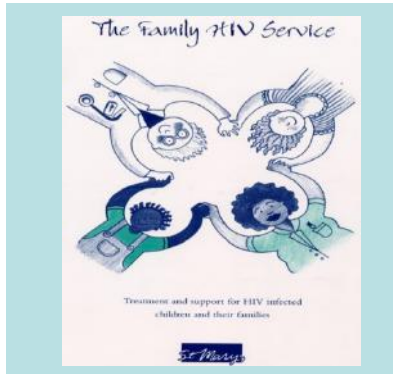


Breast Feeding for Women with HIV?

CHIVA / BHIVA



Hermione Lyall
Imperial Healthcare
NHS Trust
17.11.17



Acknowledgements:
Nell Freeman-Romilly, Pat Tookey, Claire Townsend,
Claire Thorne, Kate Francis, Helen Peters, Graham Taylor, Marc Lallement

Is it safe for me to breast feed my baby?

Scenario 1:

Well woman with HIV, 31 years old

First pregnancy - 20 weeks gestation

Conceived on ART, still on first line ART

VL < 50 for 5 years

CD4 count 770



*My family expect me to breast feed,
I also believe it's the right thing to do -*

*I have read the WHO guideline (2016)
→ it says breast is best for women with HIV
what would you advise?*

“God will cure me and my child”

Scenario 2:

G 5+0, 32/40 weeks, CD4 - 50, VL - 270,000

Denies HIV, refusing any treatment

for herself before delivery

for herself at delivery

for the infant after delivery

wants normal delivery



I want to breast feed – as I did with all my other kids

Risk of transmission to this infant?

9 yr old, 7 yr old, 5, yr old, 2 yr old – where are they, have they been tested?

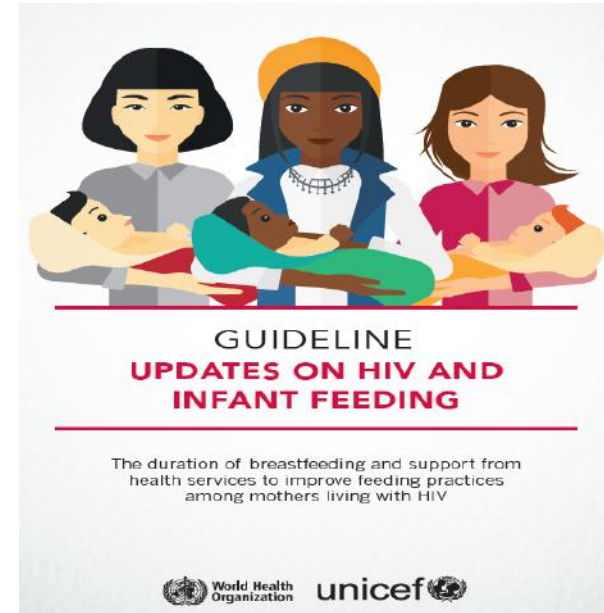


WHO Guideline on HIV & Infant feeding 2016

WHO recommends lifelong ART for everyone from the time they are first diagnosed with HIV infection.

This WHO guideline is intended mainly for countries with high HIV prevalence where diarrhoea, pneumonia and under-nutrition are common causes of infant mortality.

However, it may also be relevant to settings with a low prevalence of HIV depending on the background rates and causes of infant and child mortality



WHO Guidelines for Infant feeding 2016



Clinical Scenarios	WHO guidance for women with HIV
For how long should mothers with HIV breast feed?	<p>Mothers living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or longer, if → <i>(same as the general population)</i></p> <ul style="list-style-type: none"> • Has access to lifelong ART and HIV care • Exclusively breastfeeds for the first 6 months • Introduce appropriate complementary foods after 6 months and continue breastfeeding • Only stop once a nutritionally adequate and safe diet without breast milk can be provided
If a mother does not exclusively breastfeed: is mixed feeding with ART better than no breastfeeding at all?	<p>ART also reduces the risk of HIV transmission in mixed feeding</p> <p>Although exclusive breastfeeding is recommended - when on ART, mixed feeding is not a reason to stop breastfeeding</p>
Is a shorter duration of planned breastfeeding with ART better than no breastfeeding at all?	Any duration of breastfeeding is better than never initiating breastfeeding at all

