




Missed opportunities to prevent mother-to-child transmission of HIV in Italy

A Di Biagio ^{1,*}, L Taramasso ^{2,3,*}, G Gustinetti,² G Burastero,² V Giacomet,⁴ D La Rovere,⁵ O Genovese,⁶ C Giaquinto,⁷ O Rampon,⁷ I Carloni,⁸ TK Hyppolite,⁹ L Palandri,⁹ S Bernardi,⁹ E Bruzzese,¹⁰ R Badolato,¹¹ C Gabiano,¹² E Chiappini ¹³, M De Martino¹³ and L Galli¹³ on behalf of The Italian Register for HIV Infection in Children[†]

¹Infectious Diseases Unit, Department of Internal Medicine, Policlinico San Martino Hospital, Genoa, Italy, ²Infectious Diseases Unit, Department of Health Sciences (DISSAL), University of Genoa, Policlinico San Martino Hospital, Genoa, Italy,

³Infectious Diseases Unit, Department of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, ⁴Department of Pediatrics, University of Milan, L. Sacco Hospital, Milan, Italy, ⁵Ospedale Pediatrico Giovanni XXIII, Bari, Italy, ⁶Pediatric Intensive Care Unit, A. Gemelli Hospital, Catholic University of Rome, Rome, Italy, ⁷Department of Child's and Woman's Health, University of Padova, Padova, Italy, ⁸Pediatric Unit, Department of Child and Mother Health, Azienda Ospedaliero-Universitaria Ospedali Riuniti, Ancona, Italy, ⁹Unit of Immune and Infectious Diseases, Children's Hospital Bambino Gesù, Rome, Italy, ¹⁰Department of Translational Medical Science, Section of Pediatrics, University of Naples Federico II, Naples, Italy, ¹¹Department of Clinical and Experimental Sciences, Institute of Molecular Medicine 'Angelo Nocivelli', University of Brescia, Brescia, Italy, ¹²SC Pediatric Unit, Regina Margherita Hospital, Turin, Italy and ¹³Department of Health Sciences, University of Florence, Meyer Children's Hospital, Florence, Italy

Objectives

Vertical transmission of HIV can be effectively controlled through antenatal screening, antiretroviral treatment and the services provided during and after childbirth for mother and newborn. In Italy, the National Health Service guarantees universal access to prenatal care for all women, including women with HIV infection. Despite this, children are diagnosed with HIV infection every year. The aim of the study was to identify missed opportunities for prevention of mother-to-child transmission of HIV.

Methods

The Italian Register for HIV Infection in Children, which was started in 1985 and involves 106 hospitals throughout the country, collects data on all new cases of HIV infection in children. For this analysis, we reviewed the database for the period 2005 to 2015.

Results

We found 79 HIV-1-infected children newly diagnosed after birth in Italy. Thirty-two of the mothers were Italian. During the pregnancy, only 15 of 19 women with a known HIV diagnosis were treated with antiretroviral treatment, while, of 34 women who had received an HIV diagnosis before labour began, only 23 delivered by caesarean section and 17 received intrapartum prophylaxis. In 25 mothers, HIV infection was diagnosed during pregnancy or in the peripartum period. Thirty-one newborns received antiretroviral prophylaxis and 39 received infant formula.

Conclusions

We found an unacceptable number of missed opportunities to prevent mother-to-child transmission (MCTC). Eliminating HIV MTCT is a universal World Health Organization goal. Elucidating organization failures in Italy over the past decade should help to improve early diagnosis and to reach the zero transmission target in newborns.

Keywords: children, HIV, missed opportunities, mothers, newborns, pregnancy

Accepted 25 January 2019

Correspondence: Dr Antonio Di Biagio, Infectious Diseases, Policlinico San Martino Hospital, Padiglione Specialità Complesse, Piano-2, 16132 Genoa, Italy. Tel: +390105554646; fax: +390105556794; e-mail: adibiagioa@gmail.com

*Antonio Di Biagio and Lucia Taramasso contributed equally to this work.

[†]Details of the Italian Register for HIV Infection in Children are presented in Appendix 1.

