# *infezione da HIV e gravidanza:*

## *c'è ancora qualcosa da dire?*

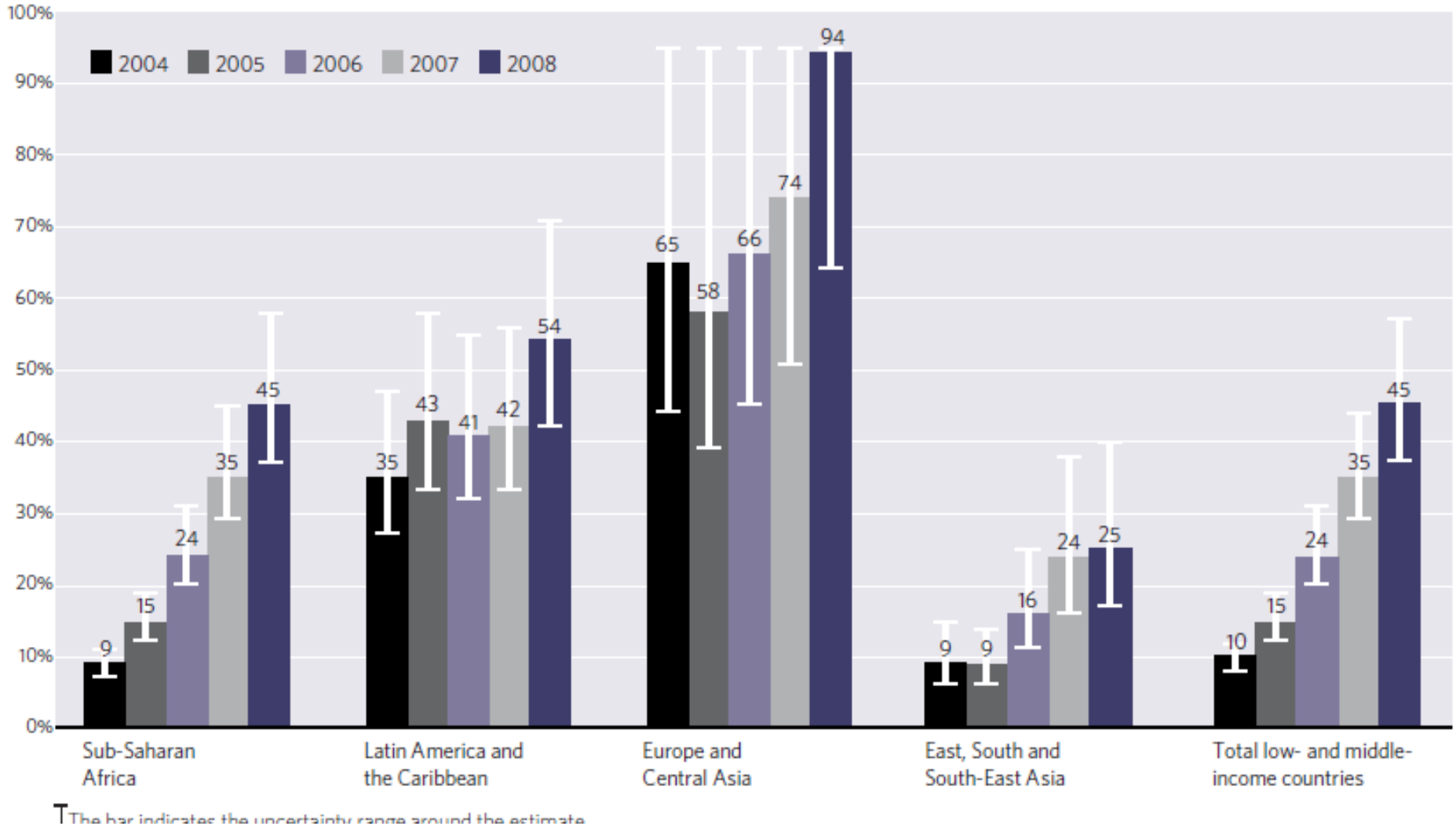
Bologna,18 aprile 2013

anna degli antoni-parma

# UNAIDS GOAL:"VIRTUAL" ELIMINATION MTCT by2015

-new pediatric infections reduced by 90% from 2009 level (<40000/year )

-MTCT decrease to <5% worldwide

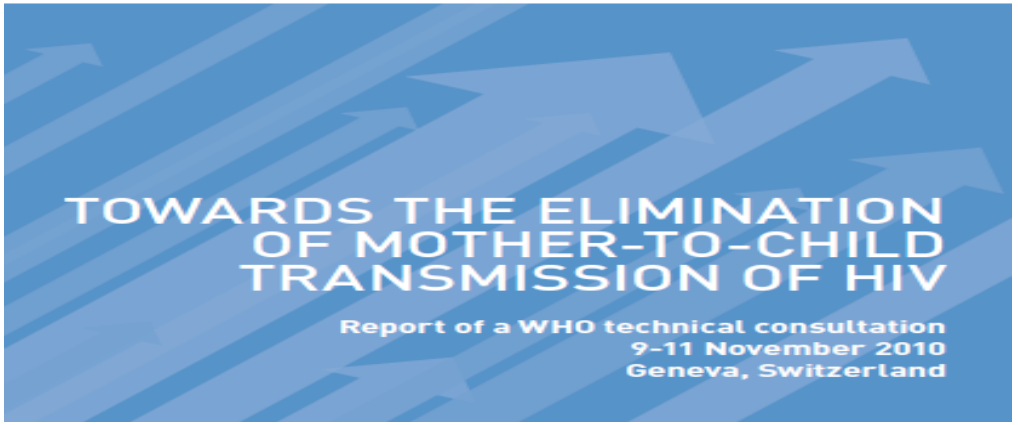



The bar indicates the uncertainty range around the estimate

Source: WHO, UNAIDS, UNICEF. *Towards universal access: scaling up priority HIV/AIDS interventions in the health sector. Progress report 2009.* p 99.