British HIV Association (BHIVA) and Children's HIV Association (CHIVA) Position Statement on Infant Feeding in the UK

BHIVA/CHIVA Writing Group on Infant Feeding in the UK

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**BHIVA Guidelines 2017
Formula Feeding
Still advised**

Risk Factors for HIV transmission & Breast Feeding



Viral Load

CD4 count

HIV sero-conversion during BF

Mastitis

Cracked nipples

Duration of BF

Mixed feeding

Infant oral thrush

Major Risk Factors for MTCT

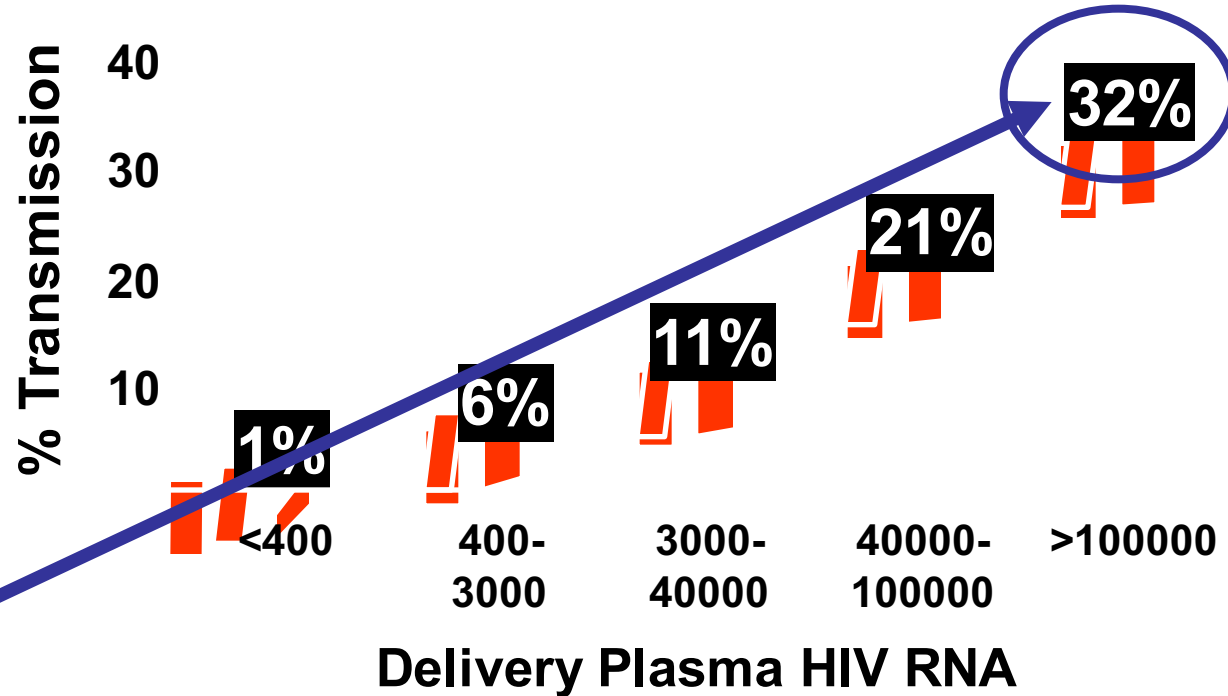
Maternal

Plasma viral load
CD4 count
Advanced HIV

Delivery

Premature delivery
Mode of delivery
Duration of rupture of
Membranes
Infection in the birth canal

Breast feeding
- No ART



Blattner W et al. WITS study, 1990-1999. *XIII AIDS Conf*,
July 2000, Durban S Africa (LBO4)