Introduction

Mother-to-child transmission (MTCT) rates for women diagnosed with HIV infection have fallen to around 1–2% in recent years in developed countries, thanks to effective antiretroviral therapy (ART), appropriate management of delivery and avoidance of breast feeding [1–5]. Nevertheless, the world-wide rate of MTCT of HIV is still far from reaching the zero transmission target, even in countries with consolidated screening programmes and standardized protocols of HIV management during pregnancy. In 2016, the incidence rate of HIV infection in Italy was 5.7/100 000 inhabitants [6]. In Italy, vertical transmission rates dropped significantly from 5.1% [56 of 1049 cases; 95% confidence interval (CI) 3.98–6.70] in 1996–1999 to 1.0% (13 of 1298 cases; 95% CI 0.46–1.55) in 2005–2010 [7].

The main weakness of the system is that many women fail to receive an HIV diagnosis before delivery [8] as a result of either absent or inadequate prenatal care [9], with a consequent absence of any form of prophylaxis for the child. As effective procedures exist to reduce the rate of transmission virtually to zero, each single infected newborn represents an unacceptable missed opportunity for safeguarding the health of the new generation.

In Italy, the National Health Service guarantees universal access to prenatal care for all women [10]. Moreover, HIV testing is free nationwide. The Italian guidelines for the care of women during physiological pregnancy recommend offering an HIV test to all pregnant women in the first trimester and repeating it after week 28 of pregnancy, regardless of the presence or absence of risk factors for HIV infection [10]. Women who are aware of being HIV positive, or who discover that they are HIV positive at the time of screening, but are not taking ART, are recommended to start ART immediately [11]. For women who do not have an undetectable viral load, peripartum prophylaxis with zidovudine (ZDV) and caesarean delivery are advised for further reduction of the risk of transmission. Furthermore, all women are counselled not to breast feed if artificial feeding is a viable and practical solution [12]. Infant formula is given free of cost to children born to HIV-infected mothers [13]. In addition, these infants start antiretroviral prophylaxis at birth. In such a context, we expect the rate of HIV MCTC to be close to zero. With the aim of determining how many vertical infections still occur in Italy and what improvements to the system are needed, we reviewed data for all patients recorded as being HIV-infected in the Italian Register for HIV Infection in Children and tried to identify the causes of HIV transmission.

Methods

Data collection

Existing anonymous surveillance data for perinatally HIV-infected children were extracted from The Italian Register for HIV Infection in Children, which was started in 1985 and involves 106 hospitals throughout the country [14]. The approval of local Ethics Committees and informed consent obtained from parents or legal guardians were required for participation. Children < 13 years of age reported to the aforementioned Register between January 2005 and December 2015 were eligible for inclusion in the study. Those with a confirmed diagnosis of HIV infection (persistence of HIV-1 antibodies after 18 months of life or, before 18 months, detection of HIV DNA and/or HIV RNA on at least two occasions, excluding cord blood) were included in our study, and data were retrospectively analysed. In this analysis, we only evaluated children born in Italy.

Clinical and sociodemographic information was collected on a standardized form and included the patient's date of birth, sex, gestational age, date of HIV diagnosis, type of postnatal prophylaxis or antiretroviral treatment and its duration, first HIV RNA measurement (HIV-1 RNA copies/mL), Centers for Disease Control and Prevention (CDC) stage according to the 1994 revised classification [15], age at AIDS diagnosis, last clinical observation, and outcome. For mothers, ethnicity, risk factor for HIV acquisition, timing of HIV diagnosis with regard to the child's birth, ART during pregnancy with any interruption, peripartum CD4 T-cell count (cells/ μ L) and HIV RNA (copies/mL), type of delivery, intrapartum prophylaxis with ZDV, and type of breast feeding were recorded. Additional data collection or clarification regarding missing data was carried out via telephone interviews with the clinicians involved in the care of individual patients.

