 2000 (Microsoft Corp., Redmond, Washington, USA) and analyses using SAS statistical software (v8.02; SAS Institute, Cary, North Carolina, USA).

Results

HIV-infected pregnant women

Of the 5967 mother–child pairs enrolled by December 2004, 1251 (21%) were from Ukraine, 179 (3%) from Poland and 4537 (76%) from Western European centres. Poland was the only country included without a universal antenatal HIV testing policy at this time [18] and most (136; 76%) of the pregnant women enrolled here had an IDU history; all the women were white, all but one had been born in Poland and they had a median age at delivery of 26.5 years (range, 17–43 years).

Maternal and delivery characteristics of women enrolling in the eight Western European countries and in Ukraine are presented in Table 1. Western European centres were ethnically heterogeneous, reflecting recent migration from Africa: 84% (863/1025) of black women came from sub-Saharan Africa, increasing from 4% (35/838) in 1985–1989 to 37% (478/1309) in 2000–2004 ($P < 0.002$). Women from sub-Saharan Africa enrolling in 2000–2004 were older (median age 30.3 versus 27.8 years), less likely to be married or cohabiting [71% (326/457) versus 78% (574/733); $\chi^2 = 7.42$; $P = 0.006$] and more likely to be identified as HIV-infected through antenatal testing [44% (211/267) versus 26% (220/831); $\chi^2 = 42.9$; $P < 0.0001$] than other women enrolling in Western European centres at this time. Overall, women enrolling in the Western European centres in 2000–2004 were more likely to know their HIV diagnosis before pregnancy, independent of ethnicity, mode of acquisition and parity, with an AOR of pre-pregnancy diagnosis of 10.1 (95% CI, 7.95–12.8) in 2000–2004 with 1985–1989 as baseline. Women from Ukraine were 83% less likely to be diagnosed before pregnancy than women in Western Europe (AOR, 0.17; 95% CI, 0.15–0.21) overall.

Women enrolling in the Ukraine centres were more similar to those enrolling in Western European centres in the first 5 years of the study than those enrolling more recently. In the Western centres in 1985–1989, 93% (783/846) of women were white, 35% (294/846) aware of their infection before pregnancy and 79% (668/846) IDUs. Median age in the Western European centres was 28.5 years (range, 10–47 years) overall, 25.1 years (range, 10–41 years) in 1985–1989 and 31.7 (range, 15–47 years) in 2000–2004, compared with 25.4 years (range, 14–43 years) in Ukraine. Prevalence of very young maternal age was higher in Ukraine than in Western

Table 1. Maternal and delivery characteristics.

	Western Europe		Ukraine
	Whole period $n = 4537$	2000–2004 $n = 1384$	2000–2004 $n = 1251$
Ethnicity	$n = 4364$	$n = 1326$	$n = 1234$
Black	1025 (23)	559 (42)	1
White	3158 (72)	702 (53)	1212 (98)
Other	181 (4)	65 (5)	21 (2)
Timing of first positive HIV test	$n = 4537$	$n = 1384$	$n = 1251$
Before pregnancy	2582 (57)	916 (66)	248 (20)
During pregnancy	1535 (34)	419 (30)	759 (61)
At delivery	420 (9)	49 (4)	244 (19)
Parity at enrolment	$n = 4128$	$n = 1294$	$n = 1219$
0	2191 (53)	571 (44)	710 (58)
1	1155 (28)	412 (32)	381 (31)
2	492 (12)	210 (16)	90 (7)
≥ 3	290 (7)	101 (8)	38 (3)
History of pregnancy termination	$n = 4190$	$n = 1313$	$n = 1220$
No	2565 (61)	805 (61)	692 (57)
Yes	1625 (39)	508 (39)	528 (43)
Living outside country of birth	$n = 4269$	$n = 1309$	$n = 1243$
No	2935 (69)	611 (47)	1024 (99)
Yes	1334 (31)	698 (53)	9 (1)
Reported risk factors for acquisition of HIV infection	$n = 4537$	$n = 1384$	$n = 1251$
IDU	1062 (23)	135 (10)	111 (9)
Sexual	2320 (51)	1031 (74)	318 (25)
IDU and sexual	928 (20)	139 (10)	239 (19)
Other	51 (1)	15 (1)	8 (1)
No risk factors specified	176 (4)	64 (5)	575 (46)
Gestational age	$n = 4456$	$n = 1350$	$n = 1251$
< 34 weeks	235 (5)	91 (7)	32 (3)
34–36	634 (14)	240 (18)	89 (7)
≥ 37	3587 (81)	1019 (75)	1130 (90)
Birth weight (g)	$n = 4459$	$n = 1262$	$n = 1251$
Median (range)	2932 (420–5190)	2900 (420–5190)	3085 (1200–5000)

