HIV in gravidanza: é arrivata l'ora?

Dott.ssa Prati Francesca UO Malattie Infettive ASMN, Reggio Emilia

POST ICAR 2022 Bologna, 29 Settembre 2022

Stefania, 28 anni

- Lavora come cooperante nei paesi in via di sviluppo
- Anamnesi muta, nessuna terapia in cronico
- Diagnosi HIV: 2015 durante screengin per donazione AVIS (2011 negativa)

- NADIR: Cd4= 179 (12%) - Viremia= 25.640 copie/ml
- Ceppo ricombinante: C wild-type

Stefania, 28 -35 anni

Terapia haart :

- 2015: Prevista/Norvir + Truvada
- Eviplera
- Dal 2017: Triumeq

Al controllo del 2022

- Cd4 1073 c/ml 36%
- Viremia non rilevabile da più 7 anni

Stefania 32 anni, desiderio di maternità

- Desiderio di maternità: folina
- Consueling in presenza del marito: U=U
- Mantiene Triumeq

2018: Allert DOLUTEGRAVIR in gravidanza

2022: studio Tsepamo non rischio DTN

Stefania 35 anni, gravidanza

- Consueling ostetrico
- Viremia non rilevabile da più 7 anni
- Aderenza ottimale

non controindicazioni

PARTO VAGINALE

HIV in GRAVIDANZA : spunti di confronto

- Test hiv capillare a tutte le donne gravide
- Consueling ostetrico dedicato
- Accessibilità del parto naturale

- Comunicazione ostetricia/infettivologo ?
- Difficoltà consueling anticoncezionale ?

Stefania, gravida 8°mese:

“Vorrei allattare al seno”

- 8° mese
- Esperienza in Africa
- Consapevolezza & Preoccupazioni
- Materiale informativo

LINEE GUIDA a CONFRONTO WHO 2016

Providing services to specifically support mothers to appropriately feed their infants Skilled counselling and support in appropriate infant feeding practices and ARV drug interventions to promote the HIV-free survival of infants should be available to all pregnant women and mothers.	Updated to a formal recommendation. See recommendation 2 (2016)

In settings in which national authorities have decided that the maternal and child health services will mainly promote and support breastfeeding and ARV drug interventions as the strategy that will most likely give infants born to mothers known to be living with HIV the greatest chance of HIV-free survival

2.	**Which breastfeeding practices and for how long** Mothers known to be living with HIV (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter and continue breastfeeding for the first 12 months of life. Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.	The 2016 guideline revises the recommended duration of breastfeeding and HIV treatment, see recommendation 1 (2016).

LINEE GUIDA a CONFRONTO - DHHS 2022

Counseling and Managing Individuals with HIV in the United States Who Desire to Breastfeed

Panel's Recommendations: Counseling and Managing Individuals with HIV Who Desire to Breastfeed

Panel's Recommendations
• In the United States, infant formula feeding is a safe alternative to breastfeeding in individuals with HIV. Breastfeeding presents an ongoing risk of HIV exposure after birth, because suppressive maternal antiretroviral therapy significantly reduces but does not eliminate the risk of HIV transmission through breastfeeding. Therefore, breastfeeding **is not recommended** for individuals with HIV in the United States **(AII).**
• Individuals who have questions about breastfeeding or who desire to breastfeed should receive patient-centered, evidence-based counseling on infant feeding options **(AIII).**
• Individuals with HIV who choose to breastfeed should be supported in risk-reduction measures to minimize the risk of HIV transmission to their infants **(BIII).**
• Clinicians are encouraged to consult the National Perinatal HIV Hotline (1-888-448-8765) if they have questions regarding individuals with HIV who desire to breastfeed **(AIII).**

Dal 2018 sezione dedicata Counseling nell'allattamento al seno

1: haart nella madre riduce ma non elimina rischio

2: latte artificiale è alimento sicuro

3: pochi dati sulla sicurezza dei farmaci nel latte

LINEE GUIDA a CONFRONTO: EUROPE 2021

EACS European AIDS Clinical Society

- The topic of feeding intentions should be discussed with a pregnant woman as early as possible in pregnancy, together with providing education and support to the mother
- **We advise against breastfeeding**, as in high-income settings the optimal way to prevent mother-to-child transmission is to feed infants born to mothers living with HIV with formula milk
  - To reduce the potential physical and emotional discomfort associated with breast engorgement, together with the risk of covert breastfeeding, women living with HIV should be given cabergoline to suppress lactation after delivery

parlare

consigliare

scegliere

- **In situations where a woman chooses to breastfeed, we recommend input from an interdisciplinary team including adult HIV specialist, paediatrician and obstetrician/gynecologist**
  - We recommend monthly follow-up during the whole breastfeeding period with increased clinical and virological monitoring of both the mother and the infant. Measurement of drug concentrations in the milk could be done to inform clinical practice
  - **Maternal HIV-VL > 50 copies/mL should result in cessation of breastfeeding, providing cabergoline and support from interdisciplinary team and a nursing specialist**
  - Immediate consulting by the interdisciplinary team should be provided in case of signs and symptoms of mastitis, infant mouth or gut infections
  - Currently there is no evidence supporting PrEP recommendation for the infants who are breastfed
  - **After stopping the breastfeeding, the child should undergo routine diagnostics as recommended in HIV-exposed children**

LINEE GUIDA a CONFRONTO: INGLESI 2020

BHIVA British HIV Association

9.4.1 Breastfeeding advice for women with HIV living in the UK

9.4.1	In the UK and other high-income settings, the safest way to feed infants born to women with HIV is with formula milk, as there is on-going risk of HIV exposure after birth. We therefore continue to recommend that women living with HIV feed their babies with formula milk (but see also section 9.4.4).	1D

Current WHO advice on breastfeeding for women with HIV is aimed at low- and middle-income countries where there is a high risk of infant morbidity and mortality from diarrhoea, pneumonia and other infections, and where formula feeding is not safe or affordable for many families. All women with HIV are advised to start cART as soon as possible after HIV diagnosis and continue lifelong treatment. They are advised to breastfeed their infants exclusively for the first 6 months, while adhering to cART, then to add complimentary foods as appropriate after this time. They are advised not to stop breastfeeding until other safe and adequate foods are available, and to continue up to 12–24 months of age [62].

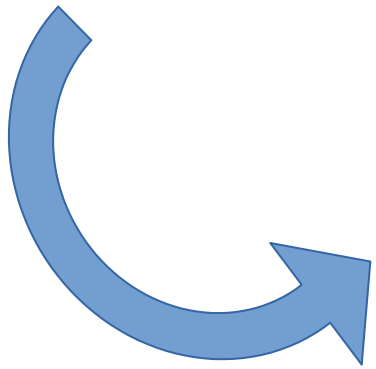
Suppressive maternal cART significantly reduces, but does not eliminate, the risk of vertical transmission of HIV through breastfeeding. The undetectable=untransmittable (U=U) statement applies only to sexual transmission, and we currently lack data to apply this to breastfeeding. Other considerations are the lack of lactation studies for most antiretroviral agents, meaning that the pharmacokinetic properties of ART in breastmilk are poorly understood, and the potential effects of exposure to ART in the breastmilk on infants who do not acquire HIV [63].

LINEE GUIDA a CONFRONTO: INGLESI 2020

BHIVA British HIV Association

9.4.4 Choosing to breastfeed in the UK

9.4.4	Women who are virologically suppressed on cART with good adherence and who choose to breastfeed should be supported to do so, but should be informed about the low risk of transmission of HIV through breastfeeding in this situation and the requirement for extra maternal and infant clinical monitoring.	1D
	When a woman decides to breastfeed, she and her infant should be reviewed monthly in clinic for HIV RNA viral load testing during and for 2 months after stopping breastfeeding.	1D
	Maternal cART (rather than infant pre-exposure prophylaxis [PrEP]) is advised to minimise HIV transmission through breastfeeding and safeguard the woman's health.	1D



Patient breastfeeding information leaflet 1

Patient breastfeeding information leaflet 2

LINEE GUIDA a CONFRONTO: INGLESI 2020

BHIVA British HIV Association

No virus

If the HIV virus in your blood is detectable, there will be HIV in your breast milk, and HIV will enter your baby's body on feeding. You should only breastfeed your baby if your HIV is undetectable.

Happy tums

Diarrhoea and vomiting show that a tummy is irritated. If your baby's tummy is irritated it may be more likely that HIV will cross into the blood steam and infect your baby. If your tummy is irritated you may not absorb your HIV medication properly. Only breastfeed if both of you have a 'happy tummy'.

Healthy breasts for mums

There may be HIV in your breast milk if your nipples are cracked or bleeding, or if you have thrush, develop an infection or have mastitis. Only breastfeed if your breasts are healthy.

The Safer Triangle means:

No Virus + Happy Tums + Healthy Breasts for Mums

General information *on* infant feeding *for* women living with HIV

The British HIV Association recommends that the safest way for a mother with HIV to feed her baby is with formula milk, as there is absolutely no risk of HIV transmission at all after birth

(BHIVA 2018)

HIV health workers understand that HIV may not be the only thing you need to think about when feeding your new baby. We have put together information that will help you make an informed decision about feeding your baby. Whatever you decide, you will not be judged. Let your HIV care team know if you decide to breastfeed your baby. They can then work with you to help make this as safe as possible, even though it will still not be as safe as feeding your baby with formula.

The most important things you can do are to keep up with your medications and appointments, enjoy this time with your new baby, and get in touch if you have any questions or difficulties.