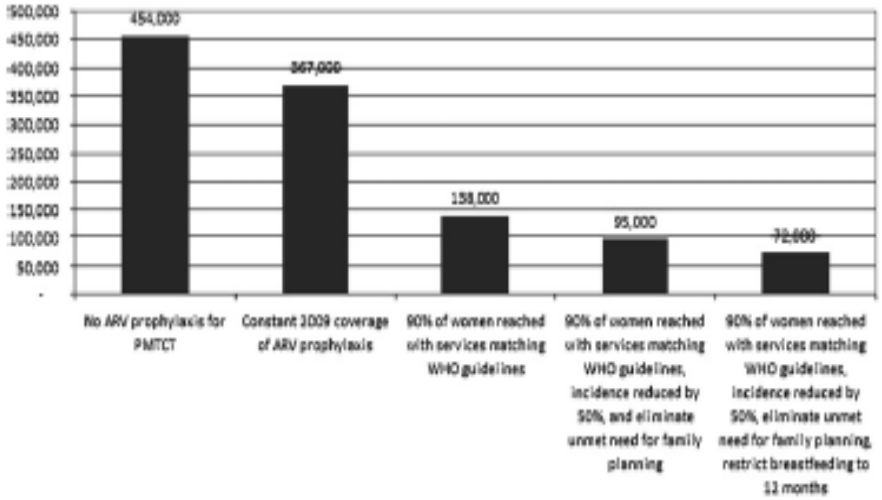
What will it take to achieve virtual elimination of mother-to-child transmission of HIV? An assessment of current progress and future needs

Mary Mahy,[1] John Stover,[2] Karusa Kiragu,[1] Chika Hayashi,[3] Priscilla Akwara,[4] Chewe Luo,[4] Karen Stanecki,[1] Rene Ekpini,[4] Nathan Shaffer[3]




**Ma 8% di riduzione di MTCT e 79% di riduzione nuove infezioni pediatriche**

>90% copertura terapeutica nelle donne gravide, >50% riduzione nuove infezioni nelle giovani donne fra 15-49 anni ed eliminazione al 100% delle esigenze di family planning per tutte le donne



# Contesto attuale

- Mother To Child Trasmission rates <1%

# *Problemi aperti*

**Raccomandazioni conflittuali fra le diverse linee guida, ad esempio:**

- **Uso di efavirenz?**
- **Aggiustamento dei dosaggi dei farmaci sulla base degli studi di farmacocinetica?**
- **Inizio delle terapie in differenti epoche gestazionali?**
- **Gestione delle cariche virali fra 50 e 1000, quale indicazione al parto?**

**FDA categories**

**A:** Adequate and well-controlled studies of pregnant women fail to demonstrate a risk to the fetus

**B:** Animal reproduction studies fail to demonstrate a risk to the fetus, and adequate but well-controlled studies of pregnant women have not been conducted

**C:** Safety in human pregnancy has not been determined; animal studies are either positive for fetal risk or have not been conducted

**D:** Positive evidence of human fetal risk that is based on adverse reaction data from investigational or marketing experiences

**X:** Contraindicated

| Antiretroviral drug | FDA pregnancy classification |
|---|---|
| Atazanavir* | B |
| Nelfinavir | B |
| Ritonavir | B |
| Saquinavir | B |
| Maraviroc | B |
| Nevirapine | B |
| Darunavir | C |
| Fosamprenavir | C |
| Indinavir | C |
| Lopinavir/r | C |
| Tipranavir | C |
| Raltegravir | C |
| Zidovudine | C |
| Efavirenz** | D |

*ATV/r use may be considered during pregnancy only if potential benefit justifies the potential risk2

**EFV is not recommended for treatment during pregnancy according to the EU Smpc

1. Public Health Service Task Force Perinatal GL 2009. Available at: http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf Accessed March 2011

| | DHHS guidelines | BHIVA guidelines | WHO guidelines |
|---|---|---|---|
| Antiretroviral therapy: efavirenz | Not recommended first trimester but if a woman is on it don't switch if this is likely to compromise virological control | No evidence for teratogenicity | Efavirenz-based regimens should not be initiated during first trimester of pregnancy. Efavirenz is listed as one of the preferred agents as a component of triple therapy for antiretroviral naive women in need of treatment for their own health. If a woman is on efavirenz and pregnancy recognized in first 28 days it should be stopped and substituted with nevirapine or a protease inhibitor, if pregnancy recognized after 28 days continue the efavirenz. |
| Therapeutic drug monitoring (TDM) | Increase lopinavir/ritonavir second and third trimester especially if protease inhibitor experienced | Routine dose alteration not recommended | No recommendations |
| | Increase atazanavir dose if antiretroviral experienced and also on tenofovir or a H2 antagonist | Consider TDM third trimester if on atazanavir and tenofovir | |
| | Darunavir should be dosed twice daily | Darunavir should be dosed twice daily | |
| Mode of delivery | Vaginal birth if maternal viral load <1000 copies/ml | Vaginal birth if maternal viral load <50 copies/ml | No recommendations |
| Intrapartum zidovudine | Recommended in all women if viral load >400 copies/ml | Recommended if viral load >10 000 copies/ml | Recommended with lamivudine (intrapartum and 7 days postpartum tail) to reduce nevirapine drug resistance among mothers and infants who receive single dose nevirapine at labour and birth |
| Duration of antiretroviral prophylaxis in the exposed neonate | 6 weeks | 4 weeks | 4–6 weeks (this may be extended in breastfeeding infants whose mother's do not continue treatment) |
| Number of antiretroviral agents for neonate if mother has detectable viral load at time of delivery | 2 drugs | 3 drugs | No recommendations |
| *Pneumocystis jirovecii* pneumonia | From 6 weeks unless adequate test information to exclude HIV infection in the neonate | Only recommended in high risk infants from four weeks (for example if viral load unknown or >1000 copies/ml) | No recommendations |

## *BHIVA pregnancy Guidelines 2012*

- Tenofovir plus emtricitabine, abacavir plus lamivudine or zidovudine plus lamivudine are acceptable nucleoside backbones
- The **third agent** in HAART **should be efavirenz** or nevirapine (if the CD4 count is <250 cells/μL) or a boosted PI

HIV Medicine(2012), **13** (Suppl.2), 87-157

# CROI 2013

**Paper #81**

## Birth Defects and ART in the French Perinatal Cohort, a Prospective Exhaustive Study among 13,124 Live Births from 1994 to 2010

Jeanne Sibiude*[1], L Mandelbrot[1,2,3], S Blanche[4], J Le Chenadec[3,5], N Boullag-Bonnet[3], A Faye[2,6], C Dollfus[7], R Tubiana[8], B Khoshnood[9], J Warszawski[3,5,10], and ANRS CO1/CO10/CO11

[1]Hosp Louis Mourier, Colombes, France; [2]Univ Diderot Paris 7, Paris, France; [3]CESP, INSERM U1018, Le Kremlin-Bicetre, France; [4]Hosp Necker, EA 3620, Univ Paris Descartes 5, Paris, France; [5]INED, Paris, France; [6]Hosp Robert Debre, Paris, France; [7]Hosp Trousseau, Paris, France; [8]Hosp Pitie Salpetriere, INSERM U943, Paris, France; [9]INSERM, UMR S953, Univ Paris-6, Paris, France; and [10]Univ Paris Sud, Le Kremlin-Bicetre, France

**Background:** The use of ARV regimens during pregnancy has led to a spectacular decrease in MTCT, now on the order of 1% in industrialized countries. Potential adverse effects including teratogenic risk have to be evaluated. We aimed to estimate the prevalence of birth defects in children born to HIV$^+$ women receiving ARV during pregnancy, and to assess the association with each *in utero* ARV drug.