IDU, injection drug user.

Europe [9% (114/1250) were aged < 20 years compared with 4% (150/4209); $\chi^2 = 64.7$; $P < 0.0001$] and Ukrainian young women were more likely to be married [39% (43/110) versus 19% (19/100); $\chi^2 = 10.1$; $P = 0.001$], less likely to have had a pregnancy termination [10% (11/113) versus 16% (29/140); $\chi^2 = 4.87$; $P = 0.027$] and less likely to report any IDU [13% (14/104) versus 26% (53/149); $\chi^2 = 14.3$; $P = 0.0002$].

Temporal trends in maternal mode of acquisition of HIV are presented in Figs 1a and 1b. In Western Europe this has shifted from IDU-related to heterosexual transmission. Since 2000, IDU has gradually declined in Ukraine, with an increase in women reporting no risk factors; that is, this latter group did not report current or past use of injecting drugs, having an IDU or other high-risk sexual partner, blood transfusions or any other high-risk sexual behaviour (e.g. multiple sex partners). Women not reporting specific risk factors in Ukraine were largely married or cohabiting (87%; 479/553), of similar age to those reporting heterosexual risk factors (respective medians, 24.7 and 25.6 years, with 52 and 45% aged < 25 years) and were significantly younger than IDUs (median age 27.2 years; 12% aged < 25 years; $\chi^2 = 370.5$; $P < 0.0001$). Prevalence of current IDU was 17% (757/4537) in Western European centres and 10% (125/1251) in Ukraine; in the West this prevalence decreased from 30% (257/846) in 1985–1989 to 5% (71/1384) in 2000–2004 ($\chi^2_{\text{trend}} = 316.5$; $P < 0.0001$). Although in Ukraine, former or current IDUs were older than other women (see above), in Western Europe women without an IDU history were older than those with (median age 29.1 versus 27.9 years, respectively), reflecting the proportional increase in older African women in recent years [19].