If you are considering breastfeeding your baby

LINEE GUIDA a CONFRONTO: SVIZZERE 2019

Table 1:

Swiss 2019 recommendations to prevent HIV MTCT. Changes from 2009 are highlighted (yellow), major changes are in bold.

Prevention measures	Optimal Scenario	Suboptimal Scenario
1. cART during pregnancy	most important prevention measure and highly recommended for all HIV-infected individuals[1]	
2. Mode of delivery	vaginal birth, if no obstetrical contraindications are present[2]	caesarean section, if possible prior to ROM (= ECS)[3]
3. nPEP	**none**	neonatal cART[4]
4. breastfeeding	**shared decision-making[5]**	contraindicated

Swiss HIV Cohort Study
& Swiss Mother and Child HIV Cohort Study

EACS 2021 Half of Swiss mothers with HIV decide to breastfeed their baby when given the choice

LG SVIZZERE allattamento al seno: rischi potenziali

Table 2:

Breastfeeding in HIV-infected mothers fulfilling the "optimal scenario with a strong wish to breastfeed"

Pro and con arguments
1) List of potential RISKS associated with breastfeeding
• HIV transmission to the child (MTCT) cannot be ruled out: i) Transmission through breastfeeding in the range of 0.3–0.9 % (6 months to 24 months of breastfeeding, PROMISE Study) has been observed when women were under effective combined antiretroviral therapy (cART) during pregnancy and the breastfeeding period but viral load measurement (pVL) data during the breastfeeding period from this study is yet missing. ii) There is no formal study evaluating the risk of MTCT by HIV-infected mothers who are under cART with undetectable HIV pVL. iii) Even if we did not identify HIV MTCT in the "optimal scenario" we cannot exclude that such a case did or might happen with lifelong consequences for the child.
• Postpartum is a vulnerable period (e.g. irregular sleep, elevated risk for mood disorders) for women with the risk of impaired adherence and consequential increased pVL. In this period particularly, support of adherence to cART is important.
• Longer exposure to maternal antiretroviral drugs; although breast milk concentrations are low, toxicity cannot be absolutely excluded.
• Episodes of mastitis might increase the risk of transmission.
• An increased risk of HIV MTCT was observed through breastfeeding if the HIV-infected mothers were untreated and when breastfeeding was accompanied by solid food (=mixed feeding). There is currently no data to support any such additional risk in the "optimal scenario" but it cannot be excluded. Exclusive breastfeeding during the first 4 months is generally recommended for all children in Switzerland.
• The role of cell-associated virus in breast milk as an additional possible risk is not fully understood.

LG SVIZZERE allattamento al seno: potenziali benefici

2) List of potential BENEFITS arguing for breastfeeding

- Recommendations to breastfeed during the six months postpartum exist in many European countries including Switzerland.

- Parents consider breastfeeding a simple, easy and free way of providing nutrition to the infant AND/OR psychologically essential for infant care and development.

- Breastfeeding has the following beneficial effects for the child [though formally not proven for children of HIV-infected mothers], among others:

  i) The human microbiome is established normally with possible beneficial health consequences; e.g. lower risk to develop allergies, overweight and diabetes;

  ii) Anti-inflammatory and anti-infective components in breast milk might have beneficial effects for immune response and immune tolerance which are important to prevent the development of allergies or infectious diseases.

- Beneficial effects of breastfeeding for the mother:

  i) Improved postpartum recovery: stimulates involution of the uterus and reduces postpartum depression

  ii) Reduction of the future risk to develop breast cancer and of glucose homeostasis with protection against type 2 diabetes

Table 3:

Guidance for a shared decision-making process to decide on breastfeeding in HIV-infected mothers with a strong wish to breastfeed their children

Guidance
1) Prerequisite conditions to minimise HIV MTCT risk ("optimal scenario")
• Suppressed HIV pVL (< 50 RNA copies/ml) throughout pregnancy
• Regular follow-up of treatment (e.g. every 2–3 months, initially in postpartum period every month) is accepted by the pregnant women to ensure maintained suppression of pVL.
• All health care providers involved should agree on an open, non-judgemental and unbiased approach towards breastfeeding.
• Inform the woman that the whole HIV care team accepts whatever the decision is and this will not affect the quality of care offered to her.
2) Shared decision-making
• Interdisciplinary process with patient and HIV care providers (including adult HIV specialist, paediatrician and obstetrician/gynaecologist)
• Start as early as possible during pregnancy but (re-)discussion required prior to delivery
• Discuss pro and con arguments of breastfeeding including open questions and admit limitations of medical knowledge (see Table 2)
• The final decision should be documented in the patient notes of the mother and distributed to all care providers involved.

LINEE GUIDA a CONFRONTO
monitoraggio durante allattamento

British: controllo viremia madre e bambino 1volta/mese fino a 2 mesi dopo il termine allattamento 1C

Swiss: madre ogni mese per 6 mesi bimbo a 1 e 6 mesi

USA: 1-2 volte al mese nella madre

Aderenza nel post-partum:

- Review 20.153 donne gravide: aderenza scenda da 76% a 53% (paesi misti)
- **UK**: studio 623 donne 10% presenta viral rebound vs. gruppo controllo 7%
- **Swiss Cohort**: 695 donne 12 % perse al follow-up nel 1° anno post-partum

LINEE GUIDA a CONFRONTO
monitoraggio durante allattamento

- Se HIV madre: > 50 c/ml sospensione immediata allattamento
- Controllo madre: ragadi mastite
- Controllo neonato: disturbi gastrointestinali

- Monitoraggio nel latte materno?

Does U=U for Postnatal Breast Milk Transmisision?

Is U=U Applicable to Breastfeeding?

EACS 2021

Lynne Mofenson, MD
Elizabeth Glaser Pediatric AIDS Foundation,
United States

What Do We Know About Breast Milk HIV Transmission?

Timing of Breast Milk Transmission (in the Absence of ART)

- Several studies suggest a substantial proportion of breast milk transmission occurs early, before 1-2 month of age – as high as an absolute risk of 6%.
- This may be due to high T-cell content of colostrum/early breast milk, which could theoretically increase risk of HIV transmission.
- However, there appears to be a continuous risk throughout lactation, with low monthly risk, on average about 0.6-0.9% per month.
- Thus, for women not on ART who breastfeed for 18-24 months, overall risk of postnatal transmission can be as high as 21-27%.

Does U=U for breastfeeding mothers and infants? Breastfeeding by mothers on effective treatment for HIV infection in high-income settings

Catriona Waitt Lancet HIV 2018; 5: e531–36

1) RAPPORTO tra VIREMIA MATERNA / VIREMIA nel LATTE & TRASMISSIONE

- Viremia plasmatica & aumenta rischio di trasmissione → non è nota una ***soglia sicura***
- *BAN Malawian*: in tutti i casi di infezione madre aveva almeno una viremia + su plasma >100
  due casi con viremia positiva su latte non su plasma
- Sud Africa: casi di trasmissione anche con viremia HIV-RNA negativa su latte

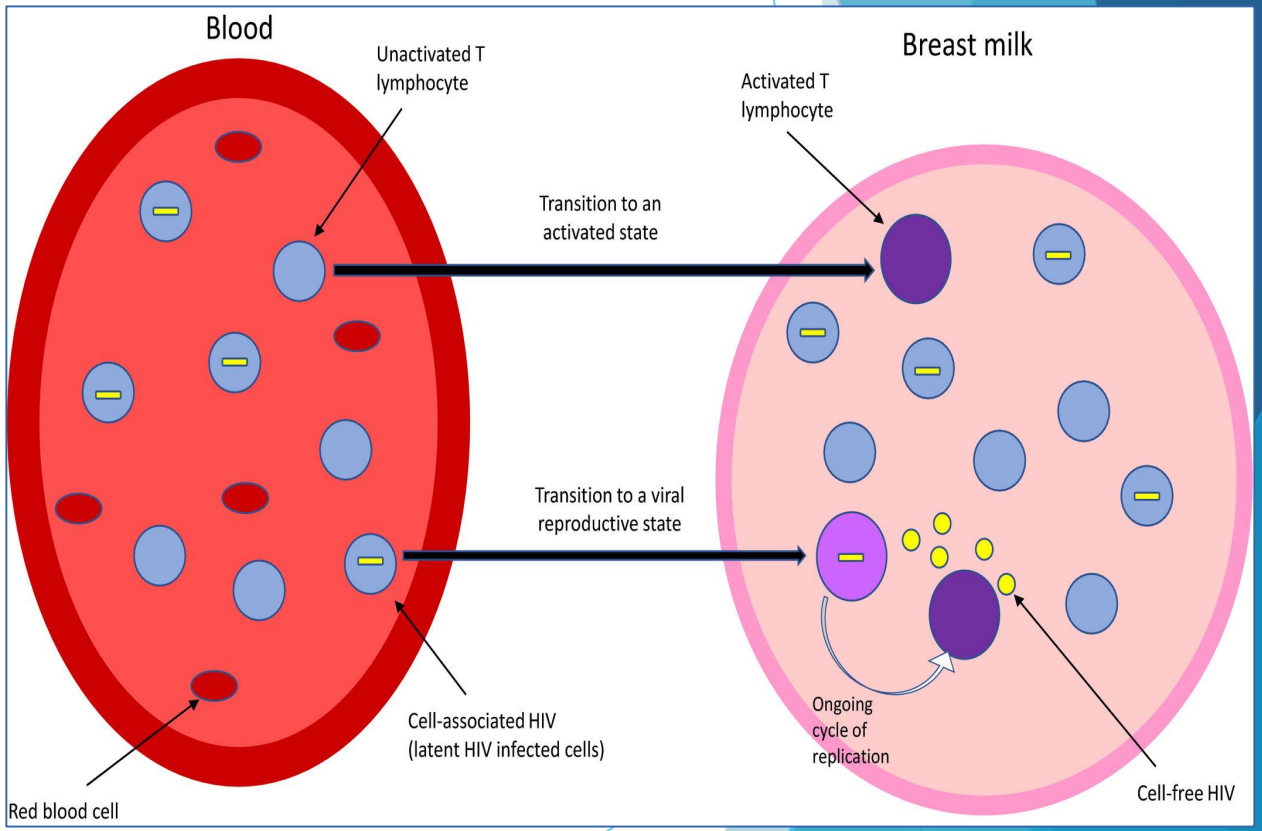
Trasmissione secondaria a HIV-DNA associato alle cellulle?