**Methods:** Since 1986, the French Perinatal Cohort (EPF) prospectively enrolls pregnant HIV$^+$ women delivering in 90 centers throughout France. Children are followed by pediatricians until 2 years of age. All live births between 1994 and 2010 were included. We excluded patients not treated during pregnancy. Birth defects were studied using both the EUROCAT and the MACDP classifications, and associations with ARV were evaluated using univariate and multivariate logistic regressions.

**Results:** We included 13,124 livebirths. The prevalence of birth defects was 4.4% % (95% confidence interval [CI] 4.0-4.7; n = 575), according to EUROCAT and 7.0% (6.5-7.4; n = 914), according to the MACDP classification, which included minor defects when 2 were present in the same child. A significant association was found between exposure to efavirenz in the first trimester and neurological defects (adjusted odds ratio [aOR] = 3.15 [1.09-9.09]). Zidovudine in the first trimester was associated with congenital heart defects (aOR = 2.34 [1.39-3.94]), and didanosine with head and neck birth defects (aOR = 2.89 [1.03-8.11]). Lamivudine and indinavir in the first trimester were also associated with birth defects, but the association with lamivudine concerned mostly minor musculo-skeletal and head and neck defects, while indinavir was not associated with any specific defects in the multivariate analysis adjusting for potential confounding variables and concomittant medications.

**Conclusions:** This study, which is the largest prospective study of birth defects in ARV-exposed infants, shows a specific association between *in utero* exposure to efavirenz and neurological defects. As in other cohort studies, the rate of birth defects may be underestimated by including only live births. Recently, WHO and US Department of Health and Human Services guidelines have been changed to authorize the use of efavirenz even in the first trimester in women already treated with this drug. The association we observed between efavirenz and neurological defects has been previously described and calls for caution and continued follow-up.

# *Terapia antiretrovirale nelle donne già in trattamento al concepimento*

Idealmente, il regime in atto al concepimento dovrebbe essere stato selezionato in epoca preconcezionale secondo criteri che ne assicurino la sicurezza d'uso in gravidanza, in maniera tale che non sia necessario modificarlo o interromperlo nelle prime settimane di gestazione per motivi di sicurezza. Nel prescrivere alle donne in età fertile farmaci potenzialmente teratogeni (es. efavirenz) la possibilità di una gravidanza non pianificata. Nelle donne in trattamento antiretrovirale in cui insorga una gravidanza non pianificata, il regime andrà rivalutato il più precocemente possibile in funzione della sua sicurezza d'uso in gravidanza [AII]. Le donne che si trovano all'inizio di

| | |
|---|---|
| **Efavirenz** | L'uso di efavirenz è stato associato ad un rischio malformativo in studi sulle scimmie, e casi sporadici di difetti del tubo neurale sono stati descritti in neonati esposti ad efavirenz durante il primo trimestre. Recenti studi di metanalisi e i dati dei registri di sorveglianza non indicano per l'esposizione ad EFV nel primo trimestre di gravidanza un rischio complessivo di difetti congeniti significativamente superiore a quello degli altri antiretrovirali. Nella prescrizione di efavirenz alle donne in età fertile, si raccomanda di fornire informazioni sui potenziali rischi connessi al suo uso in gravidanza, e di utilizzare farmaci alternativi nelle donne con progetto di gravidanza, in quelle con mancanza di utilizzo o rifiuto di metodi contraccettivi adeguati ed in quelle che iniziano terapia antiretrovirale prima che siano trascorse sei settimane dal concepimento (8ª settimana di gravidanza) [AIII]. Nelle donne in cui si verifica gravidanza in corso di trattamento con EFV, una eventuale modifica cautelativa del trattamento dovrà tenere conto della lunga emivita del farmaco ed essere congrua con l'epoca di sensibilità al difetto specifico, considerando che la chiusura del tubo neurale avviene entro la quinta-sesta settimana dal concepimento. Qualora il farmaco sia già presente in un regime in atto al concepimento con soppressione completa della carica virale, si sia superata la sesta settimana dal concepimento (8° settimana di gravidanza) e non siano presenti significativi fenomeni di tossicità, la sua prosecuzione può essere considerata. |

| | DHHS guidelines | BHIVA guidelines | WHO guidelines |
|---|---|---|---|
| Antiretroviral therapy: efavirenz | Not recommended first trimester but if a woman is on it don't switch if this is likely to compromise virological control | No evidence for teratogenicity | Efavirenz-based regimens should not be initiated during first trimester of pregnancy. Efavirenz is listed as one of the preferred agents as a component of triple therapy for antiretroviral naive women in need of treatment for their own health. If a woman is on efavirenz and pregnancy recognized in first 28 days it should be stopped and substituted with nevirapine or a protease inhibitor, if pregnancy recognized after 28 days continue the efavirenz. |
| Therapeutic drug monitoring (TDM) | Increase lopinavir/ritonavir second and third trimester especially if protease inhibitor experienced<br>Increase atazanavir dose if antiretroviral experienced and also on tenofovir or a H2 antagonist<br>Darunavir should be dosed twice daily | Routine dose alteration not recommended<br>Consider TDM third trimester if on atazanavir and tenofovir<br>Darunavir should be dosed twice daily | No recommendations |
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| *Pneumocystis jirovecii* pneumonia | From 6 weeks unless adequate test information to exclude HIV infection in the neonate | Only recommended in high risk infants from four weeks (for example if viral load unknown or >1000 copies/ml) | No recommendations |

**ATV/r 300 mg/100 mg ***

**In Pregnancy**

**In combination with TDF or H2-receptor antagonist** → **ATV/r 400 mg/100 mg ***

**may be considered**

- TDM **may be** considered to ensure adequate exposure*
- ATV/r is not recommended in combination with both TDF and H2-receptor antagonist