Missed opportunities were defined as deviations from the standard practice described in the Italian guidelines for use of antiretroviral agents and the diagnostic-clinical management of HIV-1-infected persons and in the Italian guidelines on physiological pregnancy [10,11]. The date of the first clinical observation was considered as the date of HIV diagnosis for all those children whose mothers' HIV status was unknown at the time of delivery.

Results

A total of 108 new cases of HIV-infected children in The Italian Register for HIV Infection in Children were observed between 2005 and 2015. Of these cases, 29

Table 1 Demographic, clinical, immunological and virological profile of HIV-infected children diagnosed from 2005 to 2015 in The Italian Register for HIV Infection in Children

Variable	
Year of birth	
2005	13
2006	7
2007	9
2008	11
2009	12
2010	10
2011	3
2012	6
2013	3
2014	1
2015	4
Sex	
Male	37 (47)
Female	42 (53)
CDC stage at diagnosis	
N	12 (15.1)
A	17 (21.5)
B	22 (27.8)
C	24 (30.3)
Unknown	3 (3.8)
Immunological status at diagnosis	
1	39 (49.3)
2	17 (21.5)
3	21 (26.5)
Unknown	2 (2.5)
AIDS	
Yes	25 (31.6)
No	54 (68.3)
Clinical condition	
Alive	68 (86)
Dead	2 (2.5)
Lost to follow-up	9 (11.4)
Time from birth to HIV diagnosis (days) [median (range)]	32.0 (0–2276)
Log HIV RNA load at diagnosis [median (range)]	5 (1.27–7.24)

Values are *n* (%), unless otherwise stated.

CDC, Centers for Disease Control and Prevention.

children were excluded, because the women delivered outside Italy. All 79 children included in the study were vertically infected. In Table 1, we report the clinical characteristics of the children. Their mothers came from different regions of the world: 32 from Italy and 41 born abroad. Among these, 21 were born in sub-Saharan African countries and 13 in Eastern Europe. The countries of origin of the mothers are given in Table 2.

In 32 women, the risk factor for acquiring HIV infection was sexual intercourse, and in 10 it was injecting drug use. In one woman, the risk factor was blood transfusion, while in 36 women, the risk factors for HIV infection were unknown (Table 2). Only nine women were already aware of their HIV infection before pregnancy, whereas 25 were identified as HIV positive during pregnancy or in the peripartum period. For 12 women whose HIV test was

Table 2 Country of origin of mothers

Country of origin	Number
Italy	32
Nigeria	9
Romania	7
Morocco	5
Sierra Leone	3
Ukraine	3
Ghana	3
Ivory Coast	2
Bosnia	1
Brazil	1
Bulgaria	1
Cameroon	1
Eritrea	1
Ethiopia	1
Guinea Bissau	1
Peru	1
Serbia	1
Togo	1
Zambia	1
Not reported	6

negative at the beginning of the pregnancy, an acute HIV infection developed during the pregnancy. Only five of them repeated the HIV test at the end of pregnancy and thus received the diagnosis before delivery.

In 32 women, the HIV status was unknown until the postpartum period. Only 15 of 19 women with known HIV infection received ART during pregnancy, of whom three stopped ART before the date of delivery. Of the 34 women who had received an HIV diagnosis before delivery, only 17 received an intravenous infusion of ZDV during labour. Figure 1 summarizes the timing of HIV diagnosis and the prophylactic measures adopted.

Among the 79 children, 38 were born by vaginal delivery, 28 by elective caesarean section, six by caesarean section after long labour, and three by natural spontaneous delivery. After birth, 31 of the infants started ZDV and 39 were breast-fed, nine of whom were breast-fed despite known maternal HIV infection. Missed opportunities occurred in 66 of the 79 women: 37 were not tested for HIV throughout pregnancy, and three women with a known HIV diagnosis missed the opportunity to take therapy during pregnancy. Of the 34 women who received an HIV diagnosis before delivery, 11 missed the opportunity to have a caesarean section, 18 missed the opportunity to have an intravenous infusion of ZDV during labour, and nine missed the opportunity to formula-feed their children. Moreover, eight of 34 newborns missed the opportunity to receive ZDV in the first 4 weeks of life. Only three newborns received combination ART with ZDV plus lamivudine and nevirapine. The median time from birth to HIV diagnosis was 32 days [interquartile range (IQR)