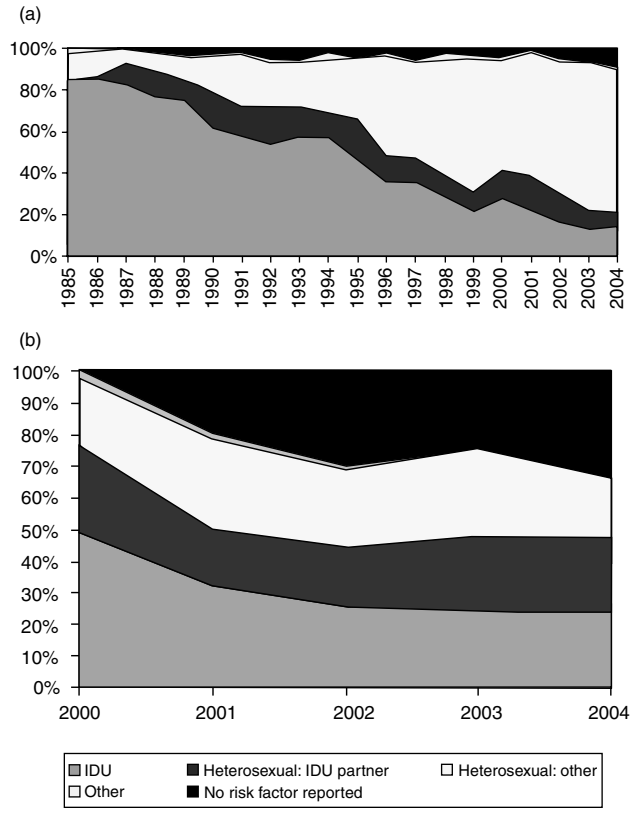

Fig. 1. Trends over time in mode of acquisition of HIV infection: (a) Western European centres and (b) Ukraine. IDU, injection drug user.

Median maternal CD4 cell count was 420 cells/μl (range, 0–2350 cells/μl) ($n = 3009$, including 71 from Ukraine). In 1135 (38%) women CD4 cell count was ≥ 500 cells/μl, in 1471 (49%) it was 200–499 cells/μl and in 403 (13%) < 200 cells/μl. Black women were more likely to be severely immunosuppressed than white (141/787 (18%) versus 240/2016 (12%); $\chi^2 = 16.9$, $P < 0.0001$). Limiting a multivariable logistic regression to data on 2205 Western European women from the period when CD4 cell count measurements were routinely recorded and allowing for ethnicity and time period (the latter used to assess maturity of the epidemic and as a proxy for trends in therapeutic management), black women remained at increased risk of severe immunosuppression than white women (AOR, 1.47; 95% CI, 1.13–1.91); women delivering in 2000–2004 were significantly less likely to be severely immunosuppressed than women delivering in 1992–1995 (AOR, 0.66; 95% CI, 0.48–0.89), independent of ethnicity.

Mother-to-child transmission

In the following analyses, data from the Polish centres were combined with those from the Western European centres, due to small numbers in the former and very similar access to PMTCT interventions. Overall MTCT rates were 6.7% (95% CI, 4.9–8.9) (42/628) in Ukraine and 9.1% (95% CI, 8.3–10.0) (373/4092) in Western/Central Europe. The MTCT rate declined significantly in the latter centres from 16.1% in 1992–1993 to 1.7% in 2002–2003 ($\chi^2 = 70.6$; $P < 0.0001$), with no significant trend in Ukraine over 2000–2004 ($P = 0.76$).

Of the 2441 (52%) women in Western/Central European centres receiving no antenatal ART, most enrolled before 1994; 1021 (22%) women received monotherapy or dual therapy and 1252 (26%) received HAART, in 610 (49%) cases initiated before pregnancy. The 739 women in Western/Central Europe on ZDV monotherapy started this at a median of 26 gestational weeks, with most delivering before 1997. In Ukraine, two-thirds ($n = 793$) of women received sdNVP, of whom 63% ($n = 503$) also received ZDV monotherapy, as a short-course regimen, initiated at a median 35 gestational weeks; a further fifth of women received either ZDV monotherapy ($n = 208$) or HAART ($n = 27$). Table 2 includes the crude MTCT rates in Western/Central Europe and in Ukraine, stratified by ART. Although no adjustment was made for other variables, the MTCT rate in Western/Central

Table 2. Mother-to-child transmission (MTCT) rates by antiretroviral prophylaxis or treatment group.