**ATV/r 300 mg/100 mg**

**Postpartum**

Atazanavir SmPC. *Available at http://www.ema.europa.eu Accessed December 2011

# *BHIVA PREGNANCY Guidelines 2012*
# *Antiretroviral treatment*

- **Darunavir (which should be dosed twice daily) is the only adult-dose ARV that should have a dose alteration during pregnancy**
- **Consider third trimester TDM, particularly if combining tenofovir and atazanavir or if using a non-standard dose of ARV or darunavir**

# TDM Farmaci

***Monitoraggio dei livelli plasmatici di farmaco***

***In generale, il monitoraggio dei livelli plasmatici di farmaco (TDM) non è raccomandato in tutte le gravide con HIV in trattamento, ma andrebbe considerato in situazioni particolari (es.: patologie o trattamenti concomitanti in grado di interferire significativamente con il metabolismo, farmaci o regimi particolari richiesti da indicazione materna per i quali non si dispone di dati in corso di gravidanza, tossicità o inefficacia di difficile interpretazione, necessità di definire precisamente i livelli in relazione alla presenza di resistenza o fallimento, ecc.)* [CIII]. *Nonostante per alcuni farmaci sia stata riportata una riduzione dei livelli plasmatici in gravidanza, le evidenze che questa ridotta esposizione abbia conseguenze negative in termini di efficacia sono modeste, particolarmente quando siano utilizzati inibitori della proteasi associati a ritonavir. Per questa classe di farmaci, situazioni terapeutiche particolari in cui considerare monitoraggio dei livelli plasmatici, anche in funzione della situazione di carica virale, sono la somministrazione combinata di atazanavir e tenofovir e l'uso di darunavir in regime di monosomministrazione [17-***

# When should HAART be initiated in pregnancy to achieve an undetectable HIV viral load by delivery?

Phillip J. Read[a], Sundhiya Mandalia[b], Palwasha Khan[c], Ursula Harrisson[b], Claire Naftalin[d], Yvonne Gilleece[d], Jane Anderson[c], David A. Hawkins[b], Graham P. Taylor[e], Annemiek de Ruiter[a], and the London HIV Perinatal Research Group

**Results:** Viral load was less than 50 copies/ml in 292 of 378 pregnancies (77.2%) by delivery. Pretreatment viral load was associated with the time taken, and the proportion achieving a viral load less than 50 copies/ml at ($P \leq 0.001$). When baseline viral load was less than 10 000 copies/ml, gestational age at HAART initiation did not affect success up to 26.3 weeks gestation. When viral load was more than 10 000 copies/ml, deferring HAART past 20.4 weeks reduced the probability of reaching less than 50 copies/ml by delivery ($P = 0.011$). When baseline viral load was more than 100 000 copies/ml the likelihood of reaching a viral load of less than 50 copies/ml was low (37%: hazard ratio 0.31), and dependent on the length of time on HAART. The hazard ratio for a nonnucleoside reverse transcriptase inhibitor regimen achieving a viral load less than 50 copies/ml compared with a protease inhibitor was 0.7 (95% confidence interval 0.52–0.94).

**Conclusion:** With a viral load more than 10 000 copies/ml and especially with a viral load more than 100 000 copies/ml, the probability of achieving either less than 50 copies/ml by the time of delivery is compromised by delaying initiation of short-term highly active antiretroviral therapy beyond 20.4 weeks gestation. Current UK and other guidelines for when to commence START may therefore limit the chance of vaginal delivery.



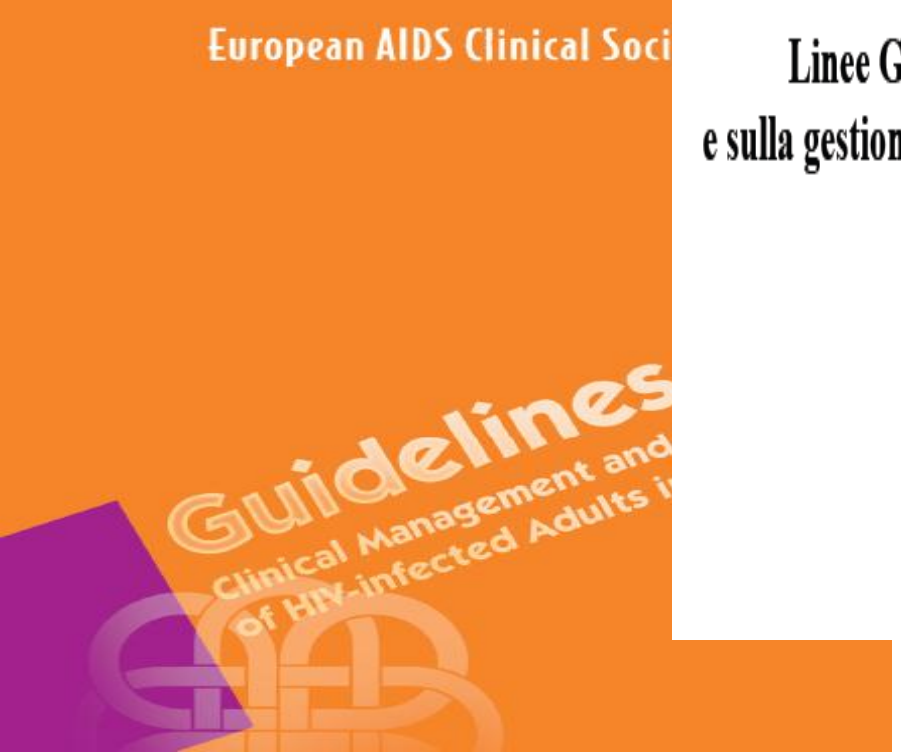
*AIDS* 2012, **26**:1095–1103

| Pretreatment viral load (copies/ml) (N=378) | Percentage, number with <50 copies/ml at delivery | Hazard ratio for <50 copies/ml at delivery (95% CI) | P value | Percentage, number with <50 copies/ml at 36 weeks gestation | Hazard ratio for <50 copies/ml at 36 weeks (95% CI) | P value | Percentage, number with <1000 copies/ml at delivery | Hazard ratio for <1000 copies/ml at delivery (95% CI) | P value |
|---|---|---|---|---|---|---|---|---|---|
| <10 000, N=200 | 91, 182 | 1 | | 80, 159 | 1 | | 98, 195 | 1 | |
| 10 000–<50 000, N=111 | 73, 81 | 0.86 (0.62–1.18) | 0.344 | 60, 67 | 0.85 (0.60–1.21) | 0.365 | 93, 103 | 0.82 | 0.205 |
| 50 000–100 000, N=24 | 54, 13 | 0.68 (0.47–0.98) | 0.038 | 50, 12 | 0.61 (0.41–0.91) | 0.016 | 88, 21 | 0.73 | 0.061 |
| >100 000, N=43 | 37, 16 | 0.31 (0.19–0.50) | <0.001 | 30, 13 | 0.35 (0.20–0.58) | <0.001 | 84, 36 | 0.53 | 0.003 |