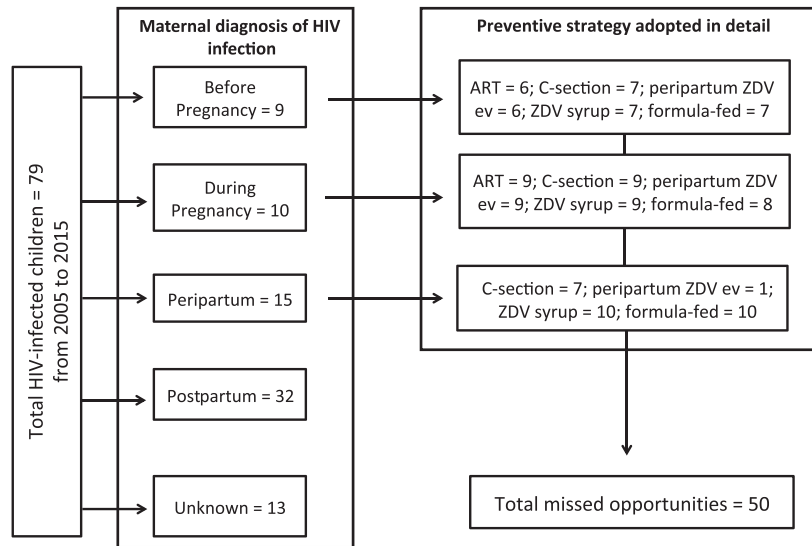


Fig. 1 Description of the time of diagnosis of HIV in mothers, and the preventive strategies adopted in the different stages ART, (maternal) antiretroviral therapy; C-section, caesarean section; ev, endovenous; ZDV, zidovudine. *Some mother–child pairs may have missed more prevention opportunities.

0–2276 days]; in 34 children, the diagnosis of infection was made > 3 months after birth, and in 13 children, it was made > 1 year after birth.

Discussion

This is the first systematic review analysis of missed opportunities to prevent MTCT in Italy. We identified 79 HIV-infected children born from 2005 to 2015, with an apparently decreasing incidence of MTCT in the last 2 years of the study (2014–2015). However, the possibilities of late diagnoses in children and late notification to the Register do not allow determination of whether the rate of MTCT is truly changing. Nevertheless, these data represent an unacceptable gap between the actual incidence of vertical HIV infection in Italy and the zero transmission rate target proposed by the World Health Organization (WHO).

Two other recent studies highlighted that children still acquire HIV infection by MTCT in Europe. Despite prevention programmes and active screening being largely available in these countries, 125 HIV-infected children were born in Spain between 2004 and 2013 and 48 in France between 2006 and 2012 [16,17]. Moreover, according to the data of the National Study of HIV in Pregnancy and Childhood in the UK, HIV status was reported for only 3988 of the 5641 children born to HIV-infected mothers, and 16 of these children acquired HIV perinatally despite known maternal diagnosis [18].

In previous studies, MTCT was linked to inadequate (or absent) prenatal care, and late booking of prenatal care was correlated with being foreign-born [18,19]. However, in our study, about 40% of women were Italian, highlighting that prenatal care and serological screening need to be optimized universally. In Italy, HIV testing is voluntary and universally free, and the current guidelines for the follow-up of physiological pregnancy produced by the National Ministry of Health recommend that HIV testing be performed both at the beginning of pregnancy and after the 28th week [10,11]. However, the guidelines of the Italian Society of Gynaecology and Obstetrics (SIGO) only mention HIV testing in the context of prenatal screening and do not recommend retesting in the third trimester [20]. Women who do not receive an HIV diagnosis during pregnancy miss the opportunity to prevent the transmission of the infection, and double checking of HIV status at two different points in the pregnancy could potentially halve the risk of MTCT compared with women who are tested only once.