	Western Europe 1985–1994		Western Europe 1995–1999		Western Europe 2000–2004		Ukraine 2000–2004	
Antenatal ART	*n* (%)	Crude MTCT rate (95% CI)	*n* (%)	Crude MTCT rate (95% CI)	*n* (%)	Crude MTCT rate (95% CI)	*n* (%)	Crude MTCT rate (95% CI)
None	2008 (96)	15.4% (282/1830; 13.8–17.1)	283 (24)	12.8% (30/234; 8.8–17.8)	148 (10)	4.65% (6/129; 1.7–9.9)	223 (18)	19.8% (19/96; 12.4–29.2)
sdNVP: mother–infant		–		–		–	290 (23)	6.8% (9/131; 3.2–12.6)
Monotherapy	73 (4)	12.3% (8/65; 5.5–22.8)	550 (47)	6.1% (28/459; 4.1–8.7)	116 (8)	4.0% (4/101; 1.1–9.4)	–	–
without sdNVP	–	–	–	–	–	–	208 (17)	7.8% (6/77; 2.9–16.2)
with sdNVP	–	–	–	–	–	–	503 (40)	4.2% (8/192; 1.8–8.0)
Dual nucleotide therapy	2	0/2	134 (11)	0.83% (1/121; 0.02–4.5)	147 (10)	0.8% (1/127; 0.02–4.3)	–	–
HAART	–	–	205 (18)	2.69% (5/186; 0.9–6.2)	1046 (72)	1.0% (8/838; 0.4–1.9)	27 (2)	0/2

ART, antiretroviral therapy; sdNVP, single dose nevirapine; CI, confidence interval.

Europe in the IDU-driven era (1985–1994) among women not receiving antenatal ART was not significantly different from that in the same group in Ukraine currently (15.4 versus 19.8%; $\chi^2 = 1.02$; $P = 0.31$).

In Western/Central Europe the elective CS rate increased from 17% (204/1220) in 1990–1994 to 47% (543/1156) in 1995–1999 and 63% (909/1438) in 2000–2004 ($\chi^2 = 589.2$; $P < 0.0001$), whereas in Ukraine the elective CS rate was 33% (418/1251), with no trends over the 5 years of data collection.

Logistic regression analyses of MTCT risk were carried out separately for Western Europe and Ukraine (Table 3). As only 71 mother–child pairs from Ukraine had CD4 cell counts, we were unable to include CD4 cell count in the analysis for this area. In Ukraine, only 170 women in the analysis had an elective CS, and although the AOR indicated a reduced transmission risk versus vaginal delivery, this did not reach statistical significance (Table 3). Overall, use of abbreviated regimens in Ukraine was associated with a 70% reduced MTCT risk. Use of sdNVP alone was associated with a 66% reduced MTCT risk after adjusting for prematurity and mode of delivery compared with no antiretroviral prophylaxis (AOR, 0.34; 95% CI, 0.15–0.82), with a similar AOR for ZDV monotherapy only (AOR, 0.44; 95% CI, 0.16–1.22), although this did not reach statistical significance probably owing to small numbers; sdNVP-boosted short-course ZDV was associated with the greatest reduction in risk (AOR, 0.23; 95% CI, 0.09–0.63) compared with no prophylaxis; however, this combination was not statistically significantly more effective compared with sdNVP alone or short-course zidovudine alone. In Western/Central Europe, maternal CD4 cell count was an important risk factor, with severe maternal immunosuppression independently associated with a doubled risk and elective CS with a two-thirds reduced risk. Women taking HAART were more than 90% less likely to transmit infection than those untreated (Table 3) and 75% less likely than women on mono or dual therapy (AOR, 0.25; 95% CI, 0.12–0.54).

Discussion

We present findings from the first epidemiological study of HIV-infected pregnant women in Ukraine. The Ukrainian HIV epidemic has been dominated by IDU [5,13], with high IDU prevalence, young age at IDU initiation, high-risk behaviours (drug use-related and sexual), low HIV prevention awareness and the intersecting epidemics of IDU and commercial sex work accelerating the epidemic [4,20,21]. By 2004, 50% of women enrolled in our Ukraine centres were IDU or reported an IDU sexual partner. Although nearly 80% women in Western European centres enrolling in 1985–1989 were IDUs

Table 3. Risk factors for mother-to-child transmission (MTCT) for Western Europe and Ukraine.