| | Weeks gestation at initiation on HAART (quartiles, n=378) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | <20.4 | | | 20.4–23.3 | | | 23.4–26.3 | | | >26.3 | | |
| Baseline VL (copies/ml) | N | Percentage with <50 copies/ml | HR | N | Percentage with <50 copies/ml | HR | N | Percentage with <50 copies/ml | HR | N | Percentage with <50 copies/ml | HR |
| <10 000 | 35 | 97 | 1 | 54 | 93 | 0.86 | 56 | 94 | 1.18 | 55 | 82 | 1.43 |
| 10 000–50 000 | 28 | 82 | 0.61* | 32 | 78 | 0.51* | 25 | 64 | 0.39* | 26 | 65 | 0.6* |
| 50 001–100 000 | 11 | 72 | 0.26* | 3 | 33 | 0.12* | 6 | 66 | 0.53 | 4 | 0 | n/a |
| >100 000 | 22 | 55 | 0.2* | 7 | 29 | 0.1* | 6 | 33 | 0.12* | 8 | 0 | n/a |

# Modalità di parto

**Non tutti la pensano allo stesso modo**




Linee Guida Italiane sull'utilizzo dei farmaci antiretrovirali
e sulla gestione diagnostico-clinica delle persone con infezione da HIV-1

*Luglio 2012*

Su mandato del *Ministro della Salute*

BHIVA Pregnancy Guidelines 2012

**Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents**

Developed by the HHS Panel on Antiretroviral G
Adults and Adolescents – A Working Group
Office of AIDS Research Advisory Council (

# Caesarean section

Issued: November 2011

NICE clinical guideline 132

www.nice.org.uk/cg132

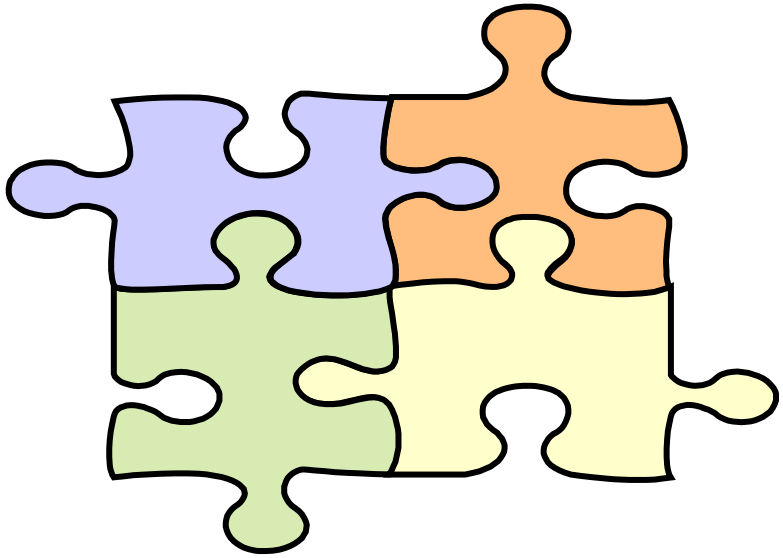
| | | | |
|---|---|---|---|
| DHHS | CS se VL>1000 o non HART | Se VL<1000 si può fare il vaginale | |
| EACS | CS se VL>50 | **Vaginale** se <50 alla 34-36 sett | Incerto il beneficio di AZT ev se VL<50 e HART |
| ITALIA | CS se VL>50 | **Si può** fare il vaginale se VL<50 o NR | Come EACS |
| BHIVA | CS se VL>50 o AZT monoterapia | **Vaginale** se VL <50 in HART | Come EACS |
| NICE | CS se VL>400 o no HART | **No CS** se VL<50 o <400 in HART | |

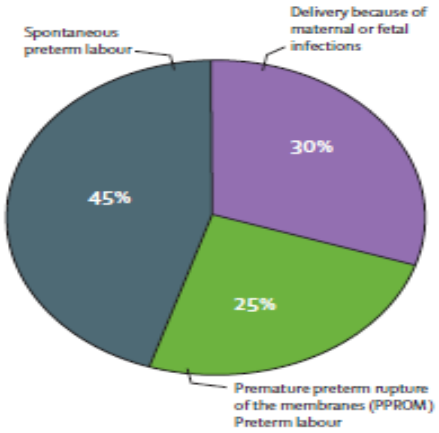
# *Parto Pretermine*

È quello che avviene <37 settimana

USA=12-13%

Europa=5-9%



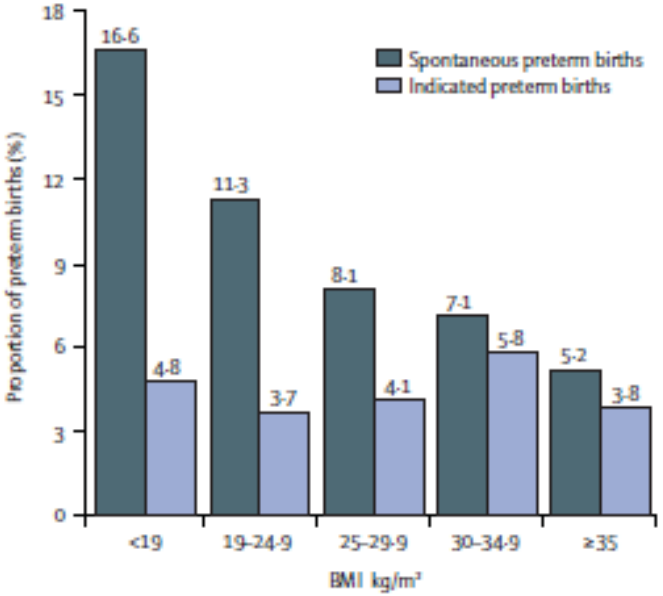


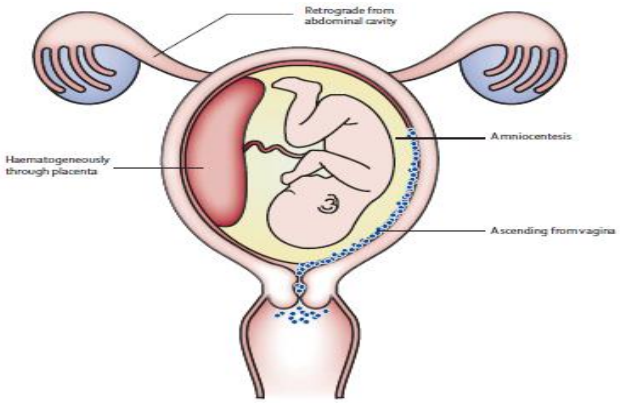

A New Piece in the Puzzle of Antiretroviral Therapy in Pregnancy and Preterm Delivery Risk