- Mastite: rialzo della viremia HIV nel latte anche in regime Haart sopressivi?

Does U=U for breastfeeding mothers and infants? Breastfeeding by mothers on effective treatment for HIV infection in high-income settings

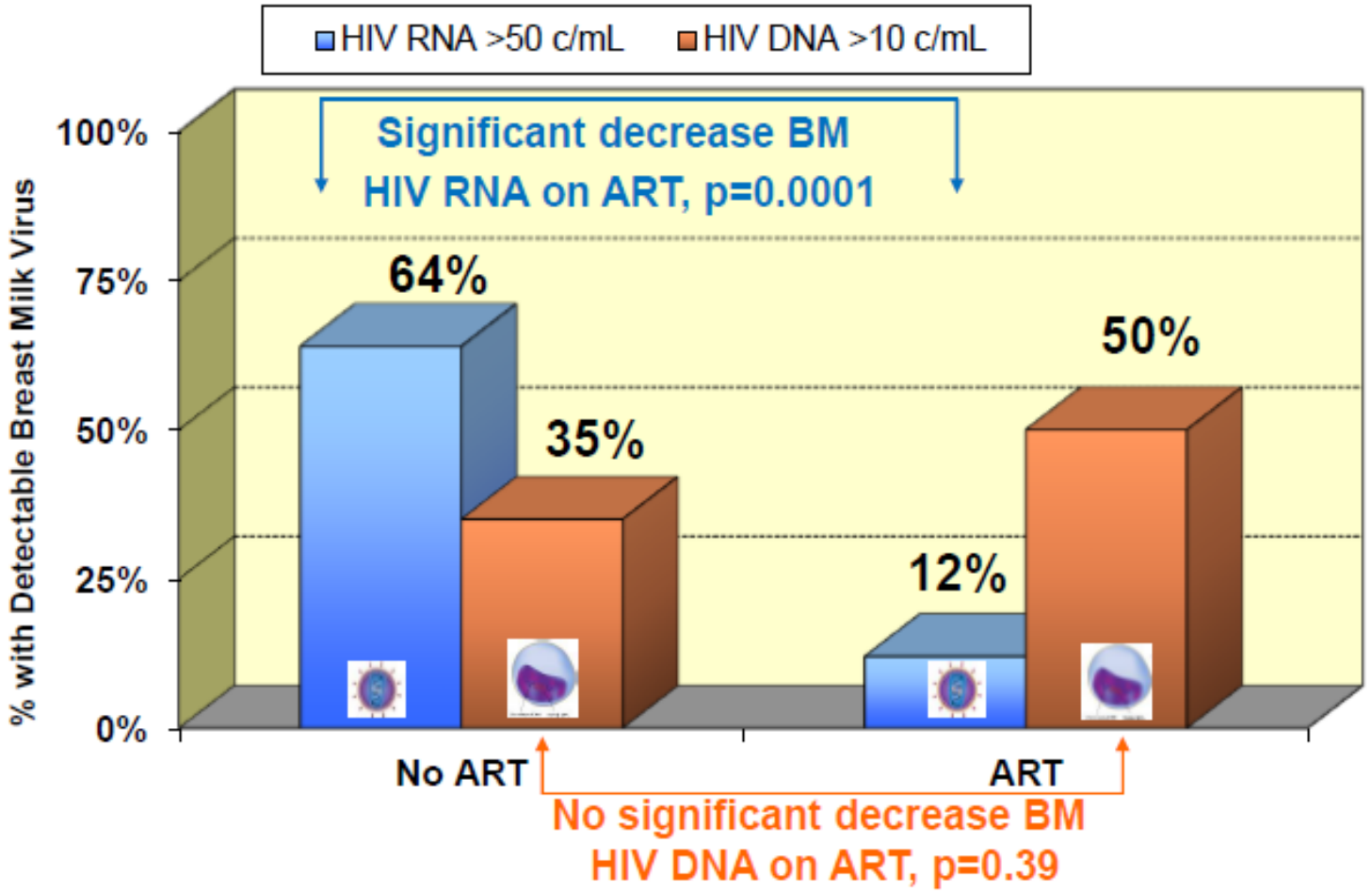
Catriona Waitt Lancet HIV 2018; 5: e531–36

- *Nel latte sono presenti **cellulle immunitarie** latentemente infette che contengono HIV-DNA provirale; hanno emivita di 44 mesi, non sono target della terapia, e constituiscono un reservoir inducibile di trascrizione di HIV-DNA*
- *Entrambe forme di HIV sono state associate alla trasmissione con latte; HIV-DNA cellulare presente nel latte è responsabile della trasmissione sopratutto **nei primi mesi***
- *Haart determina calo hiv-rna non in hiv-dna in donne in terapia da 100 gg: scarsi dati nelle donne in terapia soppressiva di lunga durata*



Association of Early Postnatal MTCT with Cell-Associated Virus is Important Because ART Reduces Breast Milk HIV Cell-Free (RNA) But Not HIV Cell-Associated (DNA) Viral Load

Shapiro R et al. J Infect Dis 2005;192:713-9



Does Undetectable Plasma Viral Load Mean Undetectable Breast Milk Viral Load?

Davis NL et al. JAIDS. 2016;73:572-80

- BAN study: Postnatal maternal ART vs infant NVP vs single-dose NVP for prevention of postnatal transmission (maternal ART and infant NVP similar significant efficacy).
- 221 mothers had paired plasma and breast milk specimens.
- Mothers with detectable plasma VL has adjusted 40-fold increased odds of detectable breast milk VL (95% CI 15-108).
- However, 2 (**0.9%**) had **undetectable plasma VL** at 6 weeks postpartum but **detectable breast milk VL** (56 and 77 c/mL).

What Do We Know About Breast Milk HIV Transmission?

Late Breastfeeding Transmission, ART, and Maternal VL

Three studies provided data on final infant infection status at the end of breastfeeding and maternal viral load during the postpartum period.

First Author (Year)	Study location	Findings
Flynn (2018)	Multi-country (PROMISE study)	2 infant infections in mothers who initiated ART postpartum with subsequent viral load <40 copies/mL
Luoga (2018)	Tanzania	1 infant infection where the maternal viral load was <1000 copies/mL but mother had a disruption in therapy
Giuliano (2013)	Malawi	1 infant infection where mother initiated ART during pregnancy and had a subsequent viral load <37 copies/mL

STUDI: donne in ART per PMTCT

Review article

Postnatal HIV transmission in breastfed infants of HIV-infected women on ART: a systematic review and meta-analysis

Stephanie Bispo[1§], Lana Chikhungu[2*], Nigel Rollins[3*], Nandi Siegfried[4*] and Marie-Louise Newell[5*]

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*These authors have contributed equally to the work.

Abstract

Introduction: To systematically review the literature on mother-to-child transmission in breastfed infants whose mothers received antiretroviral therapy and support the process of updating the World Health Organization infant feeding guidelines in the context of HIV and ART.

Methods: We reviewed experimental and observational studies; exposure was maternal HIV antiretroviral therapy (and duration) and infant feeding modality; outcomes were overall and postnatal HIV transmission rates in the infant at 6, 9, 12 and 18 months. English literature from 2005 to 2015 was systematically searched in multiple electronic databases. Papers were analysed by narrative synthesis; data were pooled in random effects meta-analyses. Postnatal transmission was assessed from four to six weeks of life. Study quality was assessed using a modified Newcastle-Ottawa Scale (NOS) and GRADE.

Results and discussion: Eleven studies were identified, from 1439 citations and review of 72 abstracts. Heterogeneity in study methodology and pooled estimates was considerable. Overall pooled transmission rates at 6 months for breastfed infants with mothers on antiretroviral treatment (ART) was 3.54% (95% CI: 1.15–5.93%) and at 12 months 4.23% (95% CI: 2.97–5.49%). Postnatal transmission rates were 1.08 (95% CI: 0.32–1.85) at six and 2.93 (95% CI: 0.68–5.18) at 12 months. ART was mostly provided for PMTCT only and did not continue beyond six months postpartum. No study provided data on mixed feeding and transmission risk.

Conclusions: There is evidence of substantially reduced postnatal HIV transmission risk under the cover of maternal ART. However, transmission risk increased once PMTCT ART stopped at six months, which supports the current World Health Organization recommendations of life-long ART for all.

Keywords: Antiretroviral therapy; HIV; prevention of mother-to-child transmission; breast feeding; systematic review; meta-analysis

STUDIE DONNE in HAART

Article

From Undetectable Equals Untransmittable (U=U) to Breastfeeding: Is the Jump Short?

Tullio Prestileo [1,2], Sanfilippo Adriana [1], Di Marco Lorenza [2,3,4,*] and Antonina Argo [5]

Table 2. Clinical, social, and demographic findings of 13 cohort female patients.