	Western Europe			Ukraine		
	N 2544	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)	*N* 498	Unadjusted OR (95% CI)	Adjusted OR[b] (95% CI)
Maternal CD4 cell count						
≥ 500 cells/μl	957	1.00	1.00	–	–	–
200–499 cells/μl	1240	1.48 (1.05–2.09)	1.88 (1.32–2.68) $P < 0.001$	–	–	–
< 200 cells/μl	347	1.76 (1.12–2.76)	2.07 (1.29–3.32) $P = 0.003$	–	–	–
Mode of delivery						
Vaginal delivery	1082	1.00	1.00	311	1.00	1.00
Emergency CS	338	0.51 (0.32–0.80)	0.69 (0.42–1.13) $P = 0.14$	17	0.55 (0.07–4.25)	0.59 (0.07–4.85) $P = 0.62$
Elective CS	1124	0.18 (0.12–0.28)	0.34 (0.22–0.52) $P < 0.001$	170	0.49 (0.22–1.05)	0.86 (0.36–2.00) $P = 0.72$
Maternal ART						
None	1052	1.00	1.00	96	1.00	1.00
sdNVP and/or SC ZDV	–	–	–	402	0.25 (0.13–0.47)	0.30 (0.14–0.64) $P = 0.002$
Mono/dual	631	0.25 (0.17–0.39)	0.34 (0.21–0.53) $P < 0.001$	–	–	–
HAART	861	0.07 (0.04–0.13)	0.09 (0.04–0.17) $P < 0.001$	–	–	–
Prematurity						
≥ 37 weeks	2066	1.00	1.00	452	1.00	1.00
< 37 weeks	478	1.31 (0.92–1.87)	1.78 (1.20–2.63) $P = 0.004$	46	3.65 (1.66–8.01)	2.19 (0.93–5.16) $P = 0.08$

[a]Adjusting for antenatal antiretroviral therapy (ART), mode of delivery, prematurity, maternal CD4 cell count and sex.
[b]Adjusting for antenatal ART, mode of delivery, prematurity and sex. OR, odds ratio; CI, confidence interval; CS, caesarean section; SC, short course; sdNVP, single dose nevirapine; ZDV, zidovudine.

this had declined to 20% in 2000–2004. The relatively low prevalence of IDU history (less than 30%) reported among pregnant women in Ukraine may reflect under-reporting due to social desirability bias or alternatively, pregnant IDU women may not have been enrolled due to a lack of antenatal care. However, these biases are likely to have remained constant over time, suggesting that the decline in IDU seen is real.

Our findings regarding mode of acquisition in Ukraine are consistent with reports of the evolving epidemic there, with evidence that HIV is spreading to bridging populations (sexual partners of IDU and sex workers) and beyond to the general population, with one-third of new HIV diagnoses in Ukraine heterosexually acquired in 2003 [1,13,21,22]. Most women not reporting any risk factors in our Ukraine centres probably acquired HIV heterosexually through unprotected sexual intercourse with casual or regular partners, including their husbands (87% were married or cohabiting), but were unaware of their exposure to HIV. Similarly, 48% of new HIV infections in women in Eastern Europe in 2004 reported to the European HIV/AIDS Monitoring Centre were in the 'other/undetermined' category [9]. Our finding of more very young women in Ukrainian versus Western European centres probably reflects their tendency to start child-bearing at younger ages, but also suggests that Ukrainian women may acquire HIV infection at younger ages [23].

The overall MTCT rate in the Ukrainian centres was 6.7% during 2000–2004. The Ukraine government implemented the use of short-course ZDV and/or sdNVP for mother and infant with formula feeding in 2001 [22]. We lacked statistical power to show a significant difference between either short-course ZDV boosted with sdNVP compared to sdNVP alone or to short-course ZDV alone, although the crude MTCT rates suggest that there might be a benefit in combining sdNVP and short-course ZDV in this population, consistent with trial findings elsewhere and WHO guidelines [11]. The overall MTCT rate in the ZDV monotherapy group in Western Europe was marginally less than that in Ukraine (6.4 versus 7.8%), despite shorter ZDV duration in Ukraine, starting at 35 weeks. The Ukrainian government recently updated its national policy, which now recommends that short-course ZDV is started at 28 weeks gestation. The in utero/intrapartum MTCT rate in the sdNVP only group here was similar to that in the HIVNET 012 trial (6.9 versus 8.1%) [24]. However, the rate at which short-course ZDV was boosted by sdNVP was somewhat higher in our non-trial situation than in the Thai PHPT2 trial [11] with longer antenatal ZDV, but lower than in the West African Ditrame Plus study where just over half were breastfed [25].