**Claire Thorne and Claire L. Townsend**

MRC Centre of Epidemiology for Child Health, UCL Institute of Child Health, University College London, United Kingdom

# Preterm births:causes




- Events leading to preterm birth are incompletely understood
- Multiple pathways include inflammation / infection, maternal / fetal stress, abnormal uterine distension, bleeding, others
- Risk factors include:

  socio-economic factors, maternal smoking, illicit drug use, maternal age, multiple gestations, maternal BMI, previous PTD, intrauterine infection, bacterial vaginosis

Goldenberg et al.Lancet 2008

# HART e parto pretermine ( PTD )

- **Preoccupazioni riguardo al parto pretermine nelle donne HIV+ sono state sollevate più di 20 anni fa (influenza di HIV e immunodepressione sull'esito della gravidanza )**
- **Dal 1996 utilizzo di una terapia combinata ( cART/HART )**
- **Primo report di una correlazione fra PTD e la terapia di combinazione nel 1998 ( case series Svizzera )**

# Rischio aumentato di PTD associato alla HART

- **In seguito numerosi studi ( soprattutto europei ma alcuni anche dagli US e altri paesi ) hanno riportato questi dati**

**- associazione con aumento del rischio da 1,5 a 3,5 volte**

**- dati aggiustati per molti ( ma non tutti ) i confounders (**accesso alla cura, condizioni socioeconomiche, storia ostetrica, cure per infertilità, BMI, fumo **)**

**-alcuni studi hanno trovato associazione solo con una HART PI-based**

European Collaborative Study (ECS) and Swiss MoCHiV 2000; ECS 2004; Cotter et al, 2006 (USA); Boer et al, 2007 (Netherlands); Schulte et al, 2007 (USA); Townsend et al, 2007 (UK and Ireland); Ravizza et al 2007 (Italy); Grosch-Wörner et al, 2008 (Germany/Austria)

# Nessuna associazione fra HART e PTD

- **Tuomala et al,2002 ( USA )**
- **Tuomala et al,2005 ( USA )**
- **Szyld et al,2006 (Latino America/Caribe)**
- **Patel et al,2010 (USA )**
- **Meta analisi di Kourtis, AIDS 2007, che include studi fino al 2006, HART non associata a rischio aumentato di PTD, OR 1.01( 95%, CI 0.8, 1.3 )**

# PTD e PI-based HART:Mma Bana study

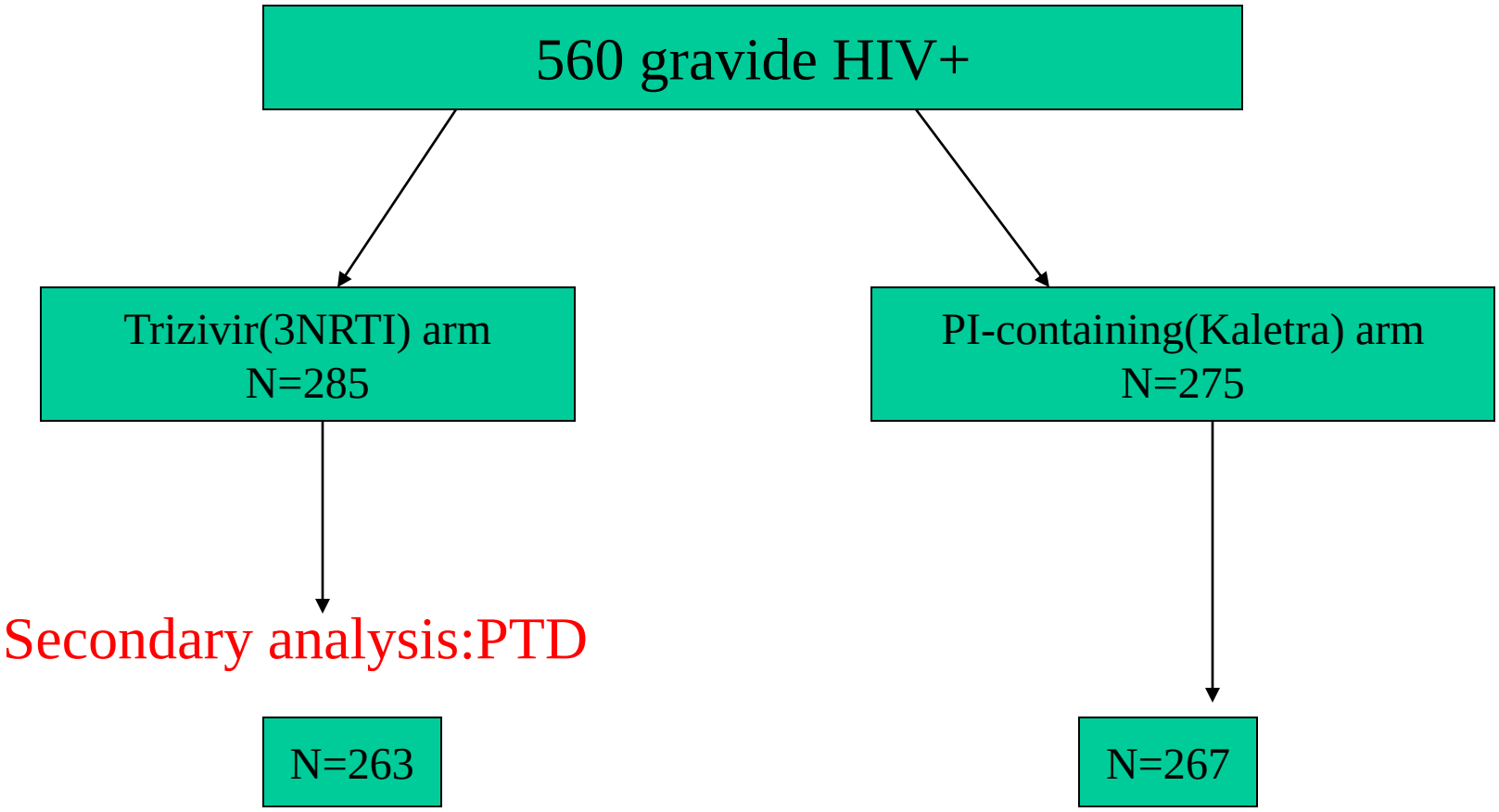
- **Trial clinico randomizzato in Botswana**
- **Confronto fra PI-based HART e triplice NRTI profilassi in PTMCT**
- **Tasso complessivo di MTCT 1.1%**

