Closing the gaps on prevention of mother-to-child transmission of HIV - EMTCT

Medical Research Council Clinical Trials Unit at University College London

Di Gibb

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PENTA 20

Outline

- Epidemiology of HIV in Pregnancy
- Timing and rates of mother-to-child transmission of HIV
- Treatment as prevention for MTCT
  - High income AND Globally
- Antenatal testing – the UK story
- EMTCT in the era of triple ART
  - Comprehensive programme to prevent MTCT
  - Triple elimination of HIV, Syphilis, Hepatitis B
- Breastfeeding – updated guidance
- Challenges
  - COVID and effects of funding cuts
- Where are we now
- HIV-exposed uninfected children

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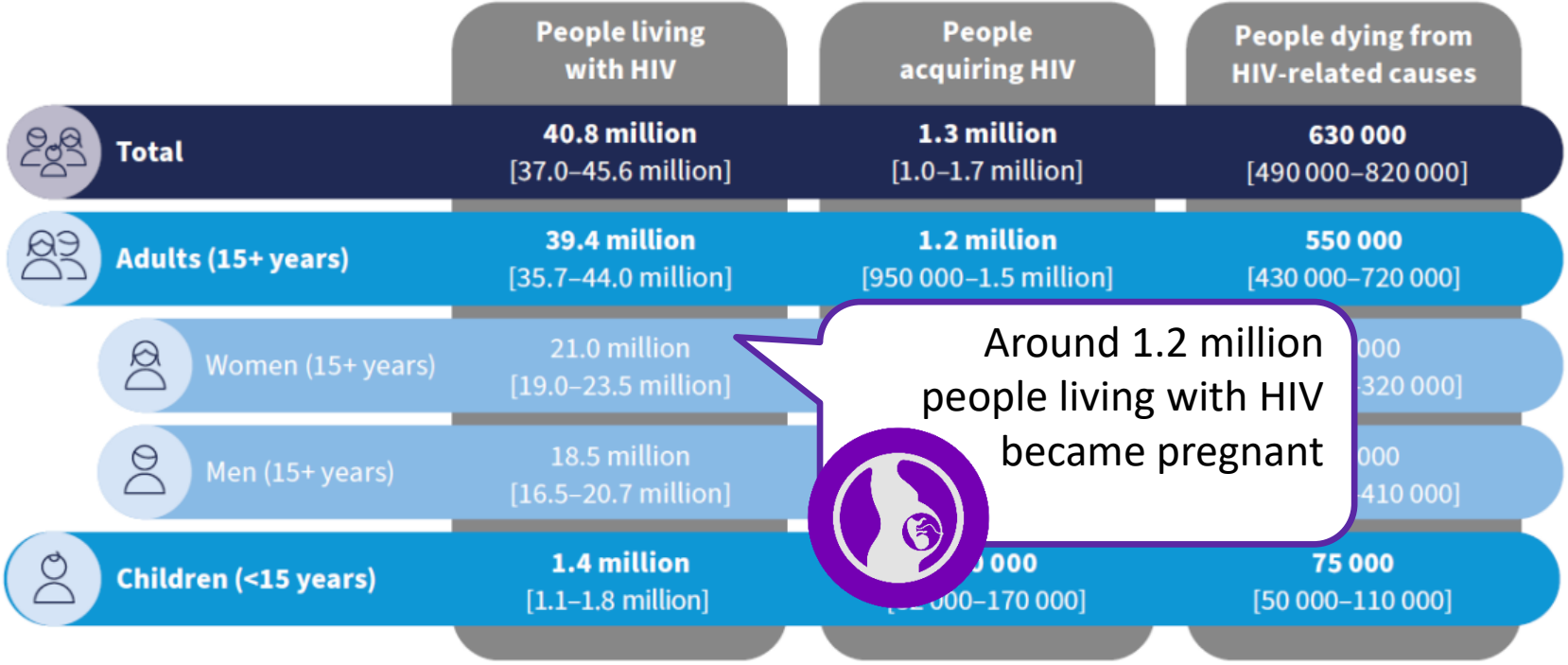
Summary of the global HIV epidemic, 2024



Source: UNAIDS/WHO estimates, 2025.

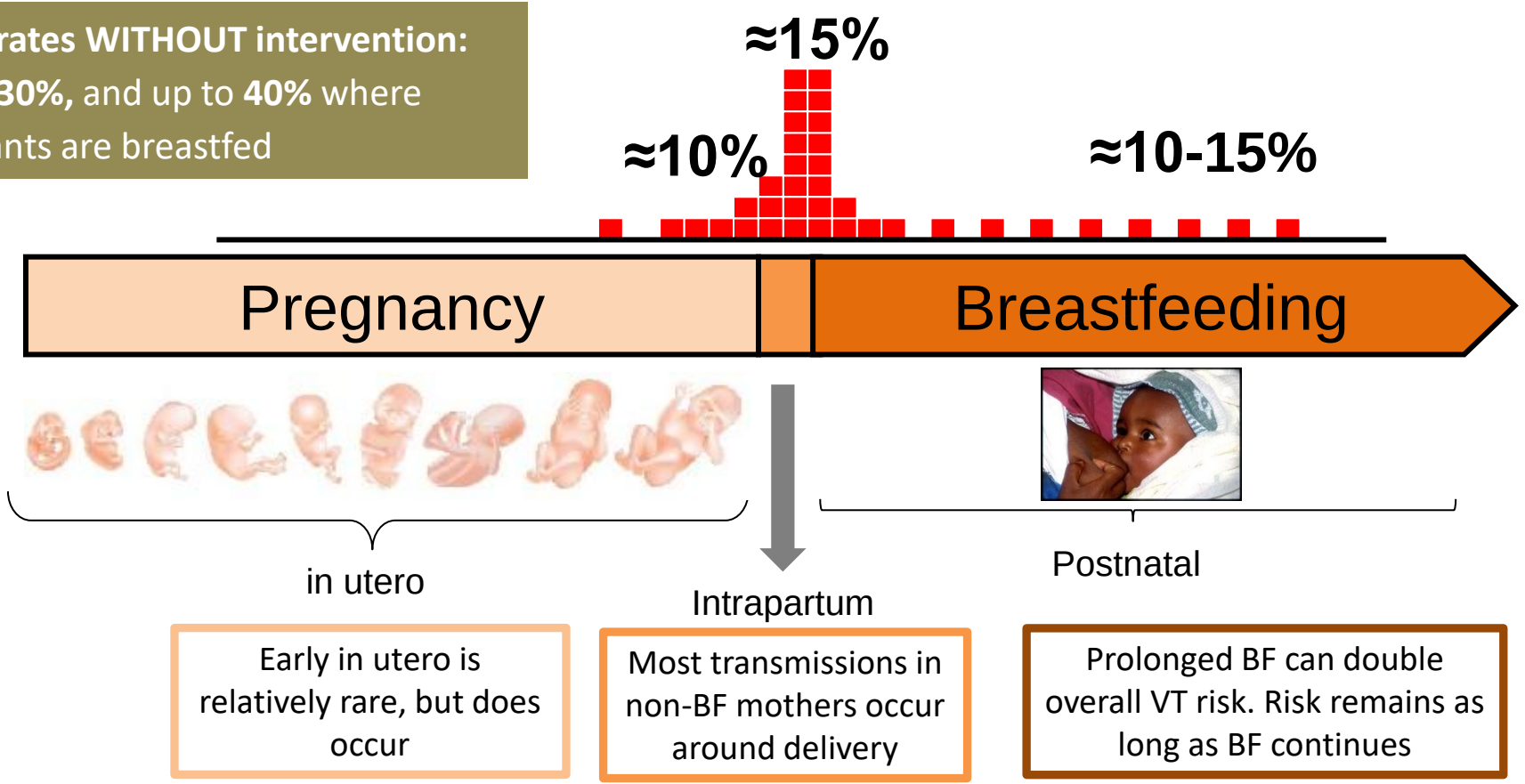
- ≈90% live in sub-Saharan Africa
- Vast majority of child HIV infections are due to vertical transmission

Children (<15 years)	**1.4 million** [1.1–1.8 million]	**120 000** [82 000–170 000]	**75 000** [50 000–110 000]

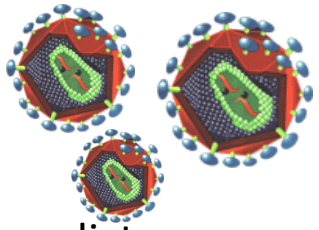
Source: UNAIDS/WHO estimates, 2025.

Timing and rates of vertical transmission of HIV

VT rates WITHOUT intervention:
15-30%, and up to **40%** where infants are breastfed



VT risk factor: viral load



- **Plasma HIV RNA level** (viral load, VL) in pregnancy is the best individual predictor of risk of VT
- VT risk increases with increasing VL

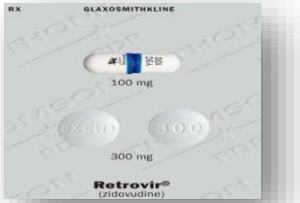
Results from the Women and Infants Transmission Study

Plasma HIV RNA	N	MTCT %
<1000 copies/ml	57	0%
1000-10,000	193	16.6%
10,001-50,000	183	21.3%
50,001-100,000	54	30.9%
>100,000	64	40.6%

Garcia et al NEJM 1999

Other risk factors include:

- Low CD4 count
- Symptomatic disease
- Co-infections (e.g., syphilis, HSV-2, malaria)
- Vaginal delivery
- Duration of rupture of membranes
- Chorioamnionitis
- Infant sex
- Mixed feeding
- Mastitis



1987:
HIV Treatment Era Begins

- AZT (ZDV) approved by FDA in March 1987 for treatment of adults

The New England
Journal of Medicine

Volume 317 JULY 23, 1987 Number 4

THE EFFICACY OF AZIDOTHYMIDINE (AZT) IN THE TREATMENT OF PATIENTS WITH AIDS AND AIDS-RELATED COMPLEX

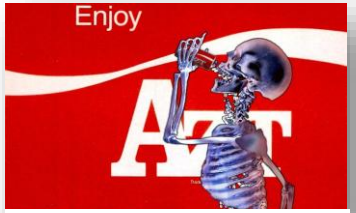
A Double-Blind, Placebo-Controlled Trial

MARGARET A. FISCHL, M.D., DOUGLAS D. RICHMAN, M.D., MICHAEL H. GRIECO, M.D., J.D., MICHAEL S. GOTTLIEB, M.D., PAUL A. VOLBERDING, M.D., OSCAR L. LASKIN, M.D., JOHN M. LEEDOM, M.D., JEROME E. GROOPMAN, M.D., DONNA MILDVAN, M.D., ROBERT T. SCHOOLEY, M.D., GEORGE G. JACKSON, M.D., DAVID T. DURACK, M.B., D.PHIL., DANNIE KING, PH.D., AND THE AZT COLLABORATIVE WORKING GROUP

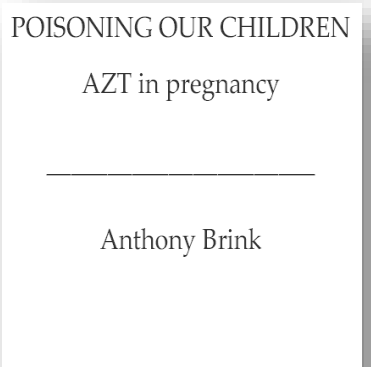
- Despite concerns about AZT toxicity, given high mortality of paediatric AIDS, paediatric and obstetric researchers proposed giving AZT to infected pregnant women to reduce MTCT.

“Treatment as Prevention”: PMTCT With AZT in 1991

- Giving a potentially toxic drug to pregnant women and exposing their fetuses was highly controversial.



- Before approving the 076 trial, the FDA held a special public meeting to discuss the ethics of giving AZT to pregnant women.



The AZT Regimen in PACTG 076 Was Designed to Target Multiple Potential Time Points of Transmission

Pregnancy

enrollment
CD4 >200

AZT 100 mg
5 times daily

TARGET:

In Utero
(after 1st trimester)

Labor/Delivery

AZT IV 2 mg/kg
→ 1 mg/kg/hr

TARGET:

Intrapartum

Pre-Exposure Prophylaxis (PrEP)

Infant

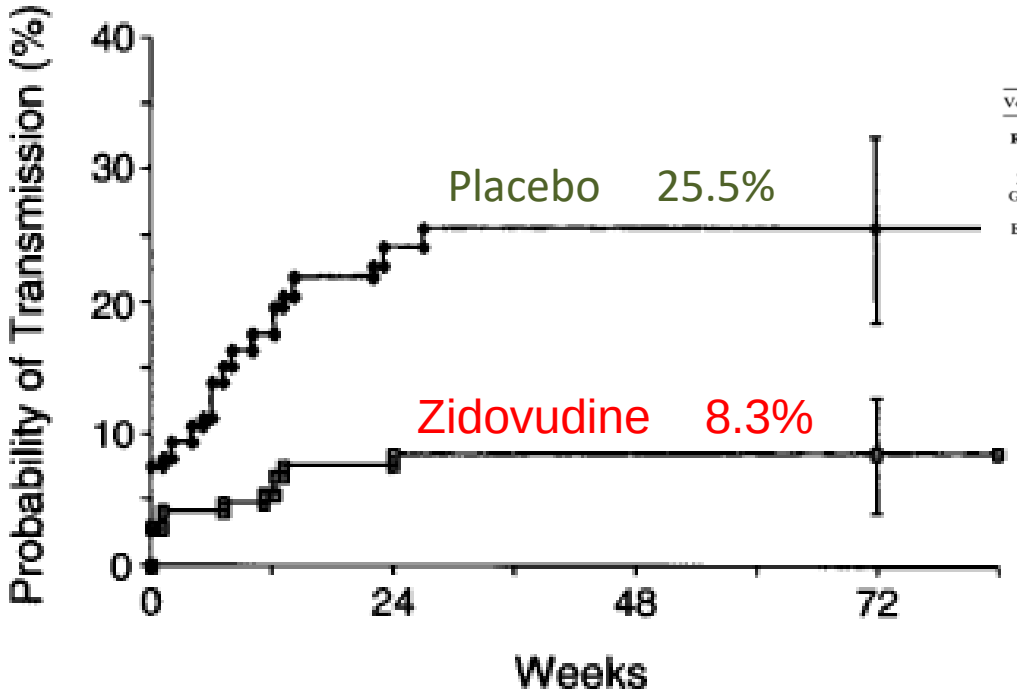
AZT 2 mg/kg
q 6 hr x 6 weeks

TARGET:

Postpartum

Post-Exposure Prophylaxis (PEP)

DSMB Stopped PACTG 076 Trial at First Interim Efficacy Analysis in February 1994



The New England
Journal of Medicine

Volume 331 NOVEMBER 3, 1994 Number 18

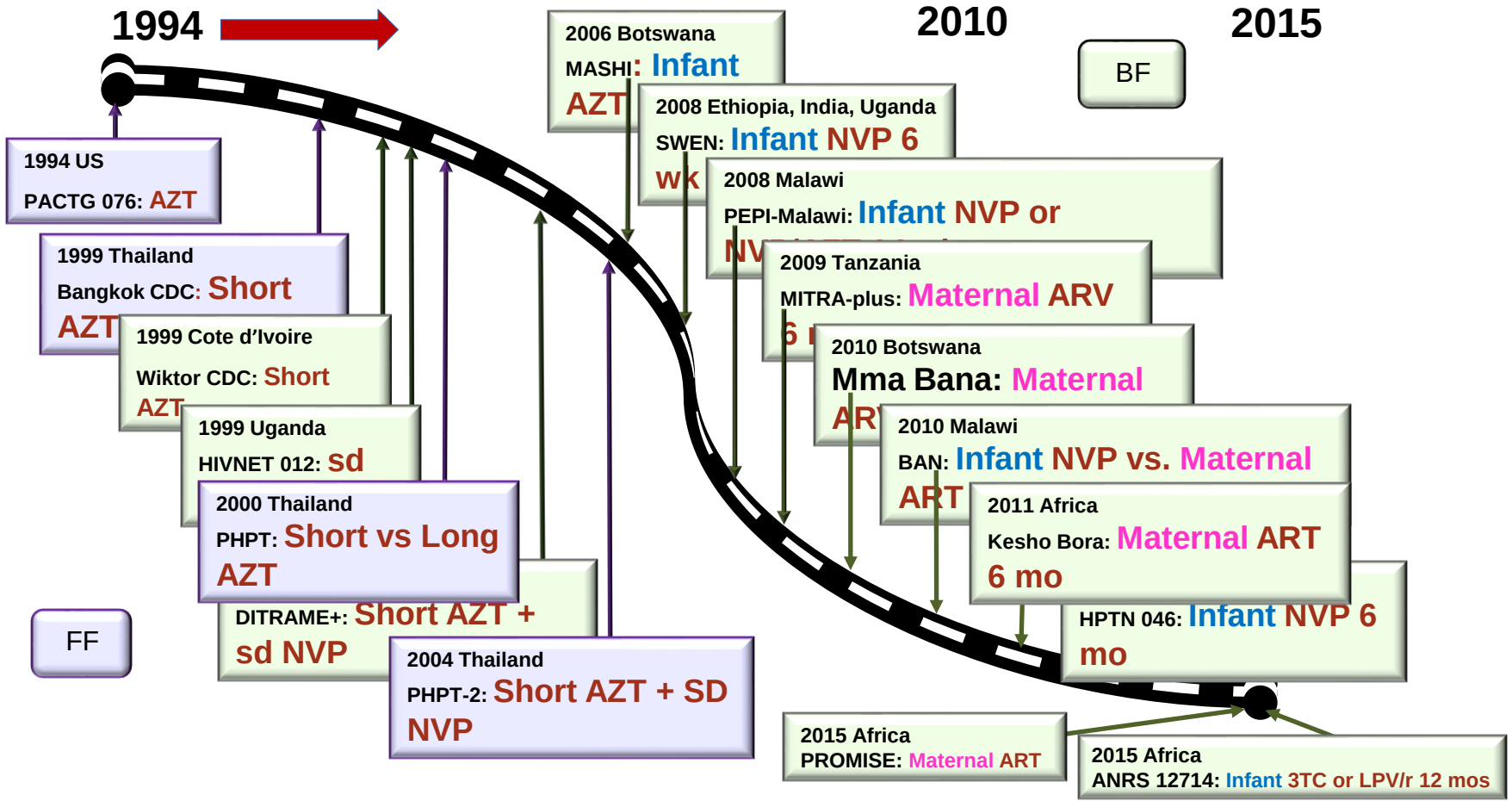
REDUCTION OF MATERNAL–INFANT TRANSMISSION OF HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 WITH ZIDOVUDINE TREATMENT

Edward M. Connor, M.D., Rhoda S. Sperling, M.D., Richard Gelber, Ph.D., Pavel Kiselev, Ph.D., Gwendolyn Scott, M.D., Mary Jo O'Sullivan, M.D., Russell VanDyke, M.D., Mohammed Bey, M.D., William Shearer, M.D., Ph.D., Robert L. Jacobson, M.D., Eleanor Jimenez, M.D., Edward O'Neill, M.D., Brigitte Bazin, M.D., Jean-François Delfraissy, M.D., Mary Culnane, M.S., Robert Coombs, M.D., Ph.D., Mary Elkins, M.S., Jack Moye, M.D., Pamela Stratton, M.D., and James Balsley, M.D., Ph.D., for the Pediatric AIDS Clinical Trials Group Protocol 076 Study Group*

67% Reduction Transmission

First demonstration of treatment as prevention!

Building the Evidence Road for Preventing Mother-to-child transmission of HIV



Strategies and guidelines have evolved as evidence has grown

2001

2004

2006

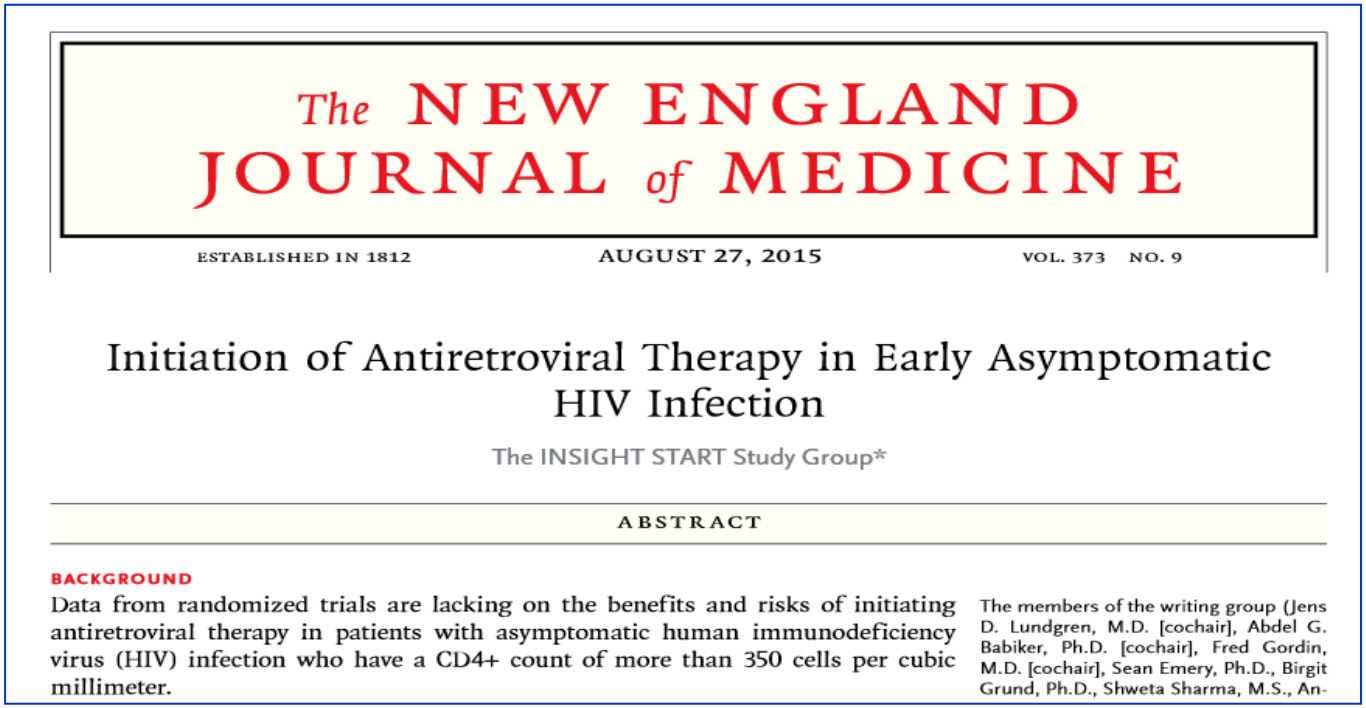
2010

2013

	2001	2004	2006	2010	2013
Treatment	No rec	ART if CD4 <200	ART if CD4 <200	ART if CD4 ≤350	ART if CD4 ≤500
PMTCT	4 weeks AZT or sdNVP	AZT from 28 wks + sdNVP	AZT from 28 wks + sdNVP + AZT/3TC 7d "tail"	**Option A** AZT/sdNVP + infant NVP if BF **Option B** ART preg/BF	**Option B** ART preg/BF **Option B+** Life-long ART

START Trial

IAS 2015
vancouver, canada
8th IAS Conference on HIV Pathogenesis, Treatment & Prevention 19-22 July 2015
IAS2015.ORG



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 27, 2015 VOL. 373 NO. 9

Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

ABSTRACT

BACKGROUND

Data from randomized trials are lacking on the benefits and risks of initiating antiretroviral therapy in patients with asymptomatic human immunodeficiency virus (HIV) infection who have a CD4+ count of more than 350 cells per cubic millimeter.

The members of the writing group (Jens D. Lundgren, M.D. [cochair], Abdel G. Babiker, Ph.D. [cochair], Fred Gordin, M.D. [cochair], Sean Emery, Ph.D., Birgit Grund, Ph.D., Shweta Sharma, M.S., An-

July 2015

Strategies and guidelines have evolved as evidence has grown

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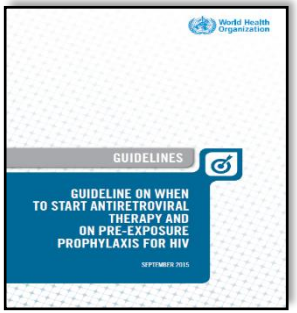
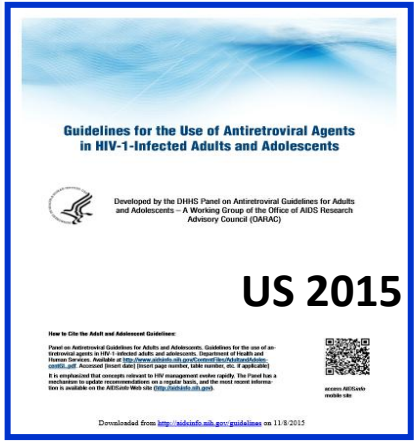
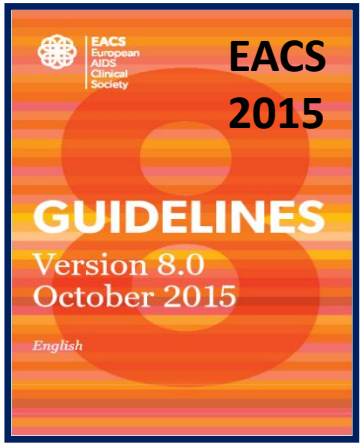


2015 TREAT ALL Strong recommendation



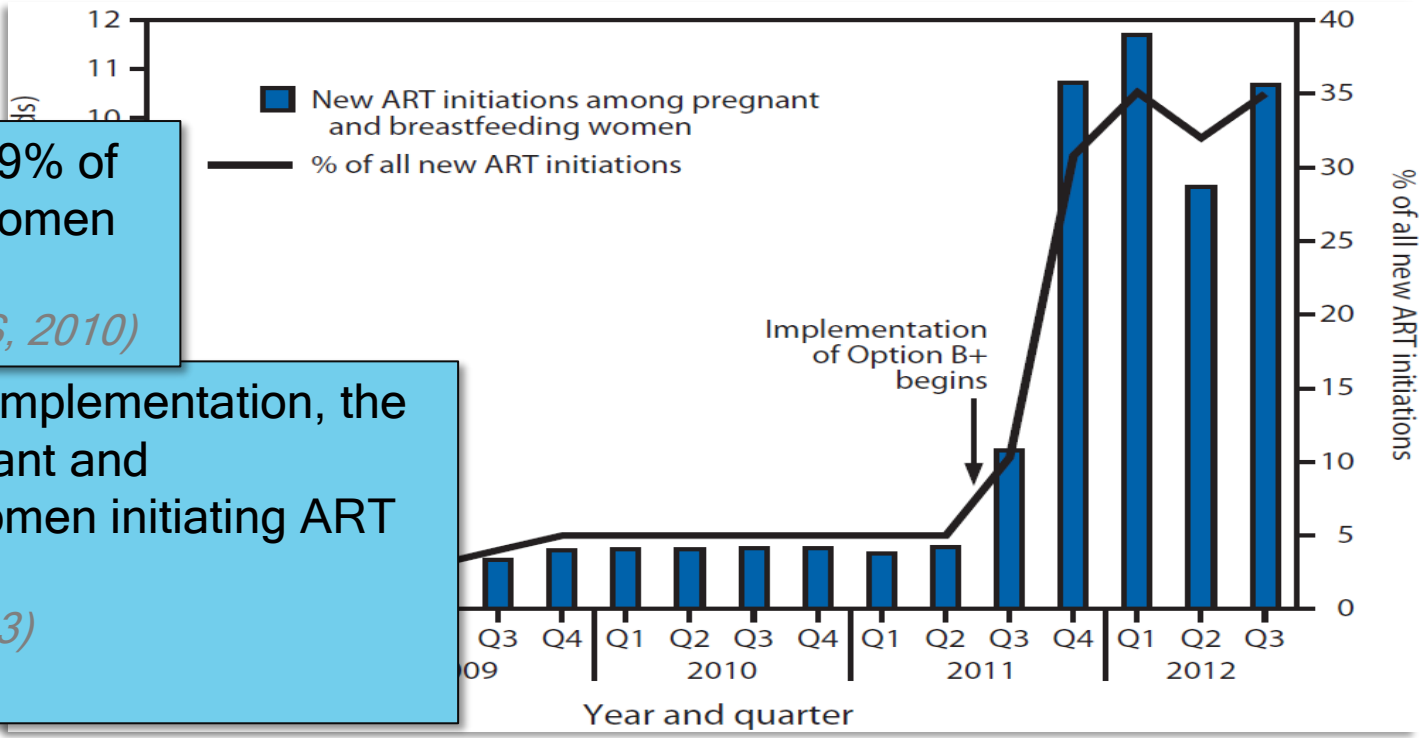


Lifelong ART started shortly after diagnosis for all, as part of a public health approach, is a key element of PVT

B Plus in Malawi – starting in 2011

2004-2008, only 9% of HIV+ pregnant women started on ART
(Braun et al, JAIDS, 2010)

In 1st year of B+ implementation, the number of pregnant and breastfeeding women initiating ART **increased 748%**
(CDC, MMWR 2013)



New ART initiations among pregnant and breastfeeding women, percentage of all new ART initiations attributed to this population, Malawi 2008-2012 (*CDC, MMWR 2013*)

New Vision, Uganda, January 28, 2015

30 NEW VISION, Wednesday, January 28, 2015 REGIONAL NEWS

New HIV prevention strategy yields results

By Cornes Lubanpakene

"…..reduction in the number of HIV-positive children born by HIV positive mothers **from 6% to 2%**, following the introduction of the option B+ treatment"

Gulu inmates get skills

GULU

By Arnest Tumwesige

A total of 43 inmates at Gulu Prison have received entrepreneurship training to help them explore business opportunities after serving their sentences.