Prevention of HIV Transmission from Breastfeeding in Africa

H. Coovadia - Plenary abst 13 CROI 2007

NOT breast feeding is unsafe in developing countries

Early cessation of breastfeeding (<6 months) reduces HIV transmission but **increases** morbidity and mortality in infants born to HIV positive African women

Continued breast feeding **reduces** morbidity and mortality in **HIV infected** infants in Africa

***Balancing the risk of:
breast milk HIV transmission versus –
early weaning – malnutrition – gastroenteritis - death***

Duration & Pattern of Breastfeeding & Postnatal HIV Transmission : Pooled Analysis from West & South African Cohorts

Becquet R, et al PLoS ONE 4(10): e7397. 2009

N = 1195 infants, not perinatally infected, & breast fed

No maternal post natal ART

	<u>18 month HIV infection risk</u>
Less than 6 months BF	3.9% (2.3-6.5)
More than 6 months BF	8.7% (6.8 – 11.0)

Exclusive BF very similar to predominantly BF (only other liquids)

Solids in first 2 months of life 2.9 fold (1.1-8.0) ↑ risk of HIV

For breast feeding mothers advise → exclusive BF & **NO early solids**

West Africa - Ditrane-Plus and South Africa – Vertical Transmission study

Feeding and mother ***not on ART*** Risk of postnatal HIV transmission

Becquet R, et al PLoS ONE 4(10): e7397. 2009

Estimated postnatal risk of transmission:

Overall risk: 9.0/100 child-years
(95% CI 6.2–11.7)

Exclusive breastfeeding: 9.0/100 child-years
(95% SI, 6.0–12.1)

Predominant breastfeeding: 8.5/100 child-years
(95%SI, 1.2–18.1)

Breastfeeding plus solids: 41.2/100 child-years
(95%SI, 1.1–74.5)

Breast feeding mother no ART - infant PEP

ANRS 12174 - PROMISE Pre-EP

Nagot et al [Lancet](#). 2016 Feb 6;387(10018):566-73. doi: 10.1016/S0140-6736(15)00984-8.

RCT 1500 M-I pairs BurkinaFaso, South Africa, Uganda, Zambia

HIV-uninfected infants at day 7 - born to mothers not eligible for ART

Exclusive breastfeeding until 26th week of life

Cessation of breastfeeding at a maximum of 49 weeks

Randomised to: infant PEP - Lamivudine or Lopinavir/ritonavir

Primary endpoint → HIV-1 Tx - day 7 - 50 weeks of age

Secondary endpoints → safety (including resistance, adverse events and growth) & HIV-1-free survival until 50 weeks.

Infant Pre-EP

2009 -2012 enrolled 1273 infants → analysed 1236

615 → lopinavir–ritonavir

621 → lamivudine

17 HIV-1 infections (8 lopinavir/rit versus 9 lamivudine)

50 week cumulative HIV-1 infection rate – no difference

Lopinavir/rit 1·4% (95% CI 0·4–2·5)

Lamivudine 1·5% (0·7–2·5)

Clinical / biological severe adverse events – no difference

Lopinavir/rit 251 (51%) grade 3–4 events

Lamivudine 246 (50%) grade 3–4 events

Breast Feeding **not on ART** & Risk of HIV Transmission

Risk of HIV Transmission to the uninfected Infant after birth

Duration of Breast feeding

6 months

12 months

Mother in Africa Not on ART

Breast Feeding for 6 months exclusively

Ditrame / VTS

3.9%
(2.3-6.5)

8.7%
(6.8 – 11.0)*

Mother in Africa Not on ART

Breast Feeding for 6 months exclusively

Infant on daily Pre-EP

Pre-EP trial (3TC/LPV/r)

PROMISE trial (NVP)

PROMISE
0.3% (0.1-0.6)

PROMISE
0.6% (0.4–1.1)

Pre-EP
1.5% (0.7–2.5)



African data

*Each additional month of BF beyond 6 mths of age → 1% risk of HIV (95%CI, 0.5–1.7)

How many women with HIV are breastfeeding in the UK (that we know of)?