National guidelines in Western Europe now recommend HAART in pregnancy as prophylaxis for PMTCT, with

continuation post-partum determined by maternal virological and immunological status, although there is still a place for ZDV monotherapy combined with elective CS for some pregnant women (e.g. those with low viral loads not requiring HAART for their own health) [26,27]. The upper 95% CI of the 1% MTCT rate among women on HAART in the Western European centres was 1.9%, just overlapping with the lower 95% CI of the 4.2% MTCT rate among Ukrainian women receiving sdNVP and short-course ZDV, at 1.8%. This highlights that a reduction in MTCT rates to very low levels without widespread access to HAART is possible in non-breastfeeding, non-trial settings.

However, access to HAART for eligible HIV-infected mothers should be prioritized, and is not only important for maternal health, but also for the children's future health and social care, regardless of infection status [28,29]. Although expanding access to antiretroviral drugs in Ukraine is underway, only an estimated 13% of HIV-infected people eligible for ART are currently treated [13]. As we only had limited CD4 cell count data in Ukraine and no viral load information, we cannot make any conclusions regarding the need for HAART in our study population.

In terms of generalizability of our results to elsewhere in Ukraine, an estimated 20% of all pregnant HIV-infected women delivering nationally in 2001–2004 were enrolled in the ECS (Ukrainian AIDS Center, 2005 unpublished data). The ECS centres were in Southern Ukraine, the national epicenter [30], in Odessa, Micolaiev and Simferopol and include those at the forefront of the PMTCT programme in Ukraine [31]. Uptake of and access to prophylactic interventions in these centres may be somewhat greater than in areas with lower prevalence and/or less experience. In particular, the 33% elective CS rate in the Ukrainian centres here was higher than that reported for HIV-infected women in Ukraine overall, at around 14% (Dr N Zhilka, personal communication, 2005). Furthermore, our findings regarding mode of acquisition of HIV may be specific to Southern Ukraine, as the first affected region of Ukraine, particularly regarding the trends over time. With regard to generalizability to other Eastern European countries, although IDU remains a driving force in many countries' epidemics, an increasing proportion (up to 45% or more) of new reported HIV infections are due to unprotected sex in Russia, Belarus, Moldova and Kazakhstan [32].

There are similarities between the early HIV epidemics in Western Europe and Ukraine, notably the importance of IDU and sexual contact with IDUs. Access to and uptake of PMTCT prophylaxis was rapid in Western Europe [33,34], and antenatal HAART use has contributed to the very low rates of MTCT there [35–37]. Although knowledge of effective PMTCT interventions pre-dated the Ukraine epidemic, application of these is an enormous challenge here, as in all low-income settings [38–40]. These challenges include transforming national PMTCT strategies from a medically-focused vertical approach towards a horizontal approach and integrating prevention activities into maternal and child health services [41]. The Ukraine government has addressed PMTCT with substantial success, with a decreasing MTCT rate from over 25% prior to 2000 to 8% in 2002 [22] (Dr N Zhilka, personal communication, 2005). However, increasing HIV incidence and lack of widespread access to HAART is likely to result in an increasing burden of paediatric HIV infection in Ukraine. The juxtaposition between this situation and the discussion in Western Europe of the potential elimination of vertically-acquired HIV infection underscores the urgent need to scale-up the response to the epidemic in the most affected regions of Eastern Europe, including Ukraine, remembering that PMTCT not only includes application of antenatal and perinatal prophylaxis and prevention of unwanted pregnancies in HIV-infected women, but also primary prevention.

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