The training targeted inmates who are about to complete their sentences.

"It is important to have skills to explore the business world so that you can start a new life," said Stephen Ocaya of Advance Africa, one of the sponsors of the training.

This was at a function in the prison library on Friday, during which inmates were awarded certificates.

The programme, which has been introduced to inmates of Lira and Kitgum districts, will run for three years.

Margaret Obonyo, the district prisons commander, said the rehabilitation of inmates has always been a challenge due to lack of funding.

"We are supposed to equip them with skills and upon release, do a follow-up to see how they are faring in the community," she noted.

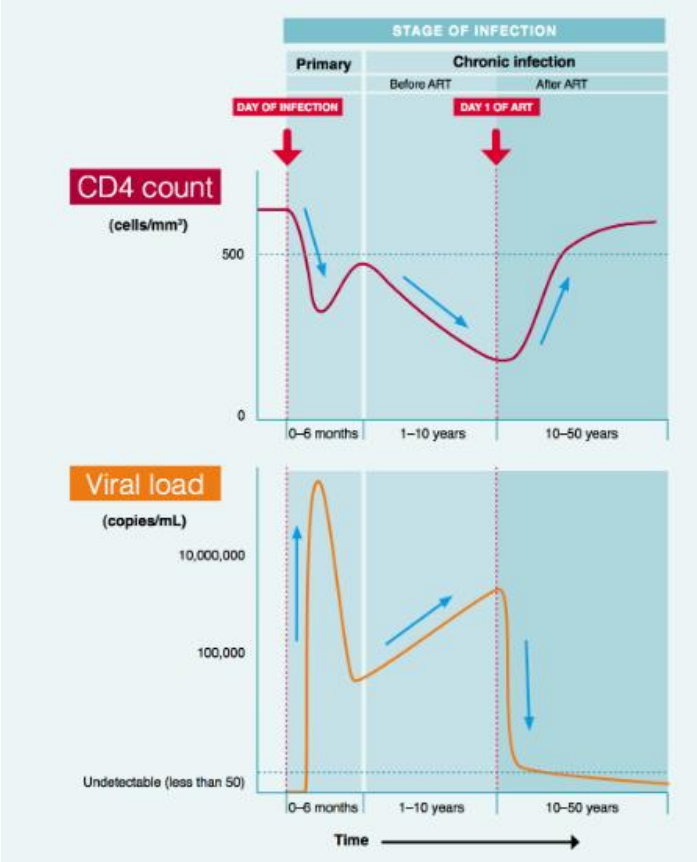
Obonyo added that despite the challenges, Uganda Prisons Services is the best in rehabilitating inmates in Africa and the seventh in the world, a standard which she said should be maintained.

"I encourage inmates to use the skills attained to start businesses," she added.

Wilfred Orwiya, speaking on behalf of the inmates, said learning new skills reduces the likelihood of indulgence in crime by ex-convicts.

How do antiretrovirals work to reduce vertical transmission?

- Diminish maternal plasma viral load to undetectable levels
- Help restore maternal immunity and general health
- Decrease HIV induced inflammation, in the placenta in particular
- Antiretrovirals that cross the placenta or that are administered to the infant (i.e., as postnatal prophylaxis) provide fetal/infant pre/post exposure prophylaxis



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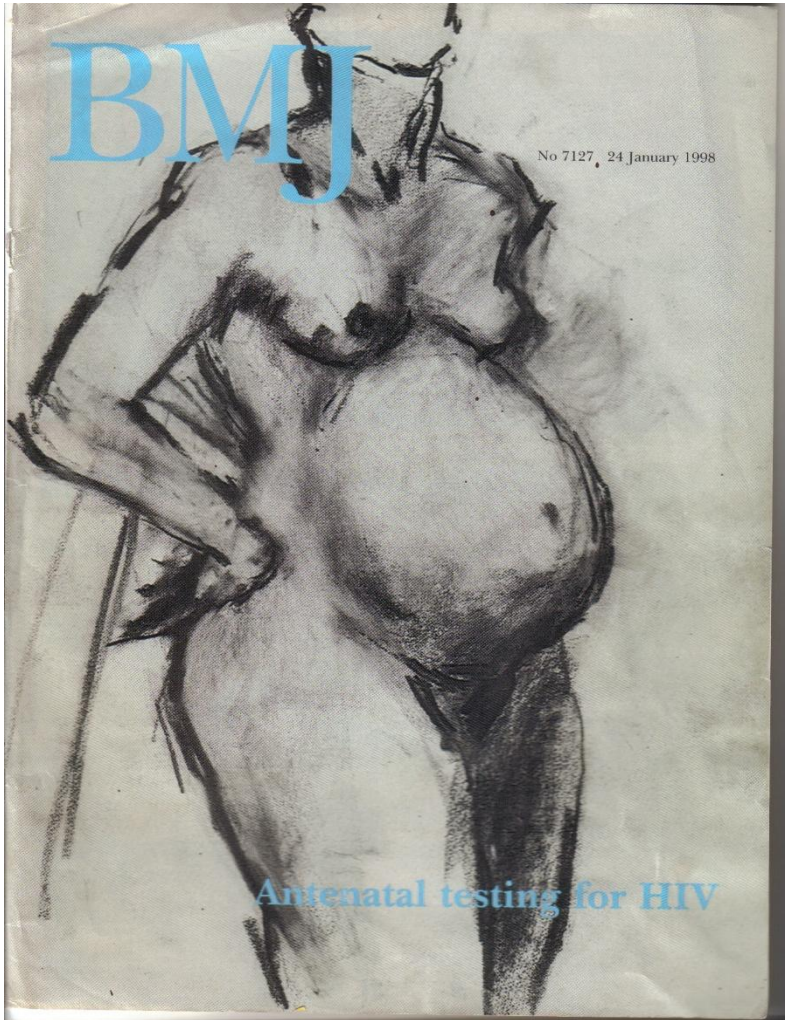
Antenatal HIV Testing

- prevention of HIV transmission to the child
- Cotrimoxazole prophylaxis to babies
- opportunity for giving information about HIV infection, sexual health
- potential to increase HIV awareness and decrease stigmatisation

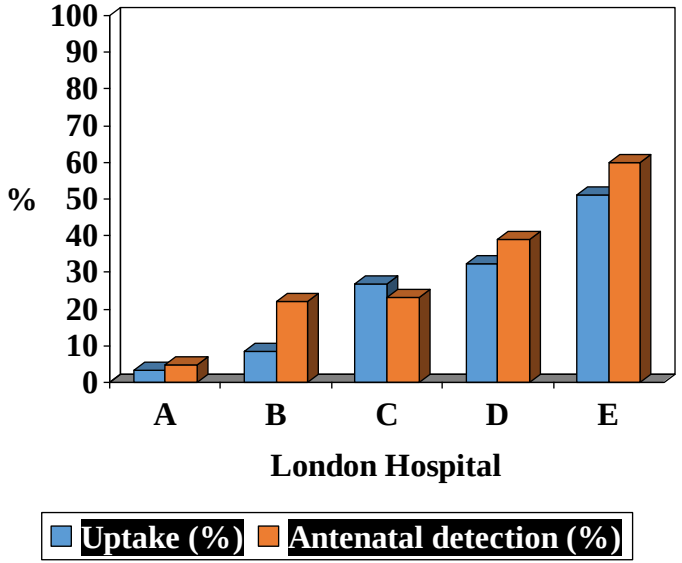
British Medical Journal 24 Jan 1998



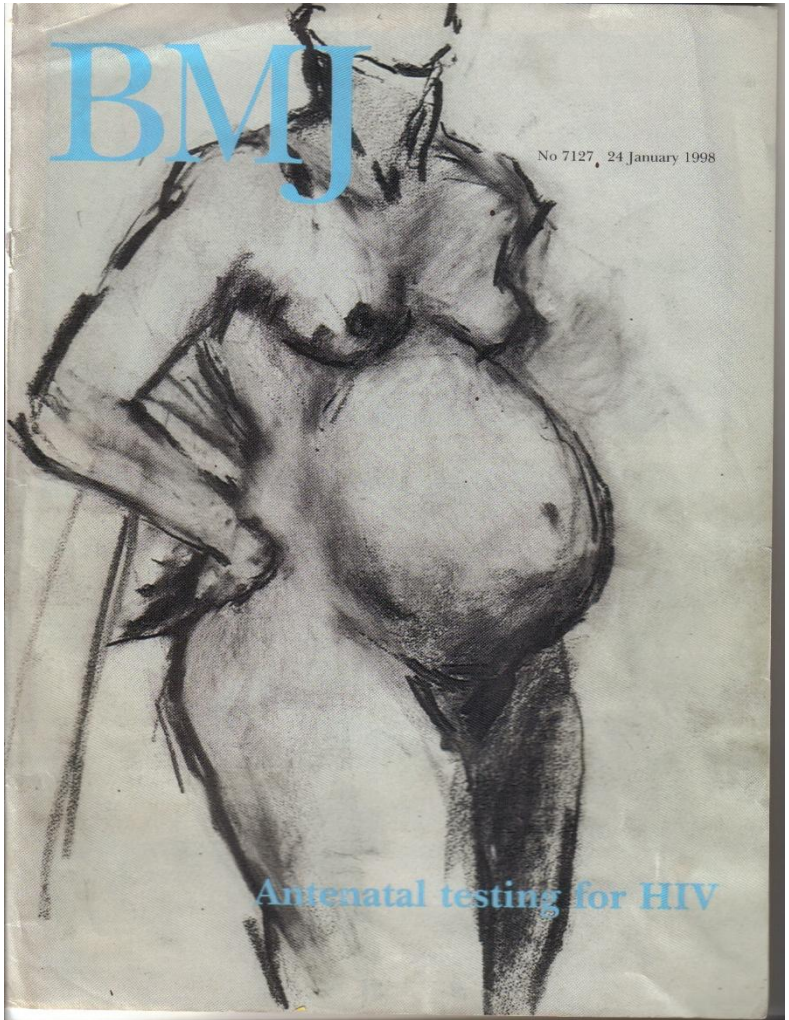
Antenatal HIV testing

Has been done badly in Britain and needs to improve

Editorial



British Medical Journal 24 Jan 1998



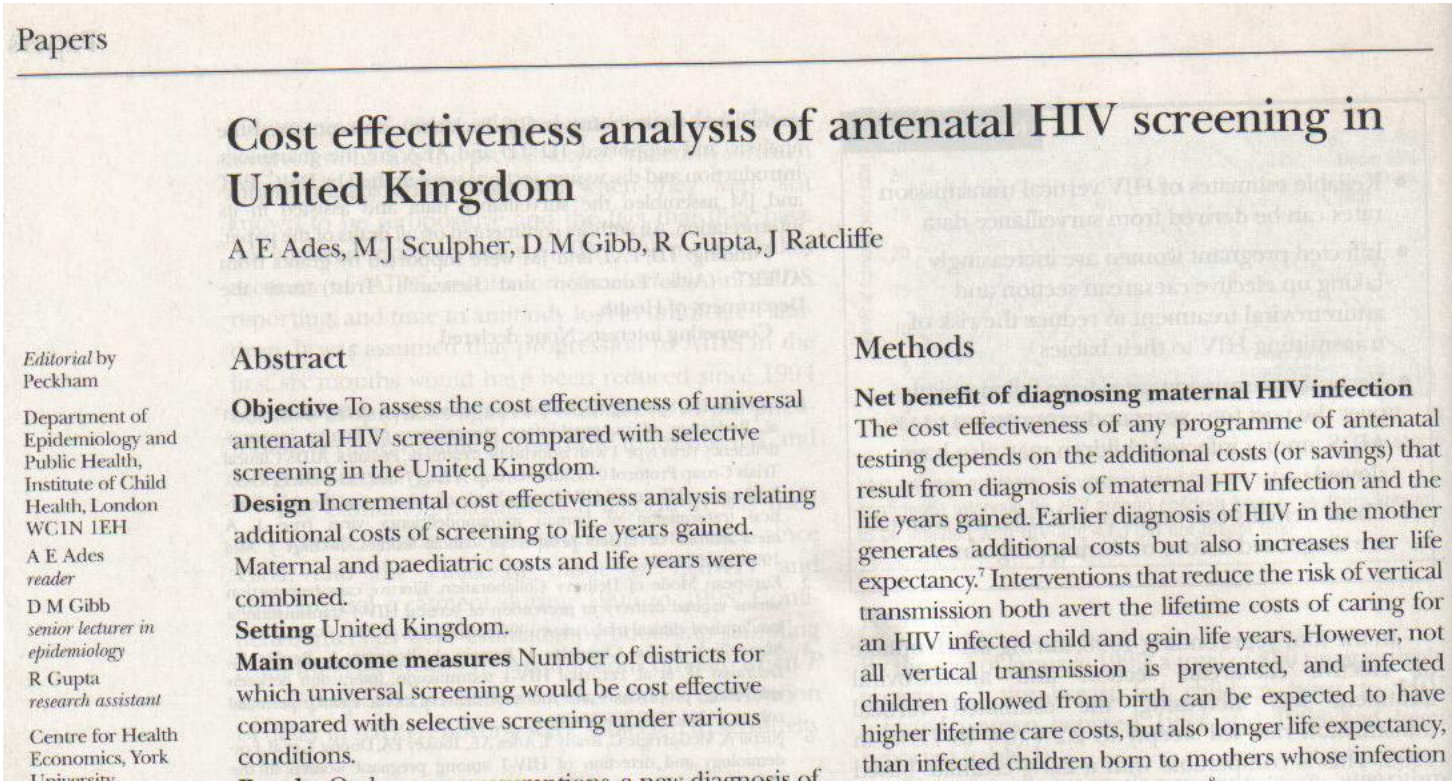
Antenatal HIV testing

Has been done badly in Britain and needs to improve

Editorial

The advantages of ascertaining a pregnant woman's HIV positive status before delivery are clear