- **Analisi secondaria:valutare fattori di rischio per PTD**

  **-tutte le donne avevano CD4>=200/mmc**

**Powis et al,JID2011**

# Disegno dello studio




Esclusi nati morti, gemelli, TC in urgenza pretermine

HART dalla 26-34 sett e fino a 6 mesi dopo

# Risultati

Tasso significativamente maggiore di PTD nel braccio PI ( **21,8%)** che nel braccio 3NRTI(**11,8%**)

Non associazione fra PTD e conta dei CD4, VL, età, istruzione, età gestazionale all'inizio della HART

Il tipo di HART e il reddito materno significativamente associati al rischio di PTD

-PI-HART associata a rischio 2 volte maggiore ( **OR2.03, 95% CI 1.26-3.27**) rispetto al regime NRTI

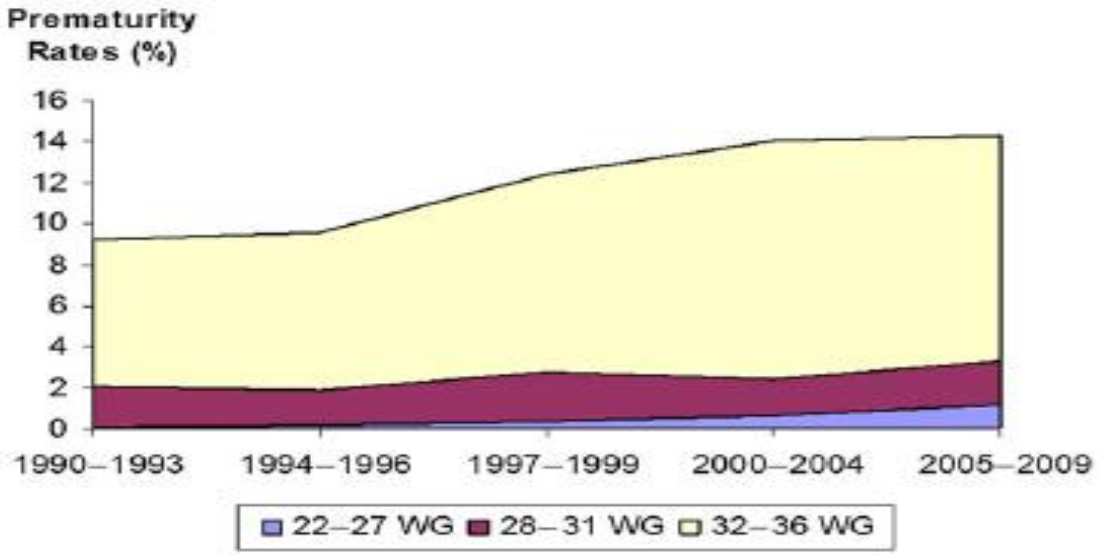
-Donne **con un reddito** rischio significativamente minore rispetto a quelle senza reddito

-nell'analisi aggiustata per il reddito, AOR per la PI-HART=**2.02**(95%,CI1.26-3.27)

# Premature Delivery in HIV-Infected Women Starting Protease Inhibitor Therapy During Pregnancy: Role of the Ritonavir Boost?

Jeanne Sibiude,[1,2] Josiane Warszawski,[1,10,11] Roland Tubiana,[4,5] Catherine Dollfus,[6] Albert Faye,[3,7] Christine Rouzioux,[8,9] Jean-Paul Teglas,[1] Dieudonné Ekoukou,[12] Stéphane Blanche,[8,9] and Laurent Mandelbrot[1,2,3]

*Results.* Prematurity increased from 9.2% during 1990–1993 (no therapy) and 9.6% during 1994–1996 (mostly zidovudine monotherapy) to 12.4% during 1997–1999 (dual-nucleoside analog therapy) and 14.3% during 2005–2009 (routine cARV therapy; $P < .01$). Prematurity was associated with cARV therapy, compared with zidovudine monotherapy, with an adjusted odds ratio of 1.69 (95% confidence interval [CI], 1.38–2.07;




CID 2012;54 (1 May)

| | Premature Birth | | Bivariable Analysis (n = 1253) | | | Multivariable Analysis (n = 945) | | |
|---|---|---|---|---|---|---|---|---|
| Variable | % | No./Total Sample | HR | (95% CI) | *P* | aHR | (95% CI) | *P* |
| Pretherapeutic viral load, copies/mL | | | | | .34 | | | .60 |
| <400 | 11.9 | (19/159) | 1 | | | 1 | | |
| 400–10 000 | 12.6 | (58/460) | 1.05 | (.63–1.77) | | 1.31 | (.69–2.48) | |
| 10 000–50 000 | 12.7 | (43/338) | 1.06 | (.62–1.81) | | 1.40 | (.72–2.71) | |
| >50 000 | 17.6 | (29/165) | 1.52 | (.85–2.72) | | 1.62 | (.8–3.3) | |
| Missing | 16.0 | (21/131) | | | | | | |
| Time of first-line initiation of ARV, gestational weeks | | | | | .18 | | | .23 |
| <14 | 10.2 | (15/147) | 1 | | | 1 | | |
| 14–20 | 13.9 | (37/267) | 1.38 | (.76–2.51) | | 1.49 | (.67–3.3) | |
| 21–27 | 16.4 | (87/529) | 1.64 | (.95–2.83) | | 1.85 | (.87–3.94) | |
| ≥28 | 8.90 | (26/292) | 0.85 | (.45–1.6) | | 0.96 | (.4–2.29) | |
| Ritonavir-boosted PI[a] | | | | | .04 | | | .03 |
| No | 9.1 | (17/187) | 1 | | | 1 | | |
| Yes | 14.4 | (153/1066) | 1.78 | (1.03–3.09) | | 2.03 | (1.06–3.89) | |