NSHPC data on breastfeeding (collected since 2012)

~ 1200 deliveries to women with HIV per year in UK

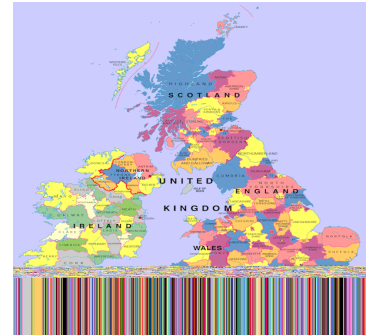
40 children reported breastfed since 2012 (all maternal VL <50)

~ 7 (0.6%) per year, no trend over time

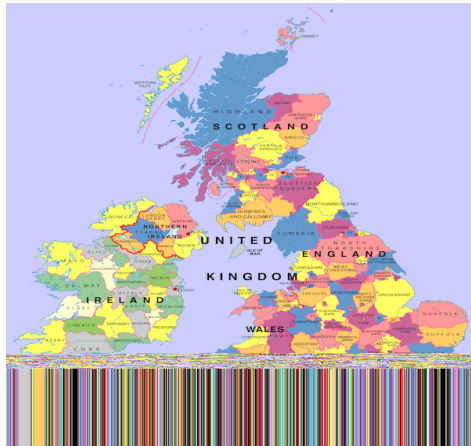
No transmissions reported to date

Duration of breast feeding: 1 day - > 1 year

On-going surveillance very important



What can we learn from African Studies on ART and Breastfeeding?



Postnatal HIV transmission in breastfed infants of HIV-infected women **on ART**- meta-analysis

Bispo S et al. Journal of the International AIDS Society 2017, 20:21251

Reviewed studies 2005 to 2015 – 11 studies selected

All mother advised to exclusively breast feed for 6 months

Outcomes: overall & postnatal HIV Tx at 6, 9, 12, 18 months:

Overall 6 months Tx rate: 3.54% (95% CI: 1.15–5.93%)

Overall 12 months Tx rate: 4.23% (95% CI: 2.97–5.49%)

Postnatal 6 months Tx rate: 1.08 (95% CI: 0.32–1.85)

Postnatal 12 months Tx rate: 2.93 (95% CI: 0.68–5.18)

ART mostly provided for PMTCT and did not continue beyond 6 months postpartum

No study provided data on mixed feeding & transmission risk

Breast Feeding on **ART** & Risk of HIV Transmission





African data

Risk of HIV Transmission to the uninfected Infant after birth Duration of Breast feeding	Mother in Africa On ART (most ART only for 6 months) Breast Feeding for 6 months exclusively then adding complementary foods Meta-analysis	Mother in Africa On ART (long term ART) Breast Feeding for 6 months exclusively then adding complementary foods PROMISE trial Taha et al IAS 2016
6 months	1.08% (0.32-1.85)	0.3% (0.1-0.6)
12 months	2.93% (0.68-5.18)	0.6% (0.4-1.1)
18 months	No data	-
24 months	No data	

Not Yet Published

UK - Breast Feeding on **ART** & Risk of HIV Tx

<p>Risk of HIV Transmission to the uninfected Infant after birth</p> <p>Duration of Breast feeding</p>	<p>Mother in UK On ART (long term)</p> <p>Formula Feeding</p> 	<p>Mother in UK On ART (long term)</p> <p>Breast Feeding</p> 	<p>Mother in Africa On ART (most ART only for 6 months)</p> <p>Breast Feeding for 6 months exclusively then adding complementary foods</p> <p>Meta-analysis*</p>	<p>Mother in Africa On ART (long term)</p> <p>Breast Feeding for 6 months exclusively then adding complementary foods</p> <p>PROMISE trial**</p>
6 months	0	No data	1.08% (0.32-1.85)	0.3% (0.1-0.6)
12 months	0	No data	2.93% (0.68-5.18)	0.6% (0.4-1.1)
18 months	0	No data	No data	-
24 months	0	No data	No data	-