…..Yet, …in Britain we are failing to test pregnant women for HIV and, as a result, to reduce the rate of vertical transmission



Papers

Cost effectiveness analysis of antenatal HIV screening in United Kingdom

A E Ades, M J Sculpher, D M Gibb, R Gupta, J Ratcliffe

Editorial by Peckham

Department of Epidemiology and Public Health, Institute of Child Health, London WC1N 1EH

A E Ades
reader

D M Gibb
senior lecturer in epidemiology

R Gupta
research assistant

Centre for Health Economics, York

Abstract

Objective To assess the cost effectiveness of universal antenatal HIV screening compared with selective screening in the United Kingdom.

Design Incremental cost effectiveness analysis relating additional costs of screening to life years gained. Maternal and paediatric costs and life years were combined.

Setting United Kingdom.

Main outcome measures Number of districts for which universal screening would be cost effective compared with selective screening under various conditions.

Methods

Net benefit of diagnosing maternal HIV infection

The cost effectiveness of any programme of antenatal testing depends on the additional costs (or savings) that result from diagnosis of maternal HIV infection and the life years gained. Earlier diagnosis of HIV in the mother generates additional costs but also increases her life expectancy.[7] Interventions that reduce the risk of vertical transmission both avert the lifetime costs of caring for an HIV infected child and gain life years. However, not all vertical transmission is prevented, and infected children followed from birth can be expected to have higher lifetime care costs, but also longer life expectancy, than infected children born to mothers whose infection

BMJ 1999

Universal Antenatal HIV Screening would be cost-effective ***throughout*** the UK

1) **Intercollegiate Guidelines (Royal Colleges of Midwifery, O&G and Paediatrics)**

2) **DOH Health Service Circular 1999/183;1999** ‘*HIV test should be offered and recommended to all pregnant women.’ National targets set*

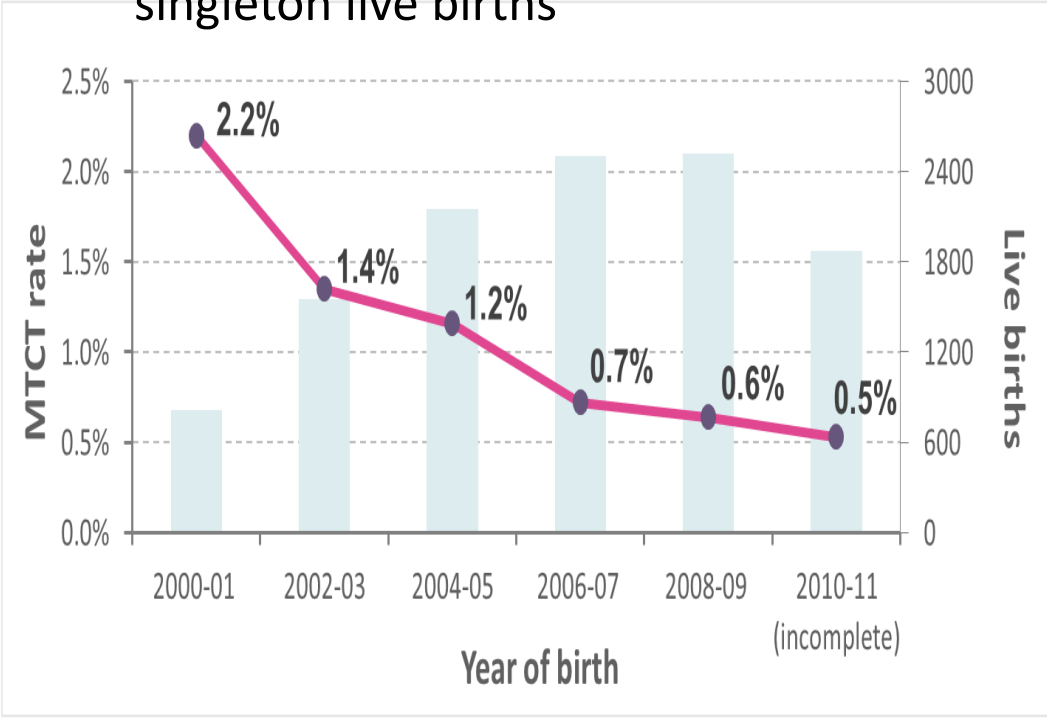
UK and Ireland

National Study of HIV in Pregnancy and Childhood
NSHPC

Universal offer of HIV testing in pregnancy 1999

MTCT rates 2000-2011

- 33 infected infants among 5788 singleton live births



"Virtual elimination" of MTCT in Europe

Country	MTCT	Time period
France	**1.0%**	2005-2009
Italy	**1.0%**	2005-2010
Denmark	**0.5%**	2000-2008
Sweden	**0.6%**	1999-2003
Spain	**1.6%**	2000-2007
Ukraine	**4.1%**	2008-2010
Russia	**3-4%**	2010
UK	**0.57%**	2007-2011

Jasseron et al 2011, von Linstow et al 2010, Naver et al 2006, Chiappini et al 2011, Prieto et al 2012, ECS unpublished data, Personal comm. Inga Latysheva

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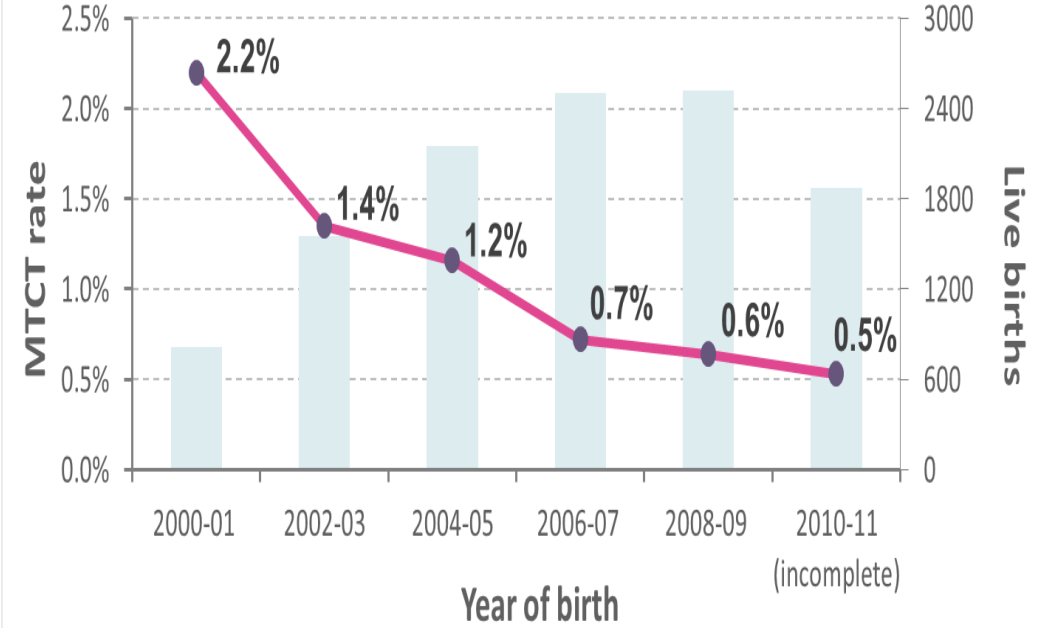

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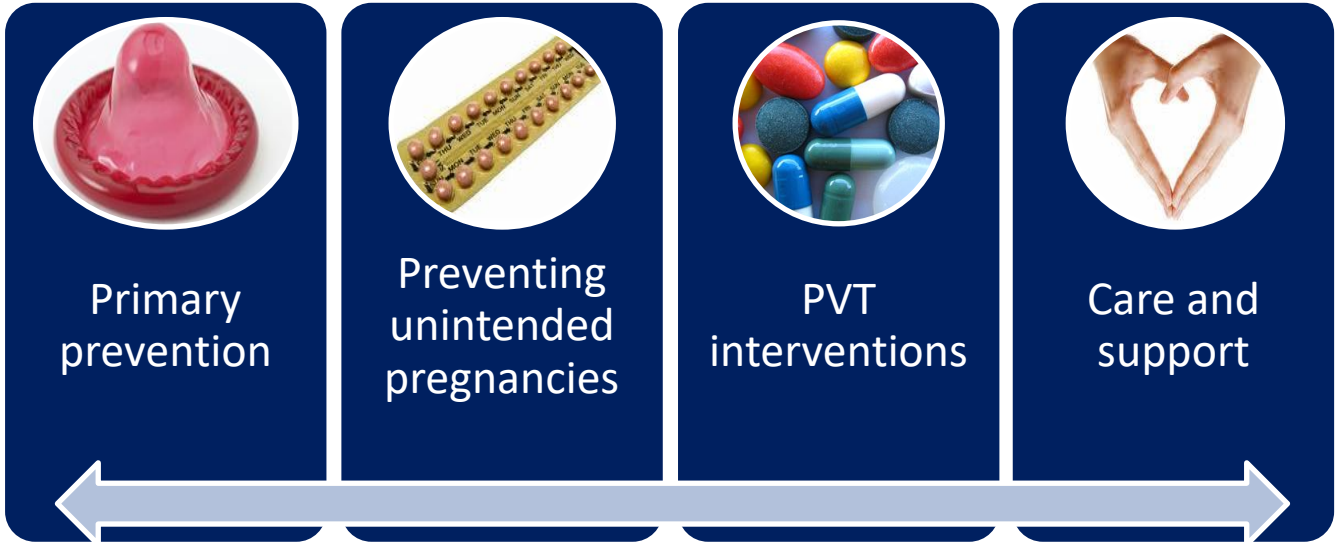
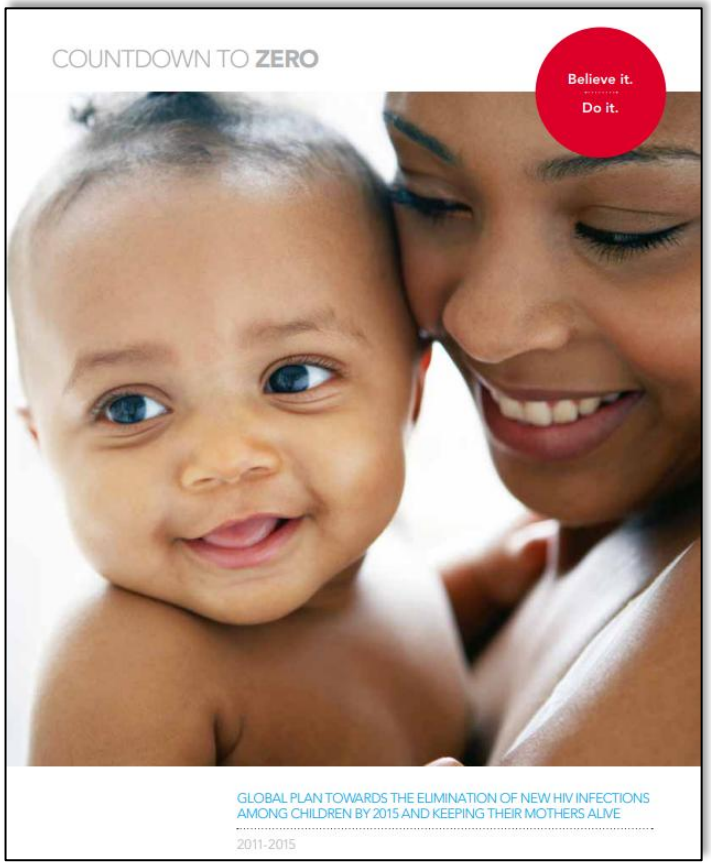
Components of a comprehensive programme to prevent HIV infection in infants

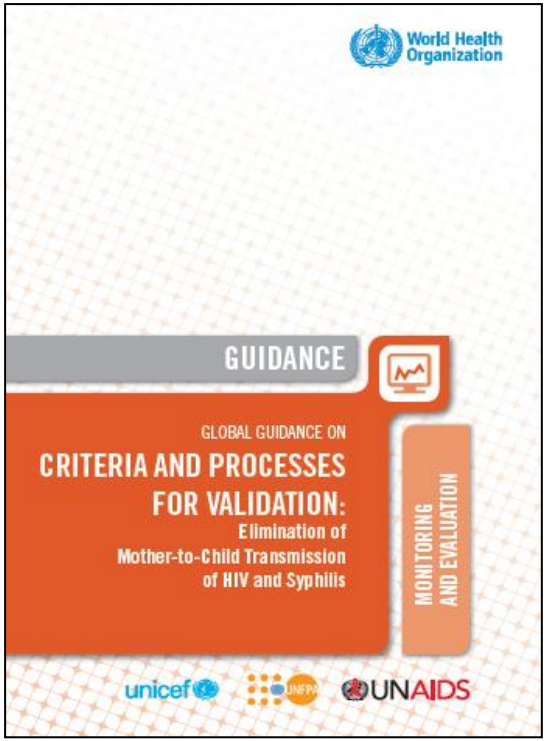


“Elimination of MTCT” / “EMTCT”