CDC	Years of Birth	Age of Delivery	Stay in Italy (Months)	Country of Origin	HIV+Diagnosis 1 (before Pregnancy) 2 (during Pregnancy)	HIV Viral Load to Delivery and during Breastfeeding	Breastfeeding Time (Months)
A-1	1999	18	6	Nigeria	1	not detected	6
A-2	1997	20	6	Mali	2	not detected	6
A-1	1987	30	48	Ivory Coast	1	not detected	11
A-1	1991	26	11	Nigeria	1	not detected	4
A-1	1993	24	6	Cameroon	1	not detected	4
A-2	1989	28	24	Ghana	2	not detected	6
A-2	1996	22	6	Ivory Coast	1	not detected	6
A-1	1985	33		Italy	1	not detected	10
A-1	1998	21	6	Nigeria	1	not detected	6
A-1	1994	34	36	Senegal	2	not detected	4
A-1	1985	33	24	Ghana	1	not detected	6
A-1	1994	28		Italy	1	not detected	6 weeks (definitive interruption for COVID-19)
A-2	1994	24	72	Nigeria	2	not detected	6

Note 1: CDC classification: Stage A-1: asymptomatic with CD4+ cell > 500/mmc, Stage A-2: asymptomatic with CD4+ cell 200–499/mm.

- **Studio retrospettivo 2017-2021**
13 donne: italiane e straniere
4 con diagnosi HIV in corso di gravidanza

- Donne testate insieme al bambino ogni **8 settimane**

- Profilassi con **AZT per 4** settimane

- Controllo a 1, 3 ,6 mesi dopo il termine allattamento:
nessuna trasmissione

Does U=U for breastfeeding mothers and infants? Breastfeeding by mothers on effective treatment for HIV infection in high-income settings

Catriona Waitt Lancet HIV 2018; 5: e531–36

2) ESPOSIZIONE NEONATO ai FARMACI PRESENTI nel LATTE: sviluppo resistenza / tossicità

- Neonato con allattamento esclusivo riceve **10% della dose/kg NNRTI e NRTI**
- il passaggio dei PI è basso
- DTG nel latte: scarsa secrezione ratio latte/plasma 0,03

- Registro gravidanze non raccoglie data sui bambini allattati al seno da mamme hiv
- Dati da studi su PVS in neonati espostiti a NVP per 18 mesi: confortanti

- Studi PMTCT mostrano che neonati che acquisiscono hiv durante allattamento da madre in terapia hanno alto tasso di **resistenze** con pattern di R differente

So – Where are We with U=U for Postnatal MTCT?

- U = U is based on data showing persons on ART achieving consistent undetectable VL (defined as <200 c/mL by CDC) have essentially no **sexual** transmission to HIV-negative sexual partners.
- Data clearly show that a viral load threshold of ~~200 cannot~~ be used when referring to peripartum and postpartum MTCT; the threshold must be 50 c/mL.
- In formula-feeding populations, data indicate that there is likely a zero risk of transmission if a mother is on ART and achieved viral suppression <50 c/mL prior to pregnancy and maintains ART and suppression through delivery – so U=U may apply here.

So – Where are We with U=U for Postnatal MTCT?

- Data on breast milk transmission and viral load are more limited and complex as our measure is virus in plasma rather than milk.
  - Plasma VL generally correlates with breast milk VL but rarely virus may be undetectable in plasma but present in low levels in milk – and visa versa.
  - Breast milk cell-associated virus is important in early transmission, and is less affected by ART.
  - For early breast milk transmission, limited data suggest U ≠ U in women who *start ART during pregnancy*, even if delivery VL is <50.

So – Where are We with U=U for Postnatal MTCT?

- Late breast milk transmission will likely require *both* plasma and breast milk virus to be undetectable from before pregnancy and through the entire breastfeeding period.
- However, data on women on preconception ART and consistently suppressed throughout pregnancy and breastfeeding are not yet available.
- However, even if residual risk, it appears extremely low (<1%).

Stefania e ...Gabriele

- Rottura prematura membrane: parto pretermine 35 settimane
- Gabriele: 3,06 Kg parto naturale
- Colloquio neonatologo

LETTERA di DIMISSIONE

Come da indicazioni Infettivologiche (visita del 05/07/2022) la paziente dopo il parto ha proseguito la terapia in atto prima del parto.
*La paziente ha discusso con infettivologo in tal occasione della sua volontà di allattare al seno ed "**è sta informata adeguatamente dei rischio residui di tale scelta e ne è consapevole fermo restando le premesse a favore di una viremia persistentemente soppressa ottima aderenza". Eseguito colloquio con neonatologo per l'allattamento dopo il parto.***

- Stefania sta allattando da 2 mesi
- Ha proseguito Triumeq

Stefania e ...Gabriele

- Collaborazione con Neonatologi
- Supporto *personale* ostetriche del servizio Latte e Coccole
- Controllo viremia mensile negativo madre e bambino (Agosto - Settembre)
- Dosaggio viremia latte

LA paziente riferisce che in seguito a confronto con medico infettivologo, ginecologo e pediatra decide di allattare Gabriele al seno.

Esame Obiettivo:

Peso nudo odierno 2868 gr (+56gr rispetto al controllo precedente del
Riferisce diuresi regolare 5/6 pannolini al die e alvo regolare colore verde-giallo
attacco al seno ogni 2h e mezza con successiva proposta di latte materno tirato circa 40ml
(a volte integra con il latte artificiale se non abbastanza latte materno tirato)

Seno regolare, assenza di zone arrossate, assenza di ragadi.
Attualmen attacca con il paracapezzolo, non riferisce dolore oppure fastidio a seno.

Conclusioni:

controllo con il PLS

Attacco al seno a richiesta (preservando la poppata notturna se possibile) e successiva integrazione con latte materno tirato/artificiale.

Terapia Consigliata:

attaccare a richiesta (senza far passare più di 2h e mezza tra una poppata e l'altra)
idratazione (almeno 2L acqua al giorno)
monitoraggio diuresi del neonato

Altre Indicazioni:

Latte e coccole 0522335511

Stefania e Gabriele: punti critici

- **Informare**: fare noi la domanda per primi

- Coinvolgimento della neonatologia: **protocollo comune**
- Coinvolgimento di **tutti** gli operatori

- Tempistiche, consenso scritto preformato, presenza del marito
- Decisione da rivalutare nel tempo *(depressione post-partum)*

- Rescue strategy… formulazioni pediatriche disponibili
- Dosaggio viremia su latte

CONCLUSIONI

Pochi casi, poca esperienza, serve condivisione e raccolta dati

Necessariamente un lavoro di equipe

FINE

MONITORAGGIO MADRE-BAMBINO ALLATTATO
LINEE GUIDA SVIZZERE 2019

3) Follow up mother and child

- Obtain a cord blood sample at birth to identify or exclude intrauterine infection of the newborn whenever possible. Previous concern about contamination by maternal HIV RNA is irrelevant in the "optimal scenario" but the unlikely event of a HIV-positive RNA result should be confirmed.

- Women deciding to breastfeed should be followed up initially monthly (during postpartum period with elevated risk of impaired adherence), afterwards every 2–3 months during the full breastfeeding period.

- Women who breastfeed should contact their obstetricians in case of signs and symptoms of mastitis. The decision to continue or to stop breastfeeding in this situation will be taken individually based on its severity, maternal compliance for cART, antibiotic treatment and the wish of the informed mother. The same holds true for hematemesis and melena in infants, where breastfeeding is the leading cause.

- HIV pVL (> 50 RNA copies/ml) must result in a stop of breastfeeding.

- All HIV-exposed children will have HIV testing as standard of care at month 1 and 6 by PCR as well as at months 18–24 by serology, if possible by a paediatric infectious disease specialist, until maternal antibodies are confirmed negative in the child. In breastfed infants the follow-up is similar, except that 1 or 2 additional follow-up visits (e.g. month 2 and/or month 4) should be considered to assure the "optimal scenario" is still granted. Additionally, HIV testing 3 months after weaning of breastfeeding is recommended.

DOLUTEGRAVIR nel LATTE

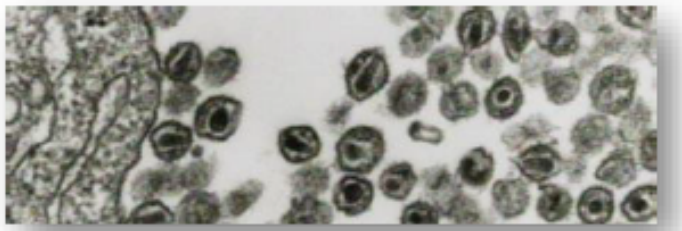
Placental transfer of DTG in an ex vivo perfusion model was high, with a mean fetal-to-maternal concentration ratio of 0.6.9 In two in vivo PK studies, the median DTG cord blood-to-maternal-plasma concentration ratios were 1.21 and 1.25.High placental transfer of DTG has also been reported in several of the case reports.

In 17 breastfeeding mothers, the median **ratio of DTG in breast milk to maternal plasma was 0.03**.

Their infants had a median maximum DTG concentration of 66.7 ng/mL (range 21–654 ng/mL) and a median minimum concentration of 60.9 ng/mL (range 16.3–479 ng/mL) at a median age of 10 days (range 7–18 days). The geometric mean ratio of infant plasma to maternal plasma DTG concentrations in these 17 mothers–infant pairs was 0.03.7

What Do We Know About Breast Milk HIV Transmission?