However, some opportunities for prevention of MTCT were also missed in women who were diagnosed before delivery. In four of 19 mothers with known HIV infection, ART was not administered, and in three of 19, ART was discontinued during pregnancy. The 2013 WHO guidelines recommend that all HIV-infected women start ART during pregnancy or continue lifelong ART [21]. ART has been associated with a decrease in HIV RNA in blood and genital secretions [22], and can also produce adequate systemic drug levels in the foetus, crossing the

Table 3 Antiretroviral regimen during pregnancy in the 15 women treated

Number of patients	Drug 1	Drug 2	Drug 3
4	Zidovudine	Lamivudine	Lopinavir/ritonavir
3	Tenofovir	Emtricitabine	Raltegravir
3	Tenofovir	Emtricitabine	Lopinavir/ritonavir
1	Tenofovir	Emtricitabine	Atazanavir
1	Zidovudine	Lamivudine	Nevirapine
1	Zidovudine	Lamivudine	Didanosine
1	Zidovudine	Lamivudine	
1	Efavirenz	Lopinavir/ritonavir	Enfuvirtide

placenta [23]. Of 15 women treated during pregnancy, the regimen was suboptimal in four patients, taking into account the historical period of reference and the guidelines that were current at that time (Table 3).

The next link in the MTCT chain is delivery. In our study, 11 of 34 women with known HIV infection did not have a caesarean section performed, although this is recommended for all women with HIV infection (or for those with RNA levels that are unknown or > 1000 copies/mL) [24,25]. Also, 18 of 34 women with known HIV infection did not receive intravenous intrapartum ZDV, and eight of their newborns did not receive ART prophylaxis. ZDV has been approved by the United States Food and Drug Administration since 2004 for the prevention of HIV transmission at different time-points in pregnancy, including intravenous ZDV during labour and syrup administration to babies.

Postnatal therapies were inadequate in almost all newborns in our cohort, representing another missed opportunity. In the past, the use of ART in the postnatal period was considered prophylaxis, but more recently physicians have begun to identify newborns at the highest risk of HIV acquisition and to initiate combination ART [26].

Finally, nine of the 34 women with known HIV infection in this study breast-fed their babies. Failure to avoid breast feeding represents another missed opportunity for prevention of MTCT, especially in Italy, where infant formula is free for all HIV-infected mothers [12]. The last important point that arose from our data is that, in addition to losing the opportunity to prevent HIV infection transmission, the opportunity to diagnose many children early was also lost, as 27 of them were diagnosed only at AIDS occurrence and six after > 1 year of life. A delay in HIV diagnosis can greatly influence a child's prognosis and impact on early treatment [27].

In 2017, the Ministry of Health released The National AIDS Plan which details principles, priorities and actions to guide the national response to the HIV epidemic [28].

This action plan was necessary, because the following issues remain unresolved. First, alarmingly, the rate of transmission of HIV infection in Italy in recent years has not diminished, with the number of new infections per year remaining stable at around 4000. Secondly, prevention and treatment of HIV infection need to be improved. In The National AIDS Plan, in the section on ways to improve control of the HIV epidemic in Italy, there is a chapter dedicated to MTCT. The provision of mandatory screening at the beginning of pregnancy and the implementation of multidisciplinary management protocols are measures that should be implemented immediately [29].

In conclusion, all women should be aware of the importance of HIV testing and consider it when planning a pregnancy. In this work, we included only missed diagnoses that caused newborn infections, but we can hypothesize that the global number of women who do not receive a diagnosis during pregnancy, and thus miss the opportunity for early treatment, is even greater. The alarming number of missed opportunities in Italy suggests that, to achieve zero transmission, it will be necessary to increase the use of diagnostic tests, improve clinical management of pregnant women at risk of HIV infection, and use ART more appropriately.

Acknowledgements

The principal investigators and sites participating in the Italian Register for HIV Infection in Children are listed in the Appendix.

Conflicts of interest: The authors have no conflicts of interest to declare.

Financial disclosure: There were no sources of funding for this work.