- Commitment to eliminate vertical transmission of HIV **as a public health threat**
- **2010**: the Pan American Health Organization (PAHO) set the original goal of EMTCT of HIV and syphilis by 2015
- **2011**: **UNAIDS Global Plan** towards the Elimination of New HIV Infections Among Children by 2015 and Keeping their Mothers Alive
- **2014**: WHO publishes first edition “**Global Guidance on Criteria and Process for Validation: Elimination of HIV and Syphilis**”



EMTCT validation



Impact elimination targets

HIV

- A case rate of <50 cases per 100,000 live births
- A VT rate <5% in breastfeeding populations or <2% in non-breastfeeding populations

Syphilis

- A case rate of <50 cases of congenital syphilis per 100,000 live births

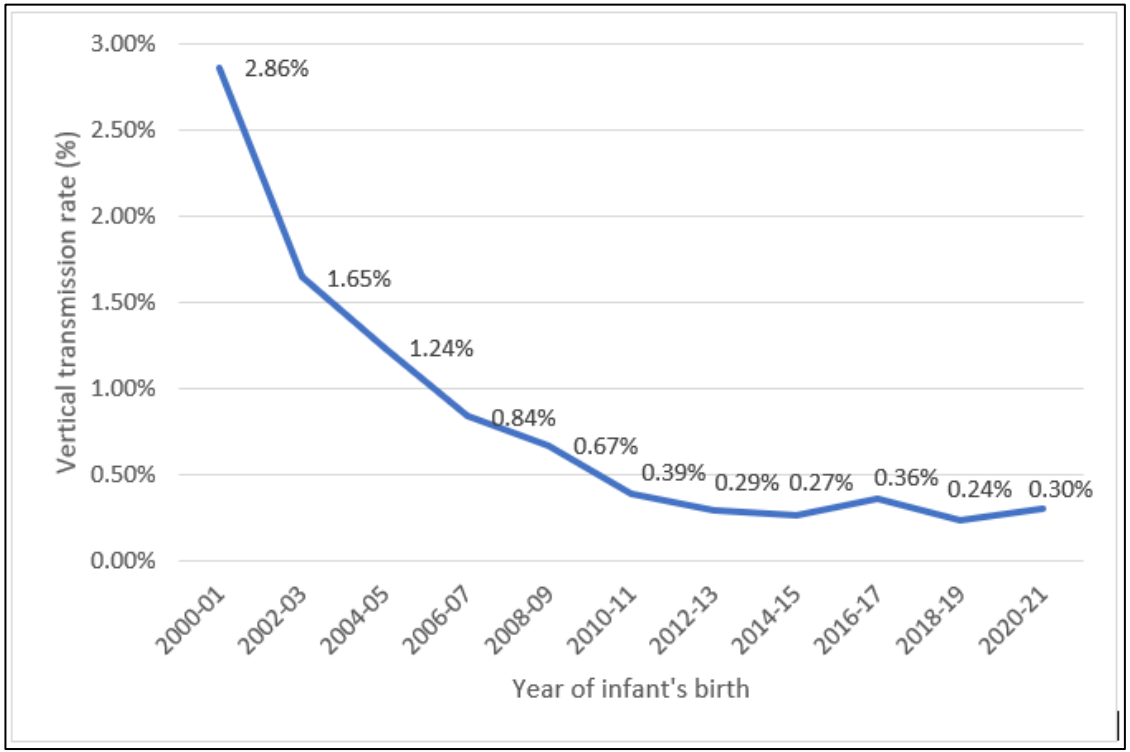
Process indicator targets

- ❖ Antenatal care coverage **≥95%**
- ❖ Antenatal HIV / syphilis testing **≥95%**
- ❖ **≥95%** pregnant women to receive treatment

Vertical transmission of HIV in England

Integrated Screening Outcomes Surveillance Service

VT rate for infants born to diagnosed women in England, 2000-21



- Data from national surveillance
- HIV screening coverage in pregnancy: 99.8%
- ≈530 pregnancies in people living with HIV in 2020-21 (vs peak of ≈1400 in 2007-2010)
- Currently, around 85% have an established HIV diagnosis before pregnancy, with 95% already on ART at conception

https://www.ucl.ac.uk/integrated-screening-outcomes-surveillance/

EPF
INSERM CESP 1018 - Hôpital de Bicêtre AP-HP
82 rue du Général Leclerc
94276 LE KREMLIN BICETRE Cedex
FRANCE

PERINATAL HIV-1 TRANSMISSION IN FRANCE: U=U FOR MOTHERS ON ART FROM CONCEPTION

00684

CROI 2022

Jeanne Sibiude[1, 2], Jérôme Le Chenadec[3], Laurent Mandelbrot[1, 2], Alexandre Hoctin[3], Catherine Dollfus[4], Albert Faye[5,6], Eida Bui[4], Emmanuelle Pannier[7], Jade Ghosn[8,2], Valerie Garrait[9], Véronique Avettand-Fenoel[10,11], Pierre Frange[10,12], Josiane Warszawski[3,13,14], and Roland Tubiana[15,16]; for the ANRS-EPF Study Group

[1]AP-HP Hôpital Louis Mourier, Colombes; [2]Université de Paris, IAME UMR 1137, INSERM, Paris; [3]INSERM CESP U1018, Le Kremlin-Bicêtre; [4]AP-HP Hôpital Trousseau, Paris; [5]AP-HP Hôpital Robert Debré, Paris; [6]Université de Paris, INSERM, U1123, Paris; [7]AP-HP, Maternité Port Royal, Paris; [8]AP-HP.Nord, Hôpital Bichat - Claude Bernard, Paris; [9]Centre Hospitalier inter-communal de Créteil, Créteil; [10]AP-HP Hôpital Necker-Enfants Malades, Paris, France; [11]Université de Paris, INSERM U1016, CNRS UMR8104, Institut Cochin, Paris; [12]EHU 7328 PACT, Institut Imagine, Université de Paris, Paris; [13]AP-HP Hôpital Bicêtre, Le Kremlin-Bicêtre; [14]Université Paris-Saclay, INSERM CESP U1018, Le Kremlin-Bicêtre, France; [15]APHP, Hôpitaux Universitaires Pitié Salpêtrière - Charles Foix, Paris; [16]INSERM, Sorbonne Université, Institut Pierre Louis d'Epidémiologie et de Santé Publique (IPLESP UMRS 1136), Paris; FRANCE.

OBJECTIVE

To estimate the perinatal transmission rate over recent time periods, in the French context of free access to care and absence of breast-feeding, according to timing of ART introduction and viral suppression.

METHODS

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Prospective national cohort including all pregnant women with HIV and their children in 90 French centres since 1986, with follow up of all children until 2 years of age.

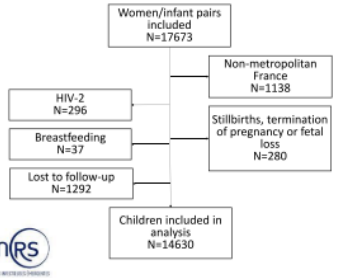
Study population: Inclusion of all HIV-1-infected mothers delivering from 2000 to 2017 and their children. No woman breastfed (Fig1).

Variables: A child was considered infected if HIV-1 DNA and/or RNA PCR results were positive for 2 consecutive samples during the follow-up or if HIV-1 antibodies were detected at ≥18 months of age. A child was considered uninfected if HIV-1 PCR results were negative ≥2 months of age and ≥1 month after ceasing all antiretroviral prophylaxis and/or if results of HIV-1 serology became negative.

Viral suppression was defined for the analysis as viral load < 50 copies/mL, or under the threshold if it was above 50 copies/mL.

Statistical analysis: We compared perinatal transmission (PT) according to time period, timing of ART initiation, maternal plasma viral load (pVL), and gestational age at birth.

Fig 1: Selection of study population. ANRS CO1/CO11.



Among 5482 HIV-infected women treated at conception, virally suppressed at delivery, and not breastfeeding, **no case of perinatal transmission was observed**: *(0/5482, 95% CI [0-0.07])* virtually eliminating in this group and this context the risk of perinatal transmission.

RESULTS

The proportion of women receiving combined ART increased from 67.7% in 2000-2005 to 97.7% in 2006-2010, and 99.2% in 2011-2017 (p<0.001), as did the proportion receiving ART from conception (28.3%, 46.3% and 65.8%, respectively, p<0.001).

Perinatal transmission rates decreased steadily between the three time periods, from 1.1% in 2000-2005 (58/5,123), 0.7% in 2006-2010 (30/4600), and 0.2% in 2011-2017 (10/4907; p< 0.001). In case of ART initiation before conception, PT rates decreased significantly across time periods, whereas in women not receiving ART at conception, PT rates were similar across time periods (Table 1).

Table 1. HIV-1 perinatal transmission rates according to time period and timing of ART initiation.

	2000-2005 N=5067 PT rate		2006-2010 N=4441 PT rate		2011-2017 N=4738 PT rate		P	All time periods N=14246 PT rate	
Timing of ART initiation	% (95% CI)	n/N	% (95% CI)	n/N	% (95% CI)	n/N		% (95% CI)	n/N
Before conception	**0.42** (0.15 - 0.91)	(6 / 1434)	**0.10** (0.01 - 0.35)	(2 / 2055)	**0.03** (0.00 - 0.18)	(1 / 3117)	0.007	**0.14** (0.06 - 0.26)	(9 / 6606)
1st Trimester	**0.31** (0.01 - 1.72)	(1 / 322)	**0.80** (0.17 - 2.32)	(3 / 375)	**0.44** (0.05 - 1.59)	(2 / 452)	0.68	**0.52** (0.19 - 1.13)	(6 / 1149)
2nd Trimester	**1.01** (0.59-1.61)	(17 / 1687)	**0.65** (0.31 - 1.19)	(10 / 1541)	**0.44** (0.12 - 1.11)	(4 / 919)	0.27	**0.75** (0.51 - 1.06)	(31 / 4147)
3rd Trimester	**1.53** (0.97 - 2.29)	(23 / 1503)	**2.55** (1.28 - 4.51)	(11 / 432)	**0.92** (0.11 - 3.29)	(2 / 217)	0.26	**1.67** (1.17 - 2.31)	(36 / 2152)
Not treated	**9.09** (4.63 - 15.7)	(11 / 121)	**10.53** (2.94 – 24.8)	(4 / 38)	**3.03** (0.08 – 15.8)	(1 / 33)	0.52	**8.33** (4.84 – 13.2)	(16 / 192)

According to viral suppression

Among 6316 women on ART at conception the proportion virally suppressed at delivery increased steadily over time: 70% in 2000-2005, 89% in 2006-2010, and 93% in 2011-2017 (p<0.001).

No perinatal transmission was diagnosed in 5,482 infants born to women treated at conception and having undetectable viral load near delivery (95%CI [0.00-0.0.7]) (Table 2).

There was no case of PT if the 1st trimester viral load was BLOQ or < 50 copies/mL (0/2358), 95%CI [0-0.16].

Table 2. HIV-1 PT rates among women on ART at conception according to viral load at delivery

	All time periods N=6316 Perinatal transmission rate	
Viral load near delivery (cp/mL)	% (95% CI)	n/N
< 50	**0.00** (0.00 - 0.07)	(0/5247)
<lower limit of quantification	**0.00** (0.00 - 1.56)	(0/235)
50 - 399	**0.20** (0.01 - 1.10)	(1 / 504)
>= 400	**2.42** (1.05 - 4.72)	(8 / 330)

According to gestational age at delivery

PT rate was higher following severe preterm deliveries (<32WG) 2.06%, than in moderate preterm (32WG-36WG) 1.34%, or in term deliveries 0.54% (p<0.001).

However, this association was not found in the period 2011-2017 (0.0 vs 0.19 vs 0.21% respectively), where a higher proportion of women were virally suppressed from the first trimester.

CONCLUSIONS

In the absence of breastfeeding, and in the French context of free access to ART and monthly pVL assessment suppressive ART initiated before pregnancy and continued throughout the pregnancy can eliminate perinatal transmission of HIV.

ACKNOWLEDGEMENTS

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Corresponding author contact information : jeanne.sibiude@aphp.fr

CROI 2022

PERINATAL HIV-1 TRANSMISSION IN FRANCE: U=U FOR MOTHERS ON ART FROM CONCEPTION

00684

EPF
INSERM CESP 1018 - Hôpital de Bicêtre AP-HP
82 rue du Général Leclerc
94276 LE KREMLIN BICETRE Cedex
FRANCE

Jeanne Sibiude[1, 2], Jérôme Le Chenadec[3], Laurent Mandelbrot[1, 2], Alexandre Hoctin[3], Catherine Dollfus[4], Albert Faye[5,6], Eida Bui[4], Emmanuelle Pannier[7], Jade Ghosn[8,2], Valerie Garrait[9], Véronique Avettand-Fenoel[10,11], Pierre Frange[10,12], Josiane Warszawski[3,13,14], and Roland Tubiana[15,16]; for the ANRS-EPF Study Group

[1]AP-HP Hôpital Louis Mourier, Colombes; [2]Université de Paris, IAME UMR 1137, INSERM, Paris; [3]INSERM CESP U1018, Le Kremlin-Bicêtre; [4]AP-HP Hôpital Trousseau, Paris; [5]AP-HP Hôpital Robert Debré, Paris; [6]Université de Paris, INSERM, U1123, Paris; [7]AP-HP, Maternité Port Royal, Paris; [8]AP-HP.Nord, Hôpital Bichat - Claude Bernard, Paris; [9]Centre Hospitalier inter-communal de Créteil, Créteil; [10]AP-HP Hôpital Necker-Enfants Malades, Paris, France; [11]Université de Paris, INSERM U1016, CNRS UMR8104, Institut Cochin, Paris; [12]EHU 7328 PACT, Institut Imagine, Université de Paris, Paris; [13]AP-HP Hôpital Bicêtre, Le Kremlin-Bicêtre; [14]Université Paris-Saclay, INSERM CESP U1018, Le Kremlin-Bicêtre, France; [15]APHP, Hôpitaux Universitaires Pitié Salpêtrière - Charles Foix, Paris; [16]INSERM, Sorbonne Université, Institut Pierre Louis d'Epidémiologie et de Santé Publique (IPLESP UMRS 1136), Paris; FRANCE.