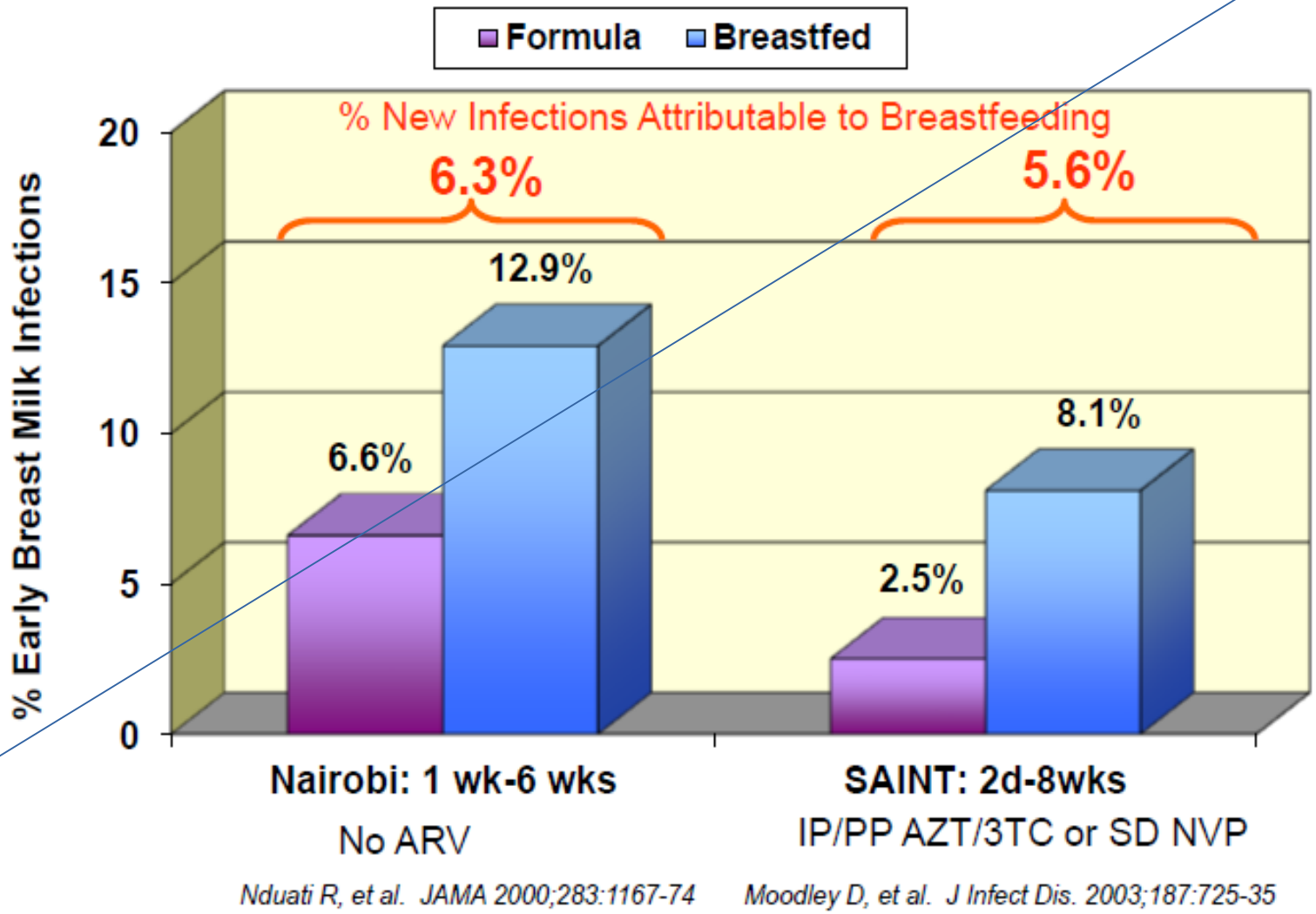
Breast Milk Viral Load vs Plasma Viral Load And Postnatal Transmission



Cellule latte

Substantial Early Breast Milk HIV Transmission:

Nairobi & SAINT Trials: Difference Between Formula & Breast-Fed Infants



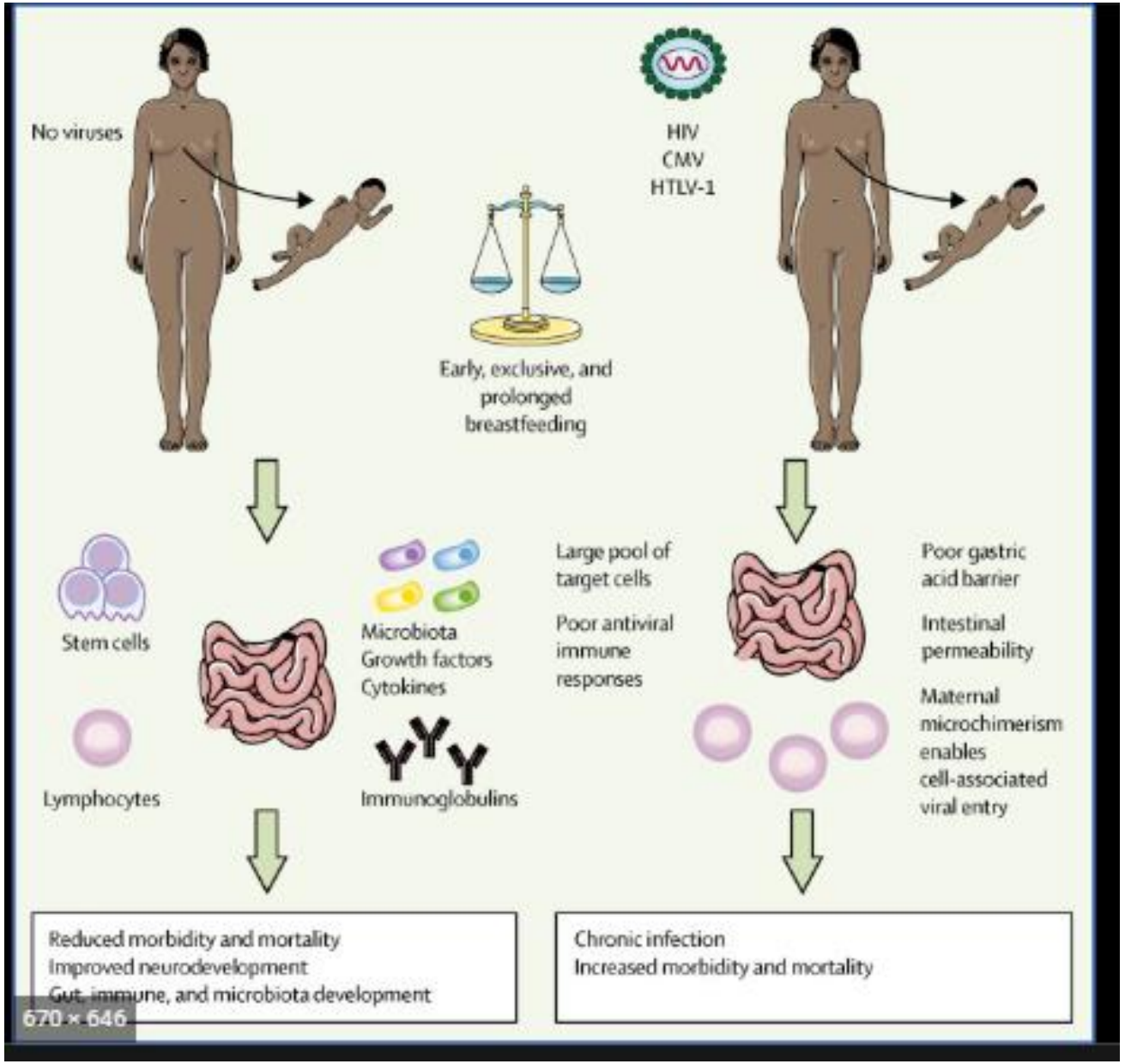
Nduati R, et al. JAMA 2000;283:1167-74

Moodley D, et al. J Infect Dis. 2003;187:725-35

Is U=U Applicable to Breastfeeding?