Breast feeding in Tanzania on ART with Viral Load monitoring

KIULARCO Study Luoga^{et al} EACS PS5/5

2013-15

methods

Mothers initiated ART before delivery

Exclusively breastfed for ≥ 5 months

Infants - negative HIV DNA-PCR at age 4-12 weeks

Mothers – VL once or twice up to 11 months post delivery

Infants - HIV antibody test at 18 months

Breast feeding in Tanzania on ART with Viral Load monitoring

KIULARCO Study Luoga^{et al} EACS PS5/5

Results

211 women - 215 pregnancies, 225 infants (10 twins)

Median time on ART 23 months (IQR 4-52)

VL measured twice in 53% (114/215) of pregnancies

During breastfeeding

91% (197/215) VL < 1000 copies/mL

75% (162/215) VL < 100 copies/mL

Duration of breastfeeding

52 weeks (IQR 44-54) (181 infants)

Breast feeding in Tanzania on ART with Viral Load monitoring

KIULARCO Study Luoga^{et al} EACS PS5/5

Results – Infants to July 2017

Lost to follow-up	10% (22/225)
Transferred	2% (4/225)
Died	8% (18/225)
Still breastfeeding	2% (4/225)

Remaining infants (78% (175/225)) HIV infected

(mother VL < 1000 copies/mL) at one month post-delivery)

(no interrupted ART during breastfeeding)

No transmission from mothers with suppressed VL test results

breastfeeding → very low risk of transmission when blood VL is suppressed

Can we say U = U for breast feeding ?

Breastfeeding with maternal antiretroviral therapy or formula feeding to prevent HIV postnatal mother-to-child transmission in Rwanda

“AMATA”
study

Cécile Alexandra Peltier^a, Gilles François Ndayisaba^a,
Philippe Lepage^b, Johan van Griensven^a, Valériane Leroy^c,
Christine Omes Pharm^a, Patrick Cyaga Ndimubanzi^a,
Olivier Courteille^a and Vic Arendt^d

Non randomised
Interventional cohort study:

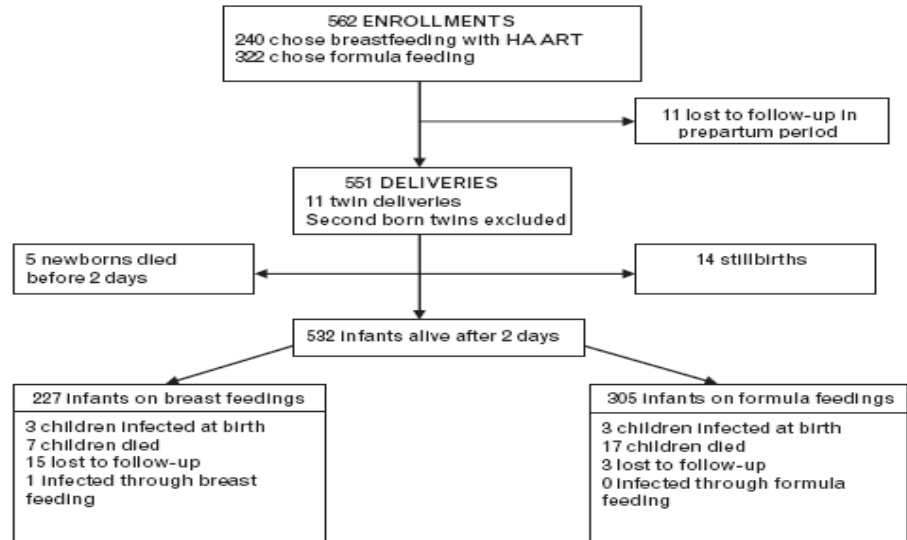
BF + ART for 6 months

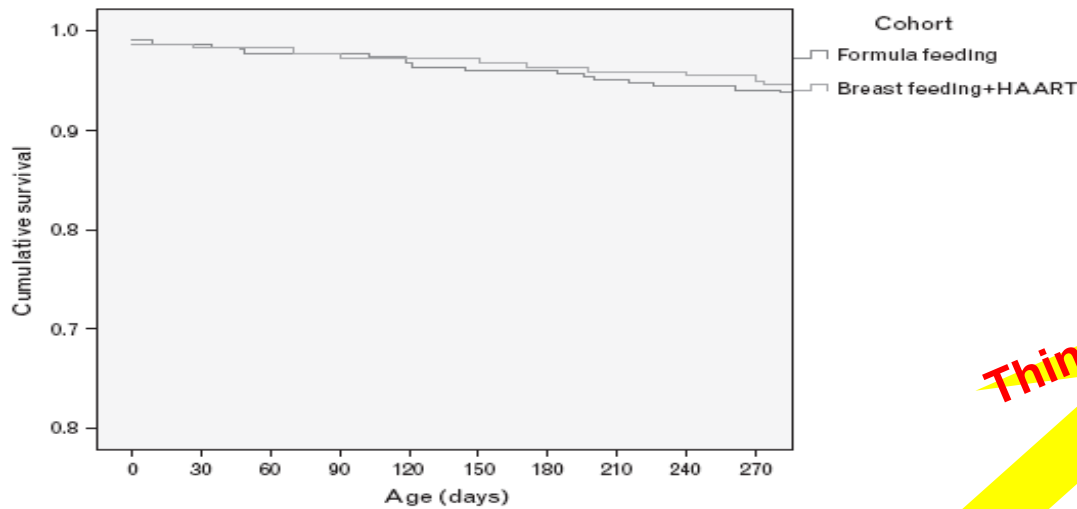
V

Formula feeding

All received ART from 28wks

9mth cumulative risk of
HIV transmission rate & HIV free
survival





**Things can go unexpectedly wrong
Mother - severe vomiting**

Overall HIV transmission → 1.3% (7 infants – 6 in-utero infections)

One infant in the BF group infected at 3-7 months

9 month post natal infection risk with BF 0.5% (95% CI – 0.1-3.4%; $p = 0.24$)

9 month cumulative mortality:

3.3% in BF group (95% CI – 1.6 – 6.9%)

5.7% in FF group (95% CI – 3.6 – 9.2%) ($p = 0.2$)

HIV free survival at 9 months:

95% in BF group (95% CI – 91-97%)

94% in FF group (95% CI – 91-96%) ($p = 0.66$)

What we learn from African Studies on ART and Breastfeeding



Maternal ART
& Formula feeding
MTCT - 0%



Maternal ART /
infant ART
& Breast feeding
MTCT ~ 0.6 - 3%

UK - Breast Feeding on ART

African infants: ↑ Death from gastro (HIV +/-); ↓ Death from

European infants: Women want to do it – is it safe?

For the mother with plasma

VL < 50, & on ART after delivery?

Will the milk plasma VL be < 50?

What about transmission

to the infant through

Risk of mother's exposure to ART?

Risk of transmitted resistance in a
breast milk HIV infected infant?

Still some unanswered questions



Antiretroviral Drug Penetration into Breast Milk and Infant Plasma: BAN Study

Corbett A et al. 15th CROI Boston, MA, 2008 Abs 648

Sampled maternal, infant, breast milk in 20 women receiving postnatal maternal ART at 6, 12, 24 weeks PP. Analysis of all sampling time points:

	3TC (N=47)	NVP (N=21)	NFV (N=26)
Breast Milk / Maternal Plasma	2.6 (1.1-3.5)	0.7 (0.5-0.9)	0.08 (0.04-0.14)
Infants Plasma / Breast Milk	0.01 (0.004-0.03)	0.2 (0-0.3)	ND
Infants Plasma / Maternal Plasma	0.06 (0.01-0.1)	0.12 (0-0.3)	ND

Infant ART exposure during breast feeding – is this a concern?