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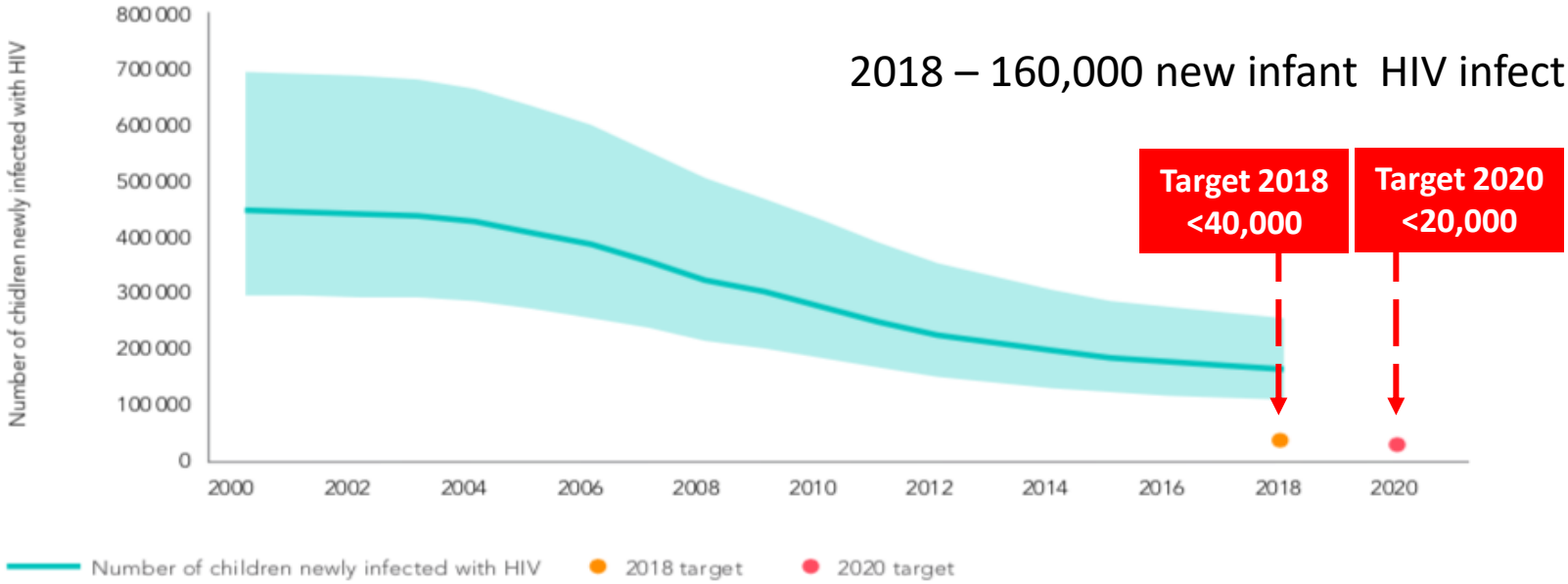
Start Free, *Stay Free, AIDS Free*

Falling short of the targets for reducing infant HIV

Figure 1. The number of children acquiring HIV is decreasing, but not rapidly enough, and the 2018 target was missed

Children aged 0–14 years newly infected with HIV in 23 focus countries, 2000–2018 and 2018 and 2020 targets

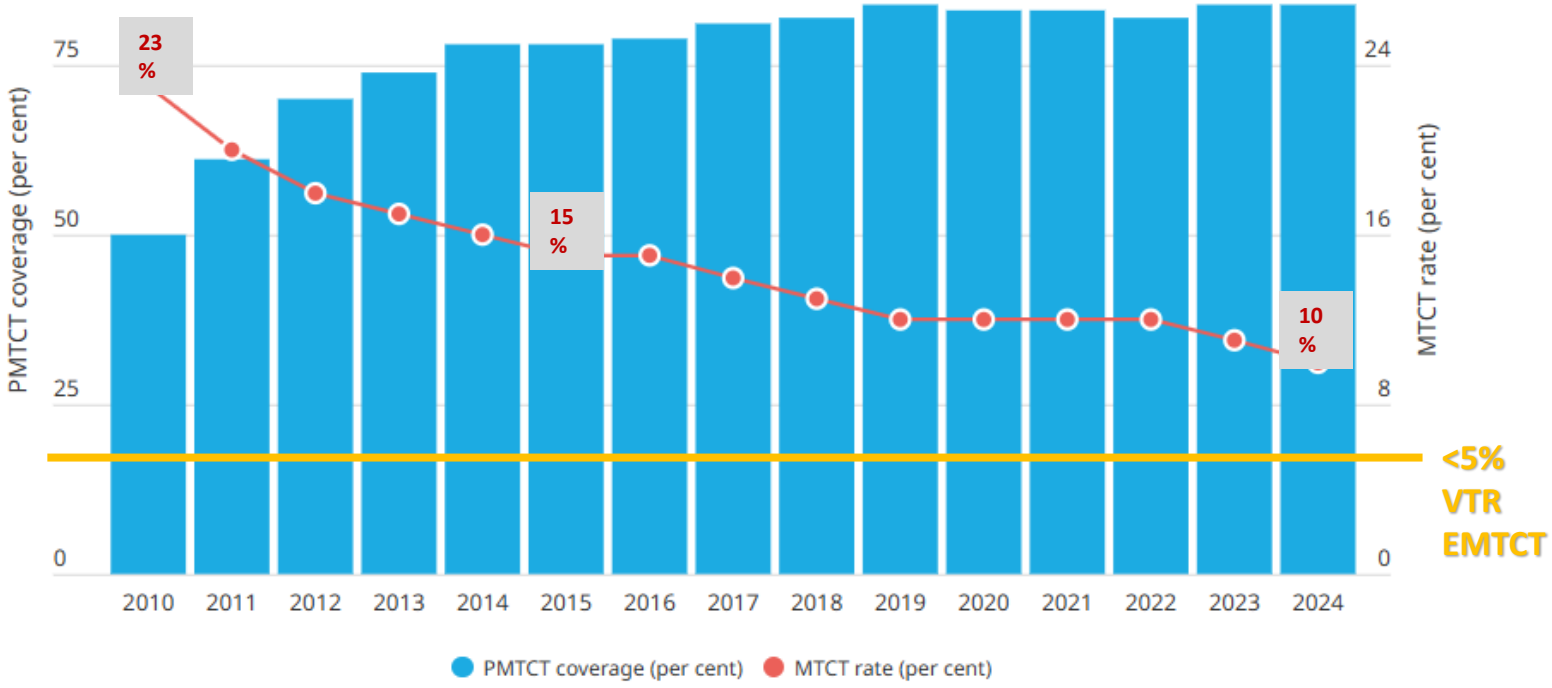


2018 – 160,000 new infant HIV infections

Target 2018 <40,000

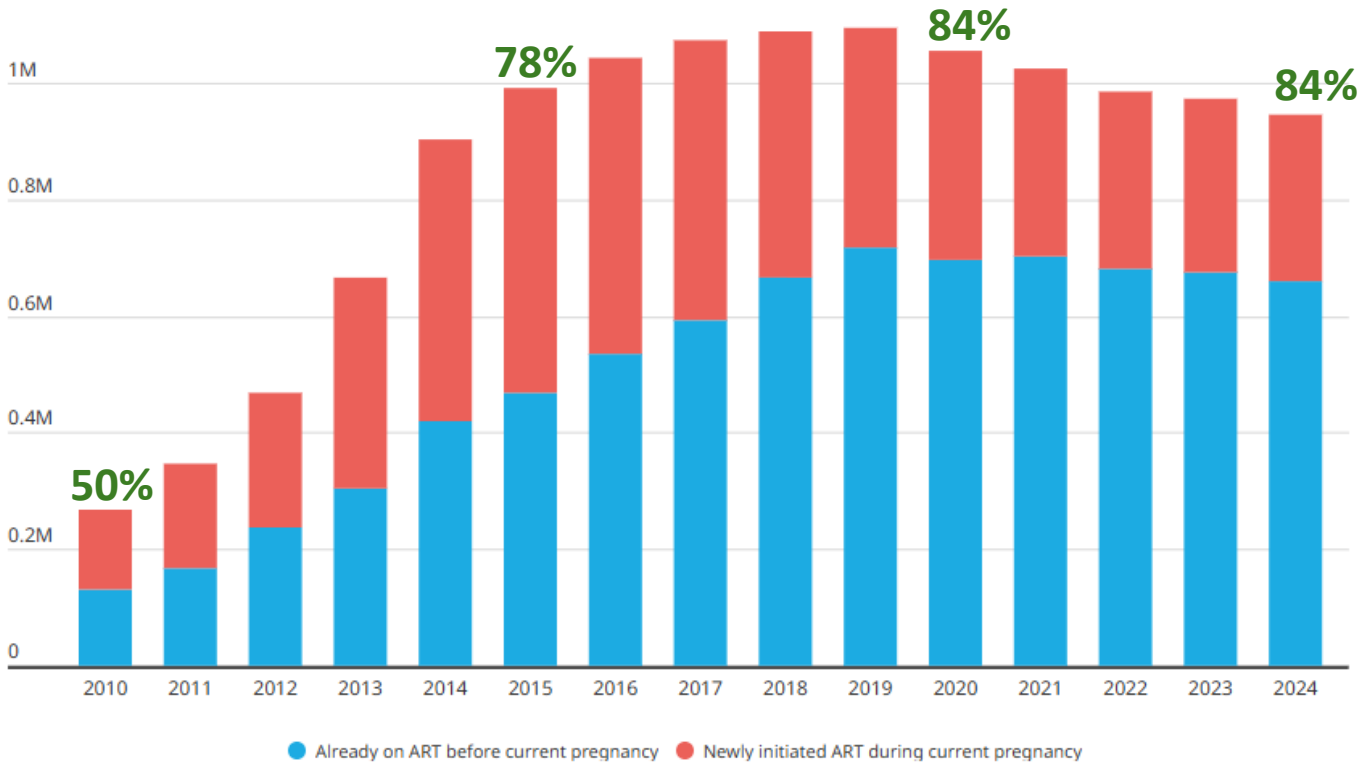
Target 2020 <20,000

Vertical transmission rate



ART in pregnancy

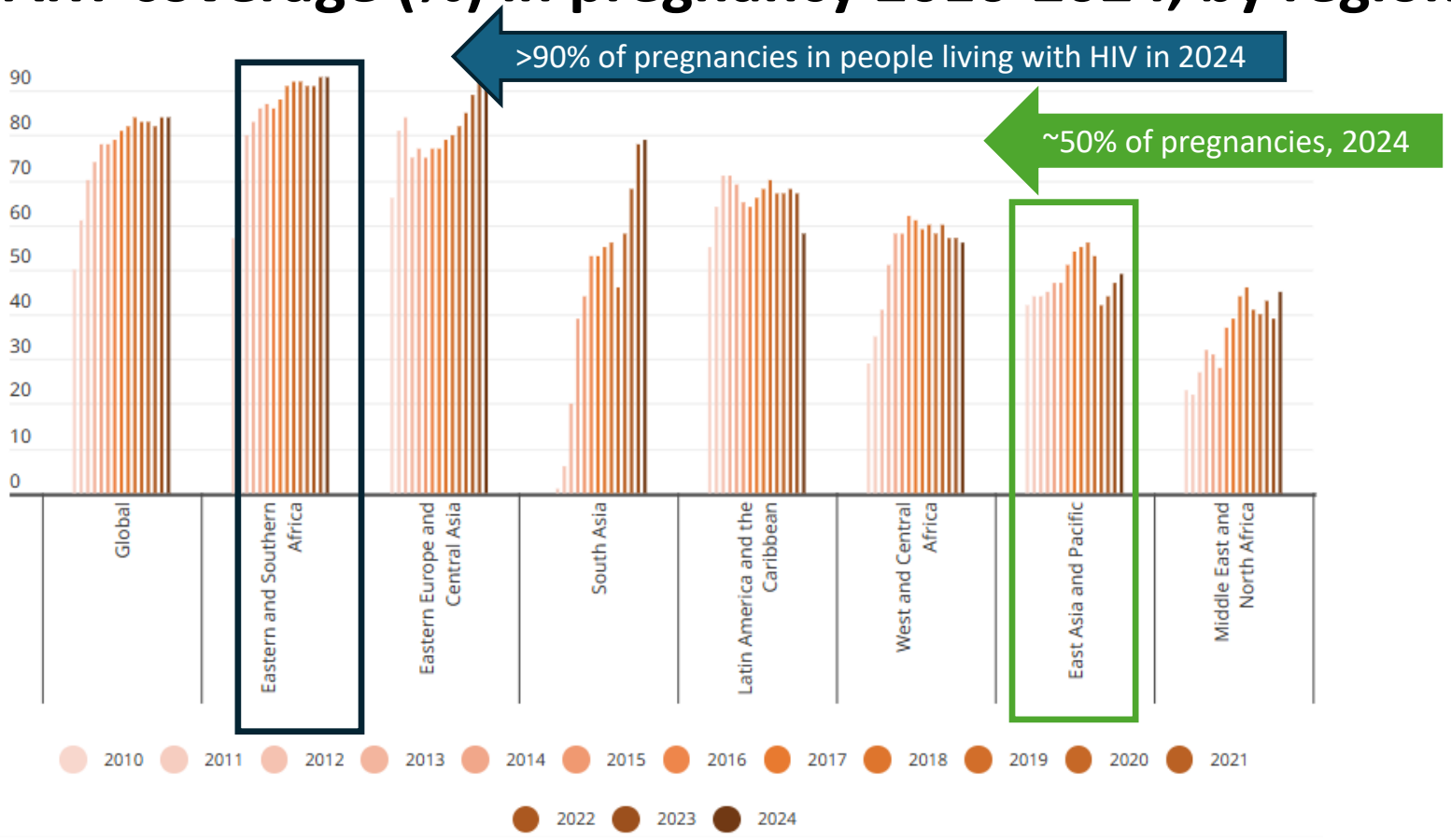
Numbers of pregnant women on ART and coverage (%)