Lynne Mofenson, MD
Elizabeth Glaser Pediatric AIDS Foundation,
United States

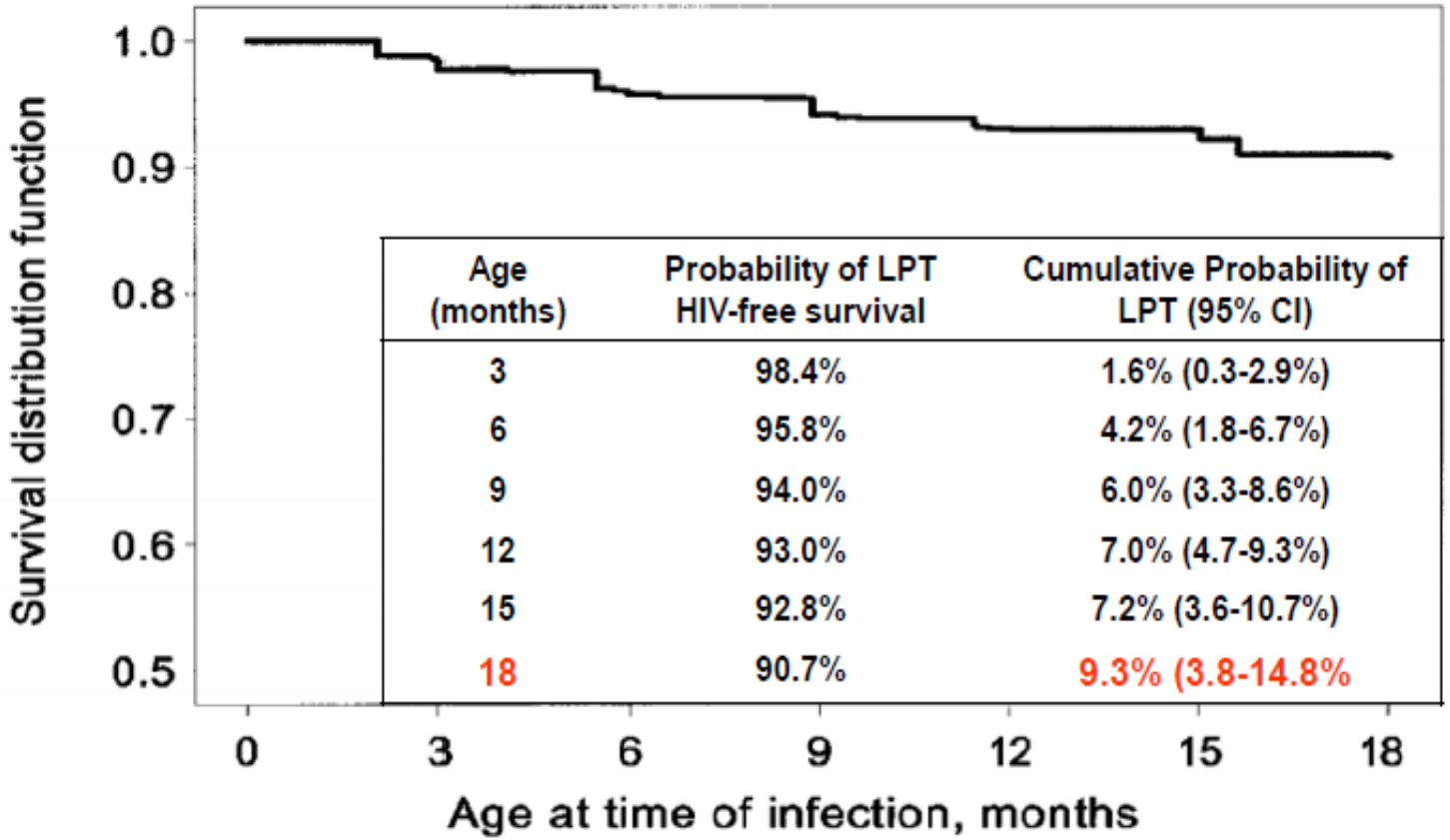
- E’ applicabile in altri setting?
- Che cosa sappiamo della trasmissione di HIV con allattamento al seno
- Cosa sappiamo U = U nella trasmissione in utero/peripartum?
- Il rischio si modifica secondo la durata dell’allattamento?
- Studi a supporto
- Tossicità HAART neonato


No viruses
HIV
CMV
HTLV-1
Early, exclusive, and prolonged breastfeeding
Stem cells
Microbiota
Growth factors
Cytokines
Large pool of target cells
Poor antiviral immune responses
Poor gastric acid barrier
Intestinal permeability
Maternal microchimerism enables cell-associated viral entry
Lymphocytes
Immunoglobulins
Reduced morbidity and mortality
Improved neurodevelopment
Gut, immune, and microbiota development
Chronic infection
Increased morbidity and mortality
670 × 646

After Age 1 Month, Risk of Late Postnatal Transmission is Constant

BHITS JID 2004;189:2154-66

- Evaluated postnatal infection rate in 4,085 breastfed children uninfected at age 1 month



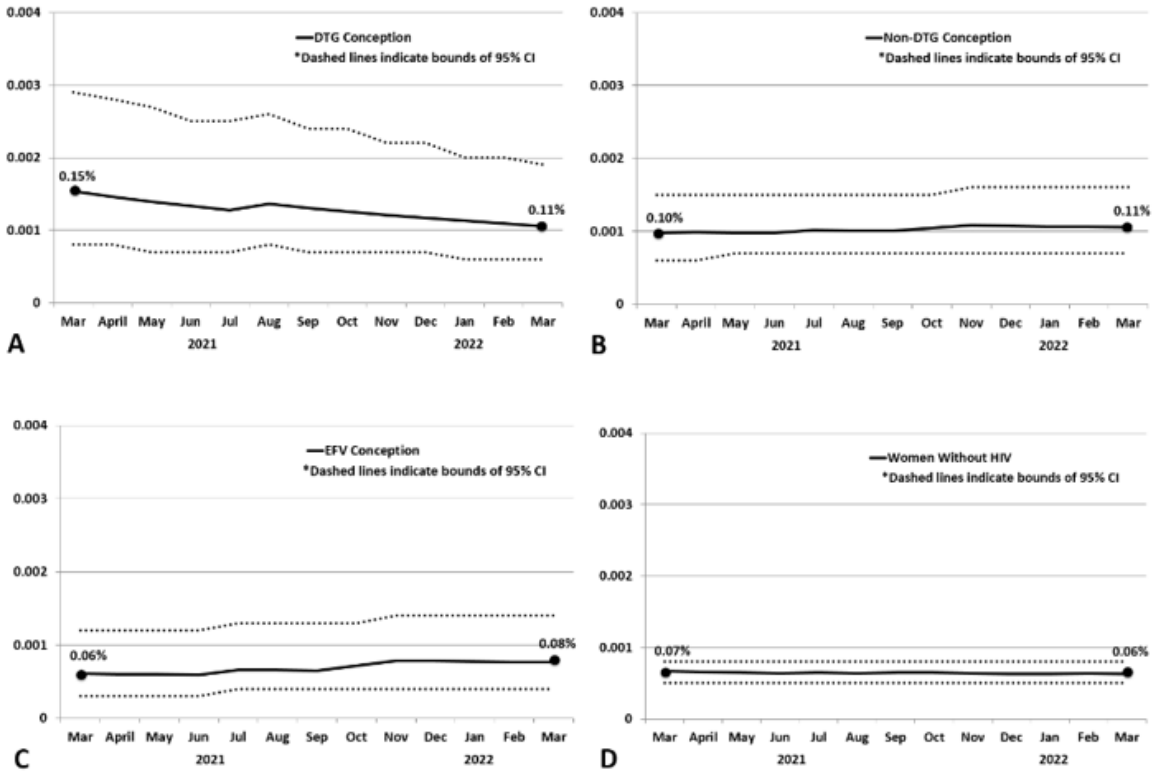
Age (months)	Probability of LPT HIV-free survival	Cumulative Probability of LPT (95% CI)
3	98.4%	1.6% (0.3-2.9%)
6	95.8%	4.2% (1.8-6.7%)
9	94.0%	6.0% (3.3-8.6%)
12	93.0%	7.0% (4.7-9.3%)
15	92.8%	7.2% (3.6-10.7%)
18	90.7%	9.3% (3.8-14.8%

Late postnatal transmission 0.74%/month breastfeeding (8.9 per 100 child-years)

HIV Treatment as Prevention and "The Swiss Statement": in for a Dime, in for a Dollar?

DOLUTEGRAVIR in Gravidanza

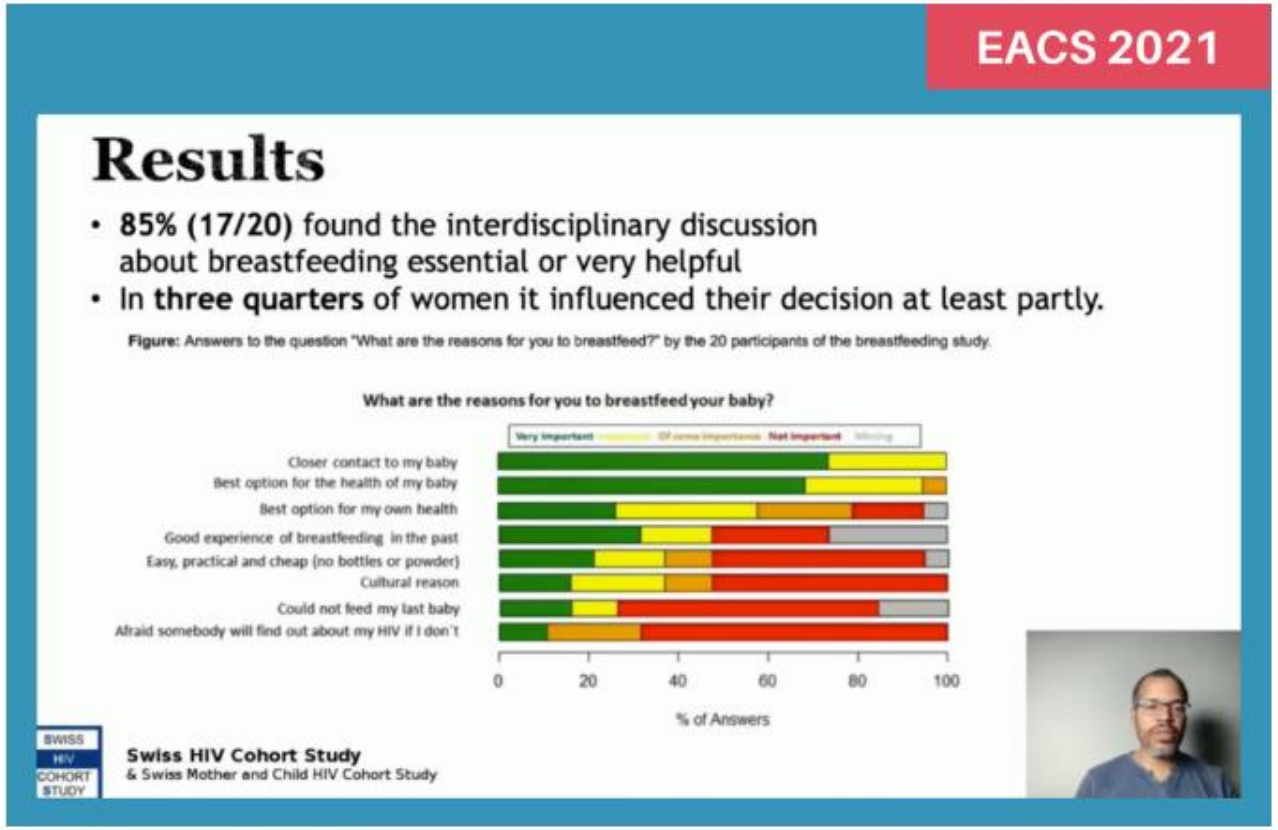
There Is No Longer Evidence of a Significant Difference in NTD Occurrence Between DTG and Non-DTG Antiretroviral Regimens When Used at Conception