References

- 1 Grignolo S, Agnello R, Gerbaldo D *et al.* Pregnancy and neonatal outcomes among a cohort of HIV-infected women in a large Italian teaching hospital: a 30-year retrospective study. *Epidemiol Infect* 2017; **145**: 1658–1669.
- 2 Preventing Mother-to-Child Transmission of HIV. U.S. Department of Health and Human Services. Available at <https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/20/50/preventing-mother-to-child-transmission-of-hiv> (accessed 16 May 2017).
- 3 Ishikawa N, Dalal S, Johnson C *et al.* Should HIV testing for all pregnant women continue? Cost-effectiveness of universal antenatal testing compared to focused approaches across high to very low HIV prevalence settings. *J Int AIDS Soc* 2016; **19**: 21212.

- 4 Elimination of Mother-to-child Transmission (EMTCT) of HIV and Syphilis. Global Guidance on Criteria and Processes for Validation. World Health Organization. Available at <http://www.who.int/hiv/pub/emtct-validation-guidance/en/> (accessed 16 June 2014).
- 5 Global Health Sector Strategy on HIV 2016–2021 Towards Ending AIDS. World Health Organization. Available at http://www.who.int/hiv/pub/who_hiv_2016.24.pdf?ua=1 (accessed June 2016).
- 6 Notiziario dell'Istituto Superiore di Sanità, 2015. Available at http://old.iss.it/binary/ccoa/cont/NotCOA2017_dati2016.pdf
- 7 Chiappini E, Galli L, Lisi C *et al.* Risk of perinatal HIV infection in infants Born in Italy to immigrant mothers. *Clin Infect Dis* 2011; **53**: 310–313.
- 8 Matos VT, Oliveira AL, Santos ER, Alencar SK, Fabbro MM. Missed opportunities for prevention of perinatal HIV infection. *Braz J Infect Dis* 2015; **19**: 554–555.
- 9 Camacho-Gonzalez AF, Kingbo MH, Boylan A, Eckard AR, Chahroudi A, Chakraborty R. Missed opportunities for prevention of mother-to-child transmission in the United States. *AIDS* 2015; **29**: 1511–1515.
- 10 Gravidanza fisiologica, aggiornamento 2011. Italian Ministry of Health, Istituto Superiore di Sanità (ISS), 2011. Available at http://www.salute.gov.it/imgs/C_17_pubblicazioni_1436_a_llegato.pdf
- 11 Antinori A, Di Biagio A, Marcotullio S *et al.* Italian guidelines for the use of antiretroviral agents and the diagnostic-clinical management of HIV-1 infected persons. Update 2016. *New Microbiol* 2017; **40**: 86–98.
- 12 Linee Guida Italiane sull'utilizzo dei farmaci antiretrovirali e sulla gestione diagnostico-clinica delle persone con infezione da HIV-1 2016. Italian Society of Infectious and Tropical Diseases (SIMIT), 2016. Available at <http://www.simit.org/medias/1047-ig-hiv-2016-c17pubblicazioni2545allegato.pdf>.
- 13 Ripartizione delle risorse finanziarie destinate alla realizzazione delle strutture sanitarie per l'attività libero-professionale intramuraria, ai sensi dell'art. 1 del D.Lgs. 28 luglio 2000, n. 254/2001. Italian Ministry of Health, June 08, 2001. Available at www.salute.gov.it/imgs/C_17_normativa_1168_allegato.pdf
- 14 Italian Multicentre Study Epidemiology, clinical features, and prognostic factors of paediatric HIV infection. *Lancet* 1988; **2**: 1043–1046.
- 15 1994 Revised Classification System for Human Immunodeficiency Virus Infection in Children Less Than 13 Years of Age. Centers for Diseases Control and Prevention (CDC), 1994. Available at <https://www.cdc.gov/mmwr/previww/mmwrhtml/00032890.htm>
- 16 Jiménez de Ory S, González-Tomé MI, Fortuny C *et al.* New diagnoses of human immunodeficiency virus infection in the Spanish pediatric HIV Cohort (CoRISpe) from 2004 to 2013. *Medicine* 2017; **96**: e7858.
- 17 Frange P, Chaix ML, Veber F, Blanche S. Missed opportunities for HIV testing in pregnant women and children living in France. *Pediatr Infect Dis J* 2014; **33**: e60–e62.
- 18 French CE, Thorne C, Byrne L, Cortina-Borja M, Tookey PA. Presentation for care and antenatal management of HIV in the UK, 2009–2014. *HIV Med* 2017; **18**: 161–170.
- 19 Trepka MJ, Mukherjee S, Beck-Sague C *et al.* Missed opportunities for preventing perinatal transmission of human immunodeficiency virus, Florida, 2007–2014. *South Med J* 2017; **110**: 116–128.
- 20 Assistenza alla gravidanza e al parto fisiologico - Linee guida di riferimento Nazionali. Italian Society of Gynecology and Obstetrics (SIGO). Available at: http://www.sigo.it/wp-content/uploads/2015/10/gravid_parto_11.pdf
- 21 World Health Organization. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendation for a Public Health Approach. Kuala Lumpur, Malaysia, 2013.
- 22 Grignolo S, Bruzzone B, Gabbi L *et al.* Vaginal HIV-1 shedding among HIV-1 infected women in the current era of combined antiretroviral therapy: a cross sectional study. *Virulence* 2017; **8**: 101–108.
- 23 Buckoreelall K, Cressey TR, King JR. Pharmacokinetic optimization of antiretroviral therapy in pregnancy. *Clin Pharmacokinet* 2012; **51**: 639–659.
- 24 European Mode of Delivery Collaboration. Elective caesarean-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. *Lancet* 1999; **353**: 1035–1039.
- 25 Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. Available at <http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf> (accessed 10 January 2019).
- 26 Andiman W, Bryson Y, de Martino M *et al.* The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1 a meta-analysis of 15 prospective cohort studies. *N Engl J Med* 1999; **340**: 977–987.
- 27 Feucht UD, Meyer A, Thomas WN, Forsyth BW, Kruger M. Early diagnosis is critical to ensure good outcomes in HIV-infected children: outlining barriers to care. *AIDS Care* 2016; **28**: 32–42.
- 28 Ministry of Health. Piano Nazionale AIDS. Rome, Italy 2017. Available at: www.salute.gov.it/imgs/C_17_pubblicazioni_2655_allegato.pdf.
- 29 Floridia M, Masuelli G, Tamburrini E *et al.* Pregnant with HIV before age 25: data from a large national study in Italy, 2001–2016. *Epidemiol Infect* 2017; **145**: 2360–2365.