Target: 100% on life-long ART

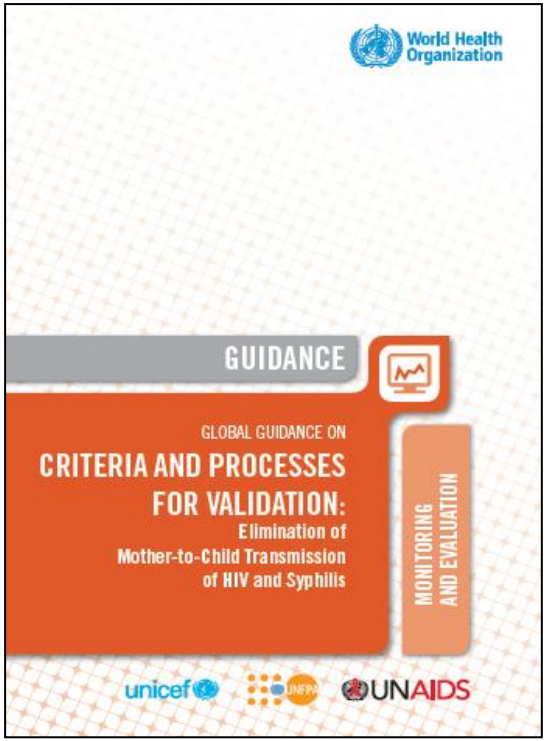
UNAIDS 2025 estimates

ART coverage (%) in pregnancy 2010-2024, by region

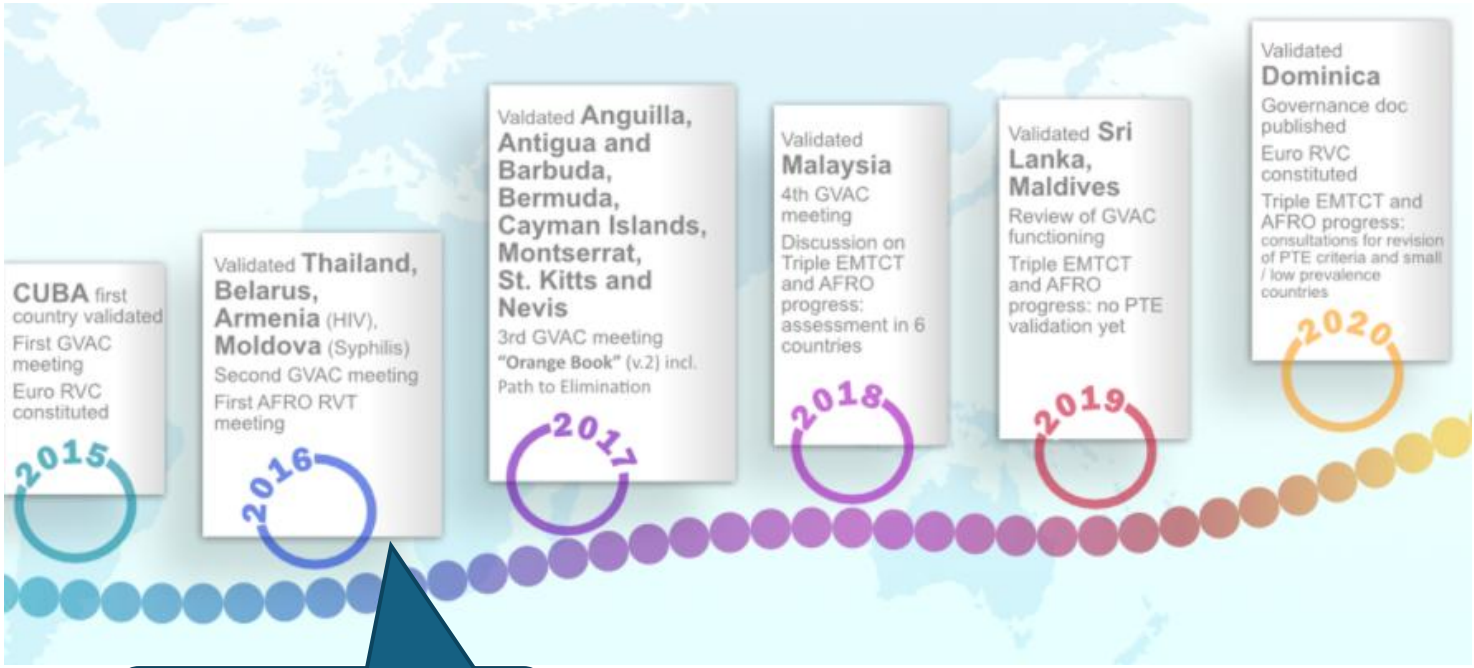


***Source**: Global AIDS Monitoring and UNAIDS 2025 estimates*

Path to VT elimination - global



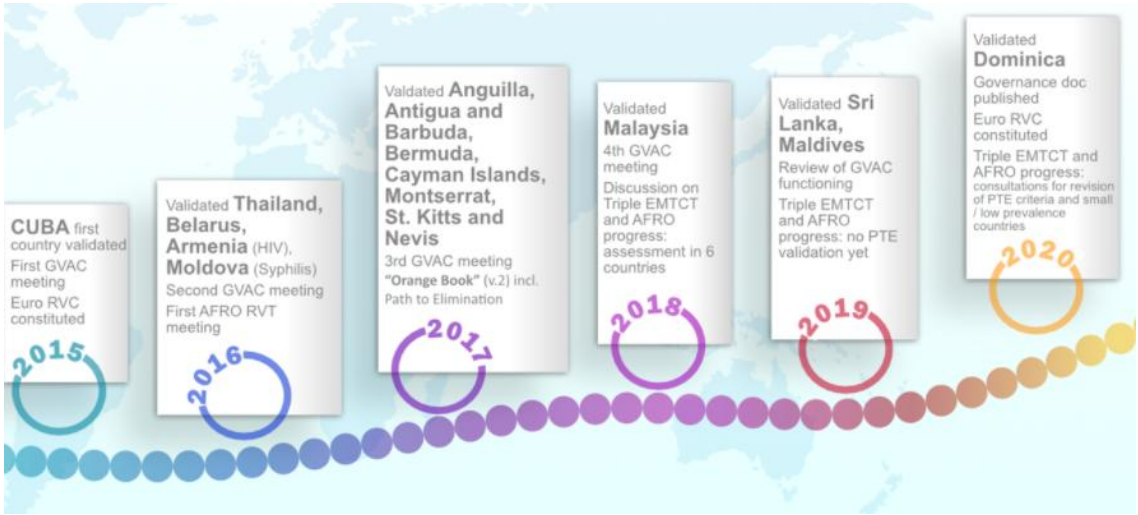
Path to VT elimination – global, 2015-2020



Thailand first country with generalised epidemic to validate EMTCT

GVAC: Global Validation Advisory Committee
RVC: Regional Validation Committee

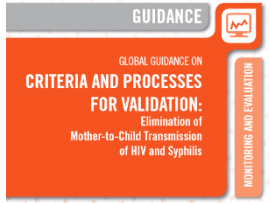
Path to VT elimination – global, 2015-2025



2021

Path to Elimination: Botswana

Botswana becomes the first country to achieve the silver tier on the path to eliminating mother-to-child transmission of HIV.



2022

Validated: Oman

2023

Path to Elimination: Namibia

Namibia is awarded the bronze tier for on the path to eliminating (PTE) mother-to-child transmission (MTCT) of HIV, and the silver tier for PTE of MTCT of HBV.

2024

Validated: Belize, Jamaica, Saint Vincent and the Grenadines

2025

Botswana achieves gold tier

GVAC: Global Validation Advisory Committee
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NEWS | 22 August 2025

nature africa

How Botswana eliminated paediatric HIV

Political will, free maternity care and digital health tools helped Botswana achieve high standards for ending mother-to-child transmission.

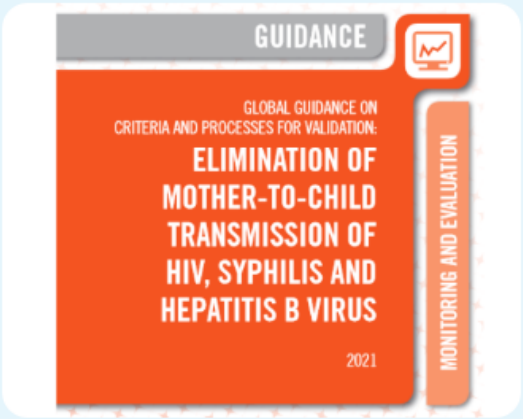
Mother-to-child HIV transmission has been eliminated in Botswana. Credit: Getty

- First high HIV prevalence setting to reach Gold tier
- VT rate declined from 4.9% in 2016 to **1.2% in 2023**
- Approach included:
  - Early adoption of Option B+ (lifelong treatment for pregnant and lactating people)
  - Free maternity care and ART for all
  - Decentralised services
- HIV Sustainability Roadmap to protect gains made in face of global health funding cuts

Gold

Case rate:
≤250 / 100 000
live births

- ANC coverage **≥95%**
- AN HIV testing **≥95%**
- ART coverage **≥95%**



2021

Third edition of the Global guidance on criteria and processes for validation

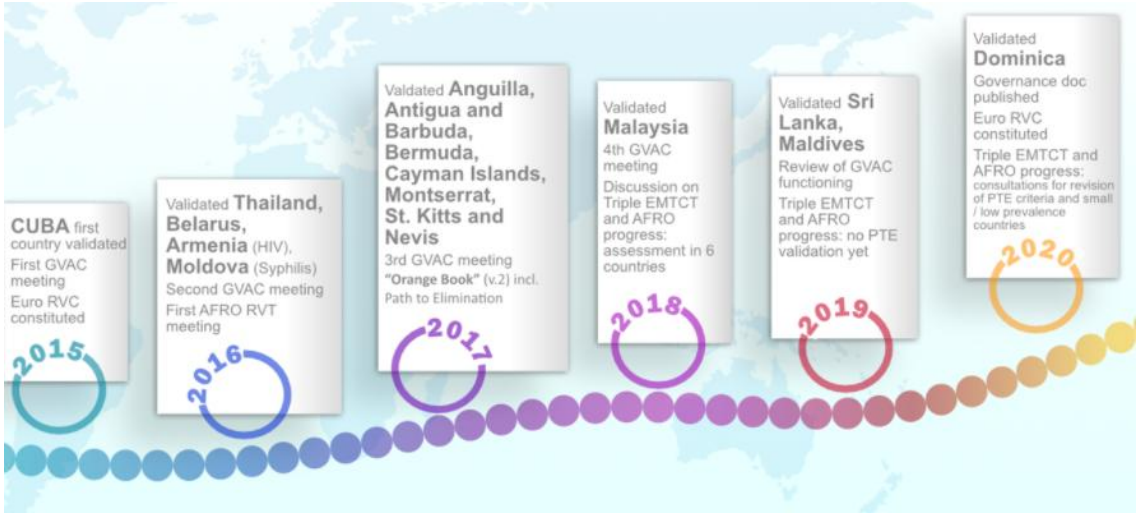
The third edition includes new criteria for the validation of EMTCT of hepatitis B virus.

World Health Organization

PATH TO ELIMINATION: RECOGNIZING PROGRESS TOWARDS EMTCT IN COUNTRIES WITH A HIGH BURDEN OF HIV, SYPHILIS AND HBV

"High burden" – e.g., for HIV, maternal prevalence >2%

Path to VT elimination – global, 2015-2025



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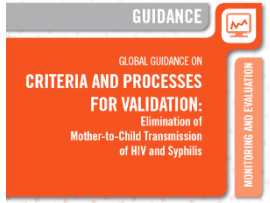

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Maldives: first country to achieve triple elimination

2025

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GVAC: Global Validation Advisory Committee
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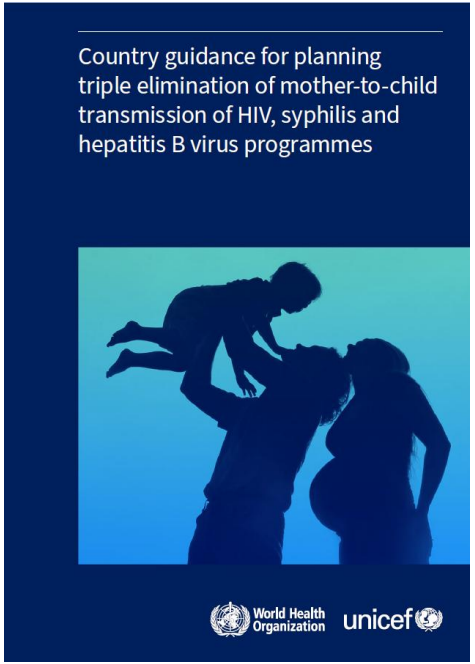
Triple elimination

- HBV has remained under-prioritised to date
  - 2024 WHO HBV guidelines should provide an additional ‘push’
- In SSA, **Namibia** is first country to achieve **Silver tier for EMTCT for HBV** (alongside Bronze for HIV)
  - ≥90% coverage of HepB3 infant vaccination
  - ≥50% coverage of universal timely HepB birth dose
- HBV testing in ANC is lagging
  - e.g., in Uganda coverage was 99% for HIV, 95% for syphilis and only 58% for HBV in 2024 (Kisaakye IAS 2025)



- **First triple test** (HIV, HBV, syphilis) prequalified by WHO
  - Fingerprick sample and multiplex rapid diagnostic testing
  - Builds on scale-up of dual HIV/syphilis rapid diagnostic tests
  - Should benefit integrated care, simplified services and improved testing coverage