- Update on neural tube defects with antiretroviral exposure in the Tsepamo study in Botswana
- Prevalence of NTDs has decreased over time from 0.94% (n=426) in May 2018
- Current analysis up to March 2022 reports 10 NTDs out of 9460 pregnancies exposed to DTG at conception: prevalence rate of 0.11% (95% CI, 0.06-0.19) compared with 0.11% (95% CI, 0.07-0.16) for non-DTG ART exposures

Trends in NTD Prevalence (95% CI) With (A) DTG, (B) Non-DTG ART, and (C) EFV Exposure at Conception and (D) in Women Without HIV, March 2021 to March 2022

Zash et al. AIDS 2022; Virtual and Montreal, Canada. Poster PELBB02.



Dr Pierre-Alex Crisinel at EACS 2021.

For new mothers with HIV, whether to breastfeed their baby has been a difficult choice. Unlike transmission through sex, viral suppression through antiretroviral therapy (ART) may not completely remove the risk of transmission.

STUDI in donne in HAART

Brief Report: No HIV Transmission From Virally Suppressed Mothers During Breastfeeding in Rural Tanzania.

Luoga E, Vanobberghen F, Bircher R, Nyuri A, Ntamatungiro AJ, Mnzava D, Mollel GJ, Letang E, Battegay M, Weisser M, Gamell A.

J Acquir Immune Defic Syndr. 2018 Sep 1;79(1):e17-e20. doi: 10.1097/QAI.0000000000001758.

PMID: 29781882

We found no MTCT from mothers who were retained in care and had suppressed VL. Breastfeeding signifies a very low risk when mothers adhere to ART. Adherence counseling, VL monitoring, and strategies to trace back those LTFU should be a priority.

Undetectable = Untransmittable

JAMA. 2019 Feb 5;321(5):451-452. doi: 10.1001/jama.2018.21167.

VIEWPOINT

HIV Viral Load and Transmissibility of HIV Infection
Undetectable Equals Untransmittable

Robert W Eisinger [1], Carl W Dieffenbach [2], Anthony S **Fauci** [1]

- U=U signifies that an HIV-infected individual on antiretroviral therapy who achieves and maintains an undetectable viral load cannot transmit HIV to their partner.

Principles of U=U

- In order for antiretroviral therapy (ART) to provide maximum benefit, taking medication as prescribed is essential. → Consistent adherence to ART required
- Achieving an undetectable viral load can take up to 6 months of ART. Once achieved, continued adherence is required. → Achieving suppression takes time - undetectability is not immediate on ART
- According to guidelines from the Department of Health and Human Services, viral load testing should be performed every 3-4 months after the plasma HIV-1 RNA level reaches undetectable (<200 copies/mL). If viral suppression and stable immunologic status are maintained for >2 years, the viral load testing can be extended to every 6 months thereafter. → Monitoring to verify remains undetectable (what defines undetectable?)
- Stopping therapy negates the validity of assuming that U = U. → Risk of stopping - U=U invalid if non-adherent

Does U=U for breastfeeding mothers and infants? Breastfeeding by mothers on effective treatment for HIV infection in high-income settings

- Profilassi neonato diverse LG
-
- DHHS: 6 settimane con NVP o AZT o entrambe
-
-

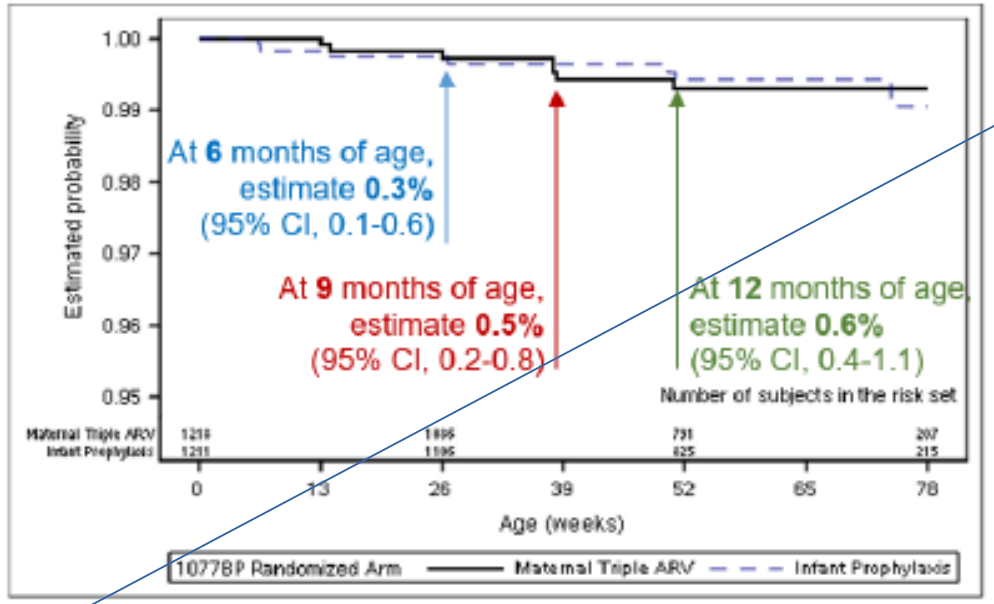
Allattamento al seno in HIV: é arrivata l'ora?

Dott.ssa Prati Francesca UO Malattie Infettive ASMN, Reggio Emilia

Bologna, 29 Settembre 2022

PROMISE Randomized Trial – Postpartum Component

- HIV+ mothers with CD4 ≥350 cells/mm3 and their uninfected breastfeeding infants randomized to start either maternal ART (n=1220) or infant NVP (n=1211) at 6-14 days postpartum at 14 sites in 7 countries.
- Plasma viral load measured at baseline and 6, 14, 26, and 50 weeks postpartum.



No statistically significant difference in probability of MTCT of HIV by study arm
Overall infant infections: 7 maternal ART, 7 infant NVP

Flynn P et al. JAIDS. 2018;77:383-92

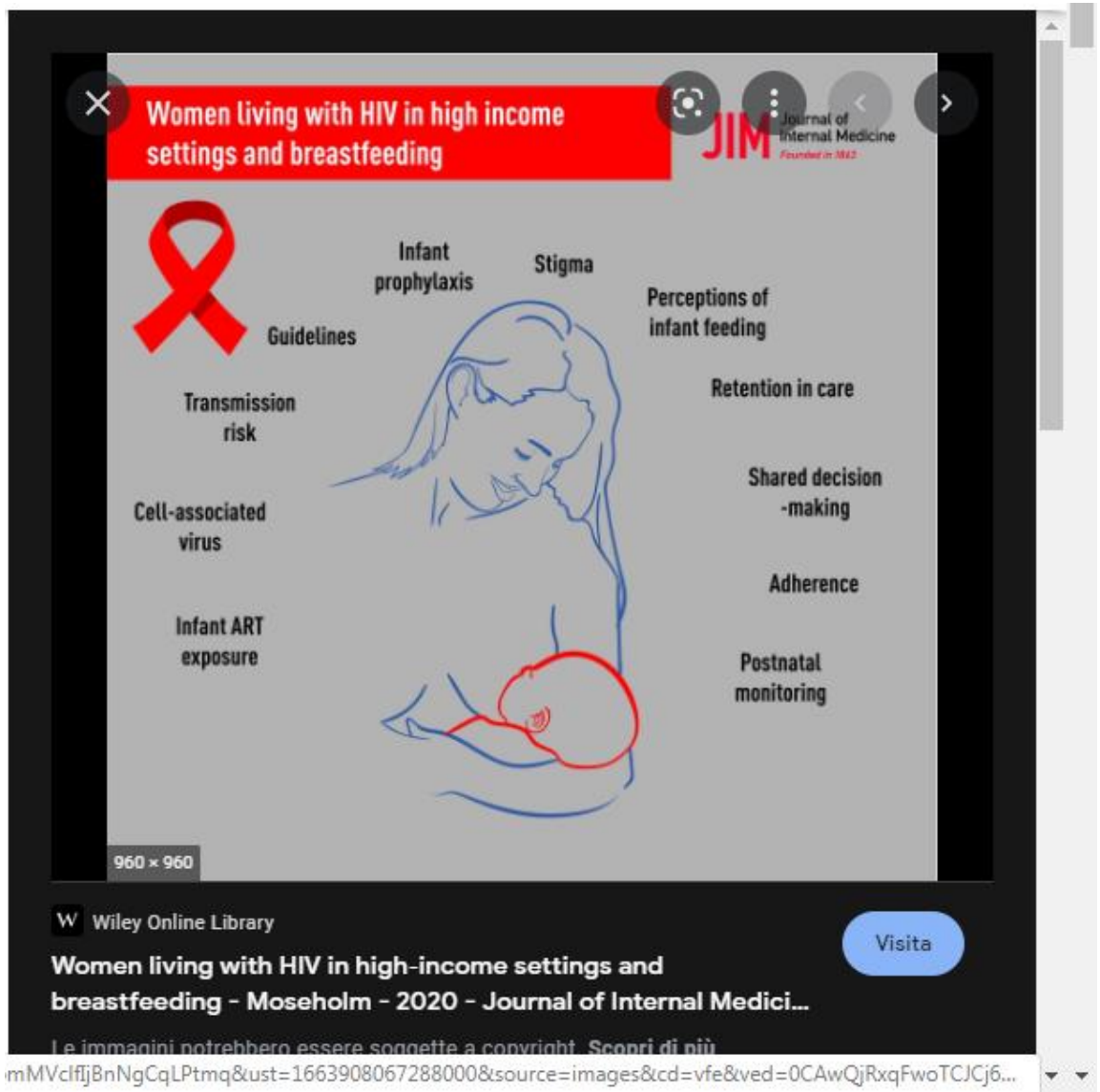
- Time-varying maternal viral load was significantly associated with infant infection in the **maternal ART** arm (HR 11.0, 95% CI 2.5-56.1) but not the infant NVP arm.
- Of 7 postnatal infections in the maternal ART arm, **2 had plasma VL <40 c/mL in the visit closest to infection** (1 week 36: <40 at all visits; 1 week 14, <40 at week14 but but 50-1000 at week 6).