Testing for HIV in infants born to breast feeding mothers with HIV on ART

Formula Fed Infant

4/5 blood tests

Birth HIV PCR

High risk infants - additional week 2-3
HIV PCR

Week 6 HIV PCR (off PEP)

Week 12 HIV PCR (off PEP)

Loss of HIV antibody at 18 months

Breastfed Infant

4 + X monthly blood tests

Birth HIV PCR

Clinical review & monthly HIV PCR when
Breast feeding

Week 4 HIV PCR (off BF)

Week 8 HIV PCR (off BF)

Loss of HIV antibody at 18 months

Back to our 2 women – breast feeding?



Scenario 1

Conceived on ART
still on first line ART
VL < 50 for 5 years

FF ~ 0% risk of HIV Tx
BF ~ 0.6% risk of HIV Tx (at 12 mths)

Open conversations,
Likely to work well with MDT

We would support BF



Scenario 2

CD4 - 50, VL - 270,000
Does not believe in HIV
Not on ART

FF ~ 15% risk of HIV Tx
BF ~ 30% risk of HIV Tx

Not engaging with MDT, unlikely to
comply with ART, → antenatal SC
referral

*We **not** would support BF*

Breastfeeding Advice as Harm Reduction

“People will make more health-positive choices if they have access to adequate support, empowerment, and education”.

Levison, J., Weber, S. and Cohan, D. (2014). Breastfeeding and HIV-Infected Women in the United States: Harm Reduction Counseling Strategies. *Clinical Infectious Diseases*, 59(2), pp.304-309.

Patient Information on HIV and Breastfeeding

Which simplifies complex (and changing)
information

+

Accounts for patient's wishes

+

Persuasively guides patients towards the safest
approach

Two Patient Leaflets

1 – for all pregnant women with HIV:

‘Feeding Your New Baby’

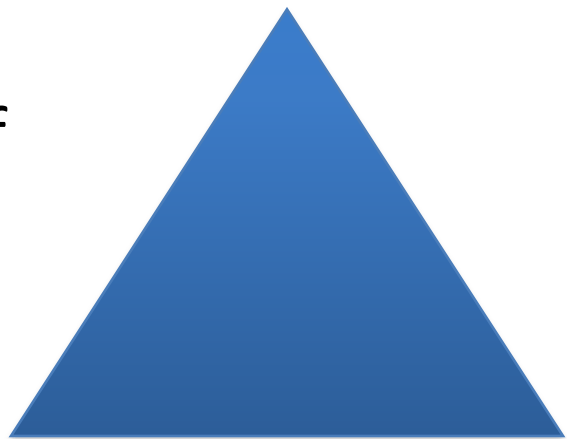
2- for pregnant women with HIV who want to breastfeed:

‘Living with HIV and Breastfeeding Your New Baby’

The Safer Triangle

No virus

Only breastfeed if
your HIV is
undetectable.



Happy tums

Only breastfeed if
both you and your
baby are free from
tummy problems

Healthy breasts for mums

Only breastfeed if your breasts
and nipples are healthy with no
signs of injury or infection.

Conclusion – Answering your child's question? New BHIVA guidelines coming out - 2017

NSHPC – enhanced surveillance

Safest thing is to formula feed – zero risk

breast feeding is an option, but women must understand →
they are taking a risk, even if very small

Any women who wishes to breast feed:

Highly adherent to ART

VL<50, ideally throughout pregnancy

Short a duration as possible

Engaged with MDT

Willing to be followed up monthly

Trouble shooting advice leaflet – the safer triangle



PACIFY Study
Questionnaire to understand
views of pregnant women with HIV
on breast feeding in UK –
Let us know if you would like to join!



Thank You