Appendix 1

The principal investigators of The Italian Register for HIV Infection in Children, by site, are: Patrizia Osimani (Ancona), Domenico Larovere (Bari), Maurizio Ruggeri (Bergamo), Andrea Pession, Giacomo Faldella (Bologna), Francesca Capra, Sara Pulcini, Valentina Zattoni, Laura Dotta (Brescia), Antonia Aliffi (Catania), Elisa Anastasio (Catanzaro), Elisa Fiumana (Ferrara), Elena Chiappini, Paola Gervaso, Carlotta Montagnani, Maurizio De Martino, Luisa Galli (Florence), Antonio Di Biagio, Lucia Taramasso, Claudio Viscoli (Genoa), Paola Erba, GianVincenzo

Zuccotti, Annarita Benincaso, Filippo Salvini, Rita Lipreri, Susanna Esposito, Anna Plebani, Claudia Tagliabue (Milan), Francesca Giubbarelli (Modena), Emanuele Nicastro, Andrea Lo Vecchio, Wilma Buffolano, Maura Agnese (Naples), Amelia Romano, Saitta Marcello (Palermo), Carlo Giaquinto, Osvalda Rampon, Martina Pennazzato (Padua), Rita Consolini (Pisa), Icilio Dodi (Parma), Domenico Zanaboni (Pavia), Orazio Genovese, Paolo Palma, Giuseppe Pontrelli, Hyppolite Tchidjou (Rome), Antonio Mazza (Trento), Pier Angelo Tovo, Erika Silvestro, Silvia Virano (Turin), Vincenzo Portelli (Trapani) and Antonio Pellegatta (Varese).