1,220 mothers on ART

VL <40 copies/mL

2 cases of MTCT
1 at Week 14
1 at Week 36

Flynn et al. 22nd IAS Conference, Amsterdam, July 2018, Abs. THPEB115


Women living with HIV in high income settings and breastfeeding
JIM Journal of Internal Medicine
Infant prophylaxis
Stigma
Perceptions of infant feeding
Guidelines
Retention in care
Transmission risk
Shared decision -making
Cell-associated virus
Adherence
Infant ART exposure
Postnatal monitoring
960 × 960
Wiley Online Library
Visita
Women living with HIV in high-income settings and breastfeeding - Moseholm - 2020 - Journal of Internal Medici...
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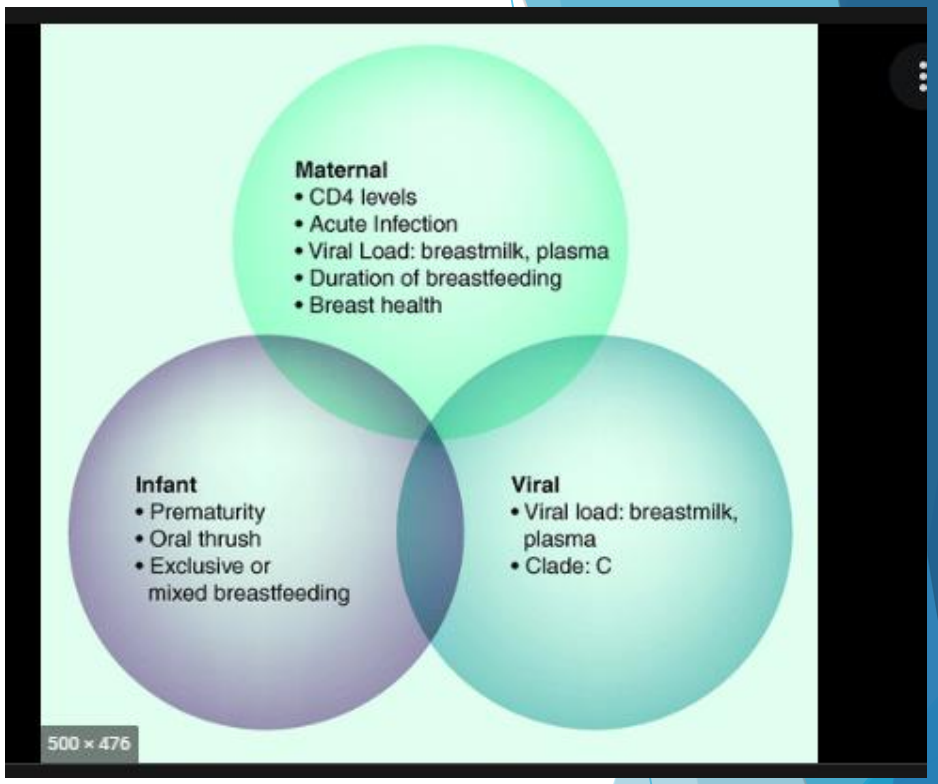

Maternal
• CD4 levels
• Acute Infection
• Viral Load: breastmilk, plasma
• Duration of breastfeeding
• Breast health
Infant
• Prematurity
• Oral thrush
• Exclusive or mixed breastfeeding
Viral
• Viral load: breastmilk, plasma
• Clade: C
500 × 476

LINEE GUIDA a CONFRONTO SVIZZERE 2018

Established in 1871

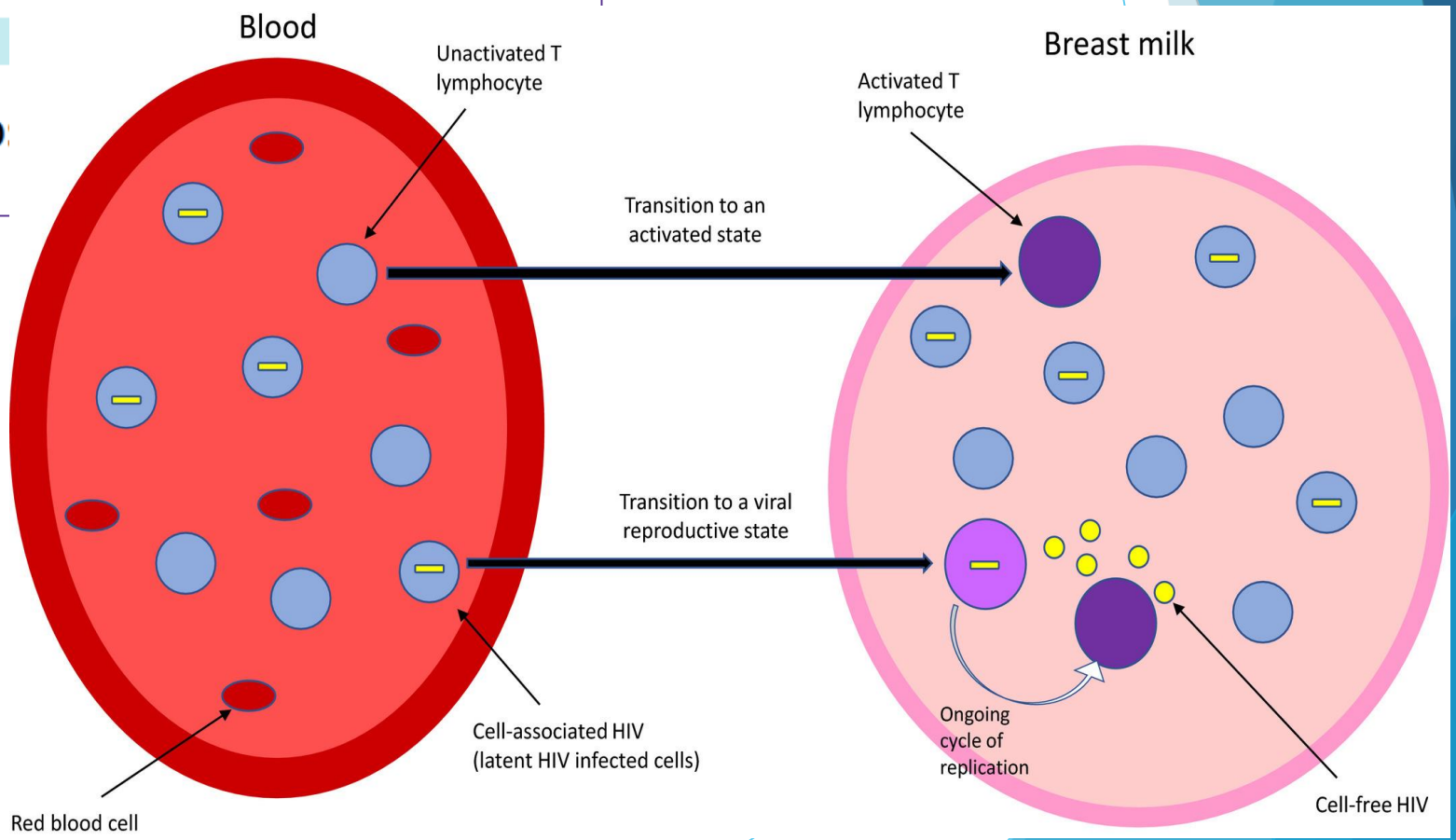
Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • www.smw.ch

Viewpoint | Published 29 July 2018 | doi:10.4414/smw.2018.14655
Cite this as: Swiss Med Wkly. 2018;148:w14655

Is breastfeeding for HIV-po
recommendable?



What Do We Know About Breast Milk HIV Transmission?

SUMMARY

Non-breastfeeding populations

If define "undetectable" = VL <50 c/mL

AND: Start ART prior to conception and plan pregnancy for after viral suppression is achieved

AND: Maintain ART and viral suppression throughout pregnancy

Breastfeeding populations

(or have extremely low risk, <1)

IF: Viral suppression <u>before</u> and <u>during</u> pregnancy <u>and</u> breastfeeding