| Complication | Total | | Boosted PI | | Nonboosted PI | | *P* |
|---|---|---|---|---|---|---|---|
| | % | No./Total Sample | % | No./Total Sample | % | No./Total Sample | |
| Preeclampsia | 1.9 | 24/1240 | 2.2 | 23/1054 | 0.5 | 1/186 | .24 |
| Gestational diabetes | 2.7 | 33/1237 | 2.9 | 30/1050 | 1.6 | 3/187 | .46 |
| Vascular or metabolic problem | 6.3 | 77/1244 | 6.8 | 71/1037 | 3.2 | 6/187 | .06 |
| Liver enzyme elevation (grade ≥1) | 12.7 | 150/1183 | 13.7 | 138/1005 | 6.7 | 12/178 | .01 |
| Bleeding | 2.4 | 30/1232 | 2.5 | 26/1045 | 2.1 | 4/187 | 1.00 |
| Hospitalization (any cause) | 26.0 | 300/1155 | 28.3 | 277/980 | 13.1 | 23/175 | <.001 |
| Premature labor[a] | 5.1 | 59/1155 | 5.6 | 55/980 | 2.3 | 4/175 | .003 |
| Vascular or metabolic problem[a] | 4.3 | 51/1155 | 4.8 | 47/980 | 2.3 | 4/175 | |
| Infection or fever[a] | 3.1 | 36/1155 | 3.5 | 34/980 | 1.1 | 2/175 | |
| Anomalies of FHR[a] | 1.7 | 20/1155 | 1.9 | 19/980 | 0.6 | 1/175 | |
| Other[a] | 11.6 | 134/1155 | 12.4 | 122/980 | 6.9 | 12/175 | |
| Type and classification of preterm births (n = 170) | | | | | | | |
| Spontaneous premature birth | 8.2 | 103/1253 | 8.4 | 90/1066 | 7.0 | 13/187 | .05[b] |
| Spontaneous onset of labor | | 51 | | 47 | | 4 | |
| Preterm premature rupture of membranes | | 47 | | 38 | | 9 | |
| Missing | | 5 | | 5 | | 0 | |
| Induced premature birth | 5.0 | 63/1253 | 5.6 | 60/1066 | 1.6 | 3/187 | |
| Preeclampsia and IUGR-associated | | 4 | | 4 | | 0 | |
| Preeclampsia alone | | 13 | | 12 | | 1 | |
| IUGR alone | | 10 | | 10 | | 0 | |
| Anomalies of FHR | | 7 | | 7 | | 0 | |
| Hepatotoxicity | | 4 | | 4 | | 0 | |
| Bleeding | | 5 | | 5 | | 0 | |
| Stillbirth or TOP | | 16 | | 14 | | 2 | |
| Missing | | 4 | | 4 | | 0 | |
| Premature birth type missing | | 4/1253 | | 3/1066 | | 1/187 | |

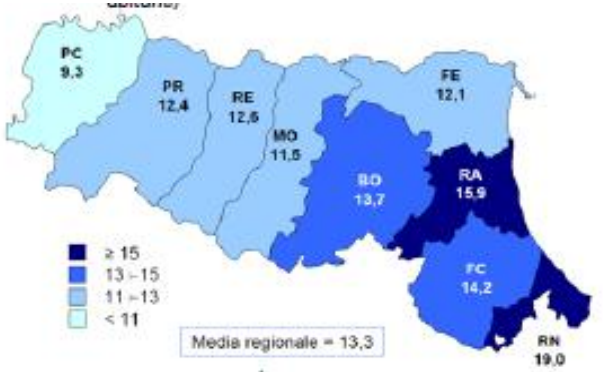
# Possibili meccanismi

- **Immunologici?** Alterazione pattern citochinico gravidico da Th2 a Th1 con aumento IL2?*riduzione IL10?immunoricostituzione?
- **Tossicità da ritonavir?**alterazione asse surrenalico materno e fetale attraverso l'interazione con CYP3A4, azione sul timing del parto?**alterazioni metabolico/vascolari materne ( preeclampsia, diabete, etc ) con aumento complicanze materne e quindi induzione del parto?

*Fiore e Ravizza 2006,**Goldemberg2008

# PC-PR-RE 2010-2013

- PC 12 gravidanze ( 2 in corso )  12 donne
- PR 50 gravidanze ( 3 in corso )  44 donne
- RE 30 gravidanze ( 5 in corso ) 30 donne
- 92 gravidanze in totale, 82 completate negli ultimi tre anni



# Popolazione studiata

- **Etnia:60 Africa(69,8%), 13 Italia (15,1%), 7 Est Europa (8,1%), 4 Sud-America(4,6%), 2 Asia(2,3%)**
- **Stadio CDC:A 67, B 11, C 7**
- **Diagnosi pre-gravidanza=64 (74,4%), gravidanza=22 (25,6%)**
- **Fattori di rischio HIV: TD=2, MTCT=2, Trasf=2,SEX=80**

# *Schemi di terapie*

- **3 NRTI:4**
- **2NRTI+NVP:12**
- **2NRTI+PI/boosted:73**
- **2NRTI+PI:1**
- 2 nessuna terapia al momento
- **2NRTI+PI/rit+Raltegravir=4**
- **Lopinavir=48, ATV=16, DRV=7, Fos=2**
- **AZT=36, TNF=33, ABC=17, d4T=2**

# Modalità di parto

- **TC elettivo: 70 (85,3%)**
- **TC urgenza:9 (10,9%)**
- **PV:2(2,4%)**
- **Aborti spontanei:1(1,2%)**
- **Parto pretermine <37 settimana:9**
- **<32settimana:0**
- **Nati morti:2**

# Soppressione virologica 32-36 sett

- **8/10 PC**
- **13/25 RE**
- **32/47 PR**

- ***64,6% di soppressione virologica a termine***

# Conclusioni ( personali )

- Indubbio il **ruolo della HART** e di quanto finora fatto sulla prevenzione della trasmissione verticale
- I **dati** disponibili riguardo all'uso di alcune terapie ( efavirenz, PI boostati ) non sono conclusivi, **richiedono continua cautela** ed attenzione e non sembrano sufficienti per modificare le indicazioni attuali
- La maggior parte delle nostre pazienti sono Africane, in buono stadio clinico, con CD4>200, hanno contratto l'infezione per via sessuale (in riduzione perciò le coinfezioni, il fumo, l'uso di droghe), spesso sono già in terapia; d'altra parte **la soppressione virologica a termine è ancora insoddisfaciente**
- Il **numero delle gravidanze è in aumento**; le donne HIV in gravidanza o che progettano una gravidanza richiedono un alto livello di presa in carico, cura e sostegno su più fronti ( HIV disclosure, aderenza, problematiche sociali o relative all'immigrazione, etc.etc)

***GRAZIE!***

E grazie in particolare ad
***Alessandra Donisi** **
***Giuliana Zoboli** ***

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