Outline

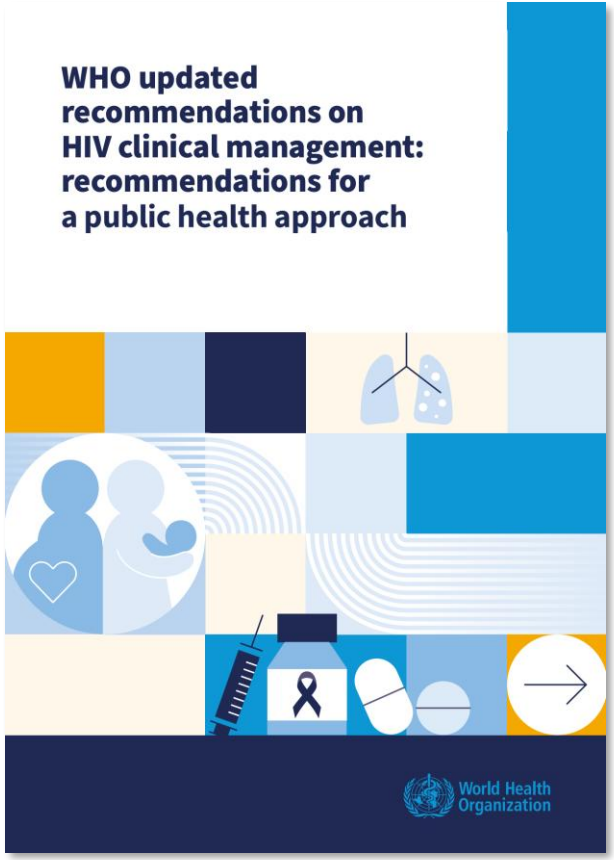
- Epidemiology of HIV in Pregnancy
- Timing and rates of mother-to-child transmission of HIV
- Treatment as prevention for MTCT
  - High income AND Globally
- Antenatal testing – the UK story
- EMTCT in the era of triple ART
  - Comprehensive programme to prevent MTCT
  - Triple elimination of HIV, Syphilis, Hepatitis B
- **Breastfeeding – updated guidance**
- Challenges
  - COVID and effects of funding cuts
- Where are we now
- HIV-exposed uninfected children

Preventing new infections in pregnant and lactating people

- Women who are pregnant or breastfeeding have increased risk of acquiring HIV, especially in high incidence settings
- Seroconversion results in higher risk of VT (high VL, missed opportunities for PVT)
- Strengthening HIV prevention in community, antenatal and postnatal settings for reproductive aged women is needed

- Testing women's partners (can include self-testing for couples)
- Providing choices for HIV prevention interventions
  - e.g., pre-exposure prophylaxis (PrEP), post-exposure prophylaxis (PEP), range of testing delivery methods and locations

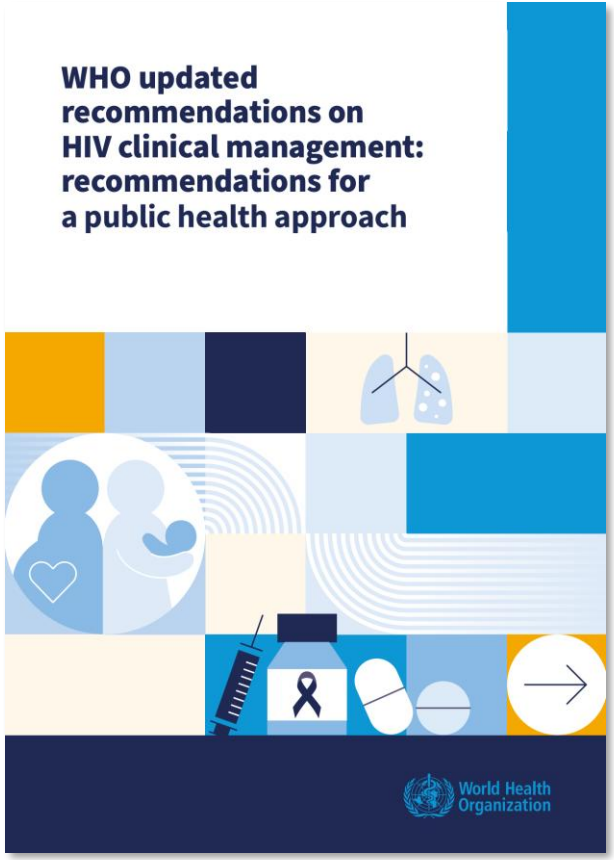
Drake et al, 2014; Thomson et al 2018, Davey et al 2020, Global Alliance Progress Report 2024



Infant Prophylaxis during Breastfeeding

- Low risk infants receive 6 weeks of single drug (NVP)
- High risk infants receive 3-drug ART:
  - ABC/3TC/DTG for 6 weeks
  - Followed by single drug until maternal VL suppressed or end breastfeeding

- High Risk equals:
  - Born to mother receiving <4 weeks ART
  - Maternal viral load >1000c/ml
  - Mother has incident infection during pregnancy or breastfeeding
  - Mother identified for first time with HIV in postpartum period



Duration of Breastfeeding **(2016):**

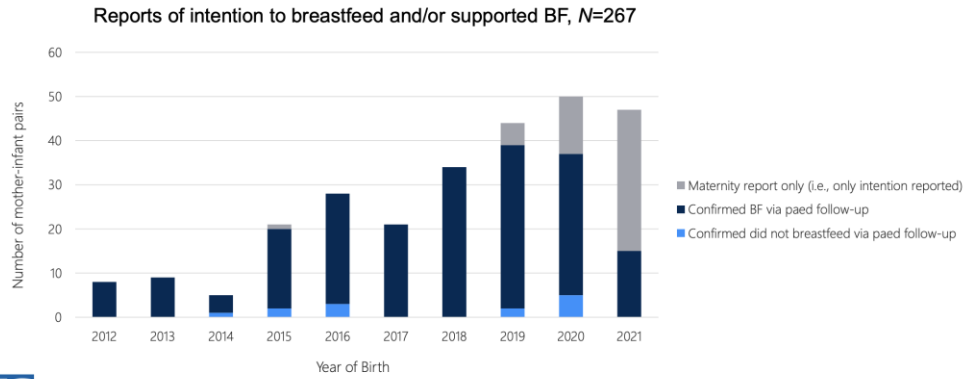
- At least 12 months or up to 24 months (as per general population
- Exclusively breastfeed for the first 6 months
- Introduce complementary feeding alongside breastfeeding up to 2 years

Where National program recommends replacement feeding **(2025):**

- mothers on ART and virally suppressed should be offered the choice to breastfeed
- Support for mothers to optimise ART adherence if breastfeeding

Infant feeding – UK data – 2012-2021

Results – cases of BF



111 breastfed infants where infant outcome known

Approx 1.3% of infants born to women living with HIV

No transmissions

Difficulties with monitoring attendance noted

10 instances where BF stopped after VL>50c/ml

Successful implementation of new Swiss recommendations on breastfeeding of infants born to women living with HIV

Pierre Alex Crisinel [a], Katharina Kusejko [b], Christian R Kahlert [c], Noémie Wagner [d], Leila Sultan Beyer [e], Begoña Martinez De Tejada [f], Irene Hösli [g], Malte Kohns Vasconcelos [h], Marc Baumann [i], Katharine Darling [j], Andrea Duppenthaler [k,1], Andri Rauch [l], Paolo Paioni [n], Karoline Aebi-Popp [l,m,*]

Deliveries 2019-2021
"Optimal Scenario"
25 decided to breastfeed
BF median 6.3 months
(0.7-25.7, IQR 2.5-11.1)
No PNP
Zero transmissions

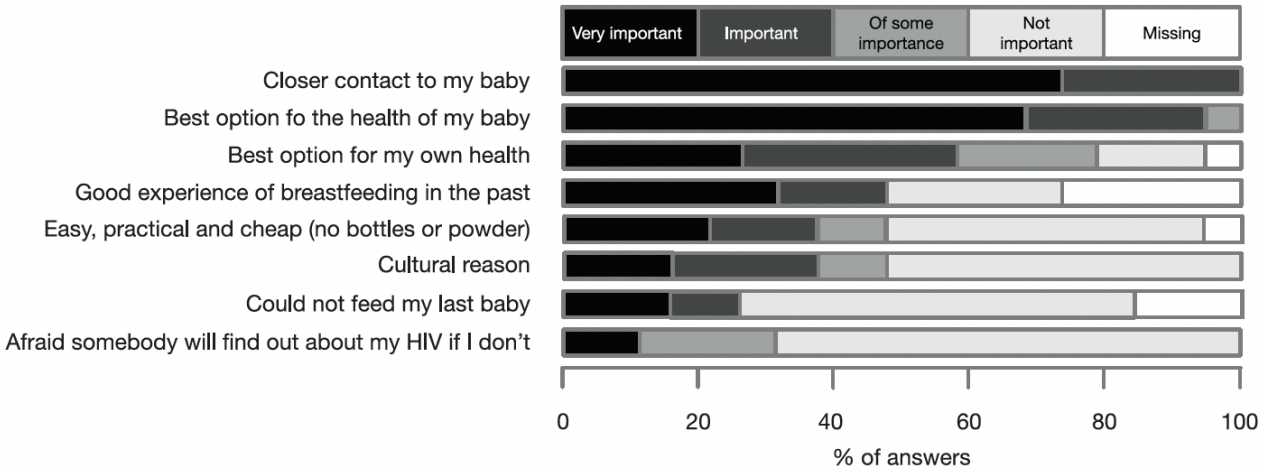


Fig. 2. Reasons of 19 included mothers to breastfeed their baby.

HIV-Positive and Breastfeeding in High-Income Settings: 5-Year Experience From a Perinatal Center in Germany

Fabian Weiss, MD,[a] Ulrich von Both, MD,[b,c] Anita Rack-Hoch, MD,[b] Franz Sollinger,[b] Josef Eberle, MD,[d] Sven Mahner, MD,[a] Ralph Kaestner, MD,[a,e] and Irene Alba Alejandre, MD[a]

Births 2016 – 2020

30 infants breastfed (25 “optimal scenario”)

Duration 2 weeks - > 12 months

PNP for 2 weeks, 4 weeks, 6 weeks, 8 weeks (5 no PNP)

No transmissions

Outline

- Epidemiology of HIV in Pregnancy
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- EMTCT in the era of triple ART
  - Comprehensive programme to prevent MTCT
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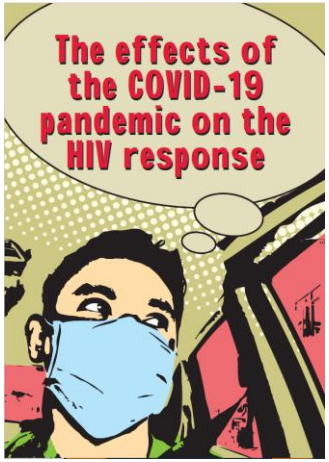
- Breastfeeding – updated guidance
- **Challenges**
  - **COVID and effects of funding cuts**
- Where are we now
- HIV-exposed uninfected children

COVID-19 pandemic and the global HIV response

- Disruptions to HIV services
- Reduction in facility-based HIV testing led to fewer diagnoses
- Supply chain issues and clinic closures
- Treatment access slowed down
- HIV prevention programmes interrupted
- PVT programme coverage dipped in parts of SSA



But some positive innovations in response included scale-up of HIV self-testing, expansion of digital health tools, and integration of HIV care with broader primary care

UNAIDS 2021

Cuts to foreign assistance could undo decades of progress

Potentially more than 4 million additional HIV-related deaths and more than 6 million additional new infections in the period 2025–2029

Figure 1.6. Number of new HIV infections 1990–2024, and projections assuming cuts in HIV funding 2025–2029, global

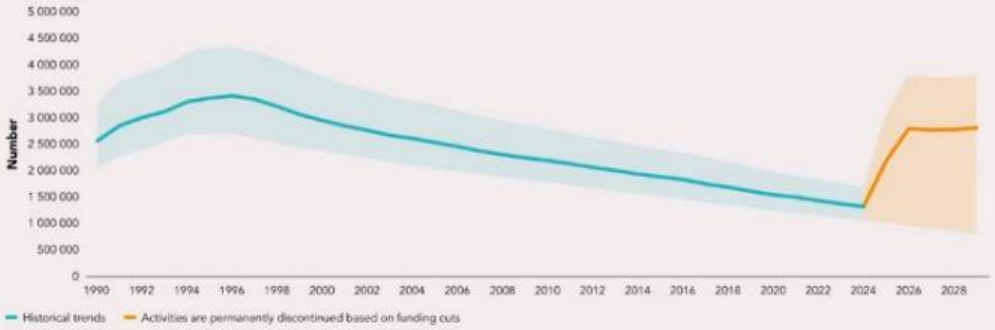
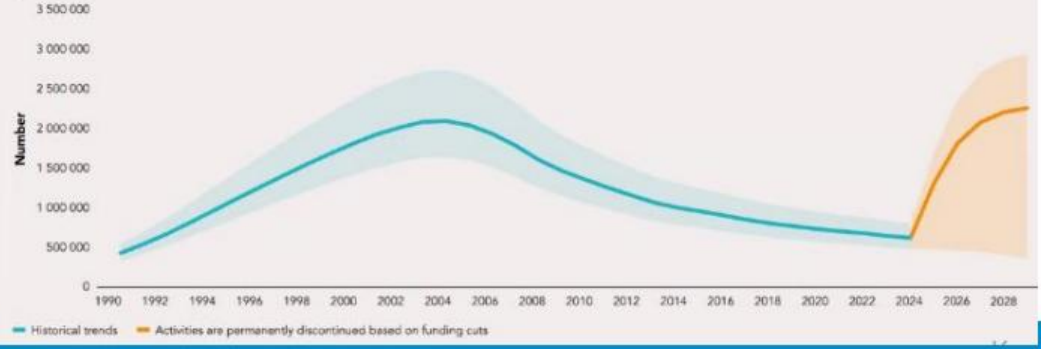


Figure 1.7. Number of AIDS-related deaths 1990–2024, and projections assuming cuts in HIV funding 2025–2029, global



Source: AIDS, crisis and the power to transform: UNAIDS Global AIDS Update 2025. Geneva: Joint United Nations Programme on HIV/AIDS; 2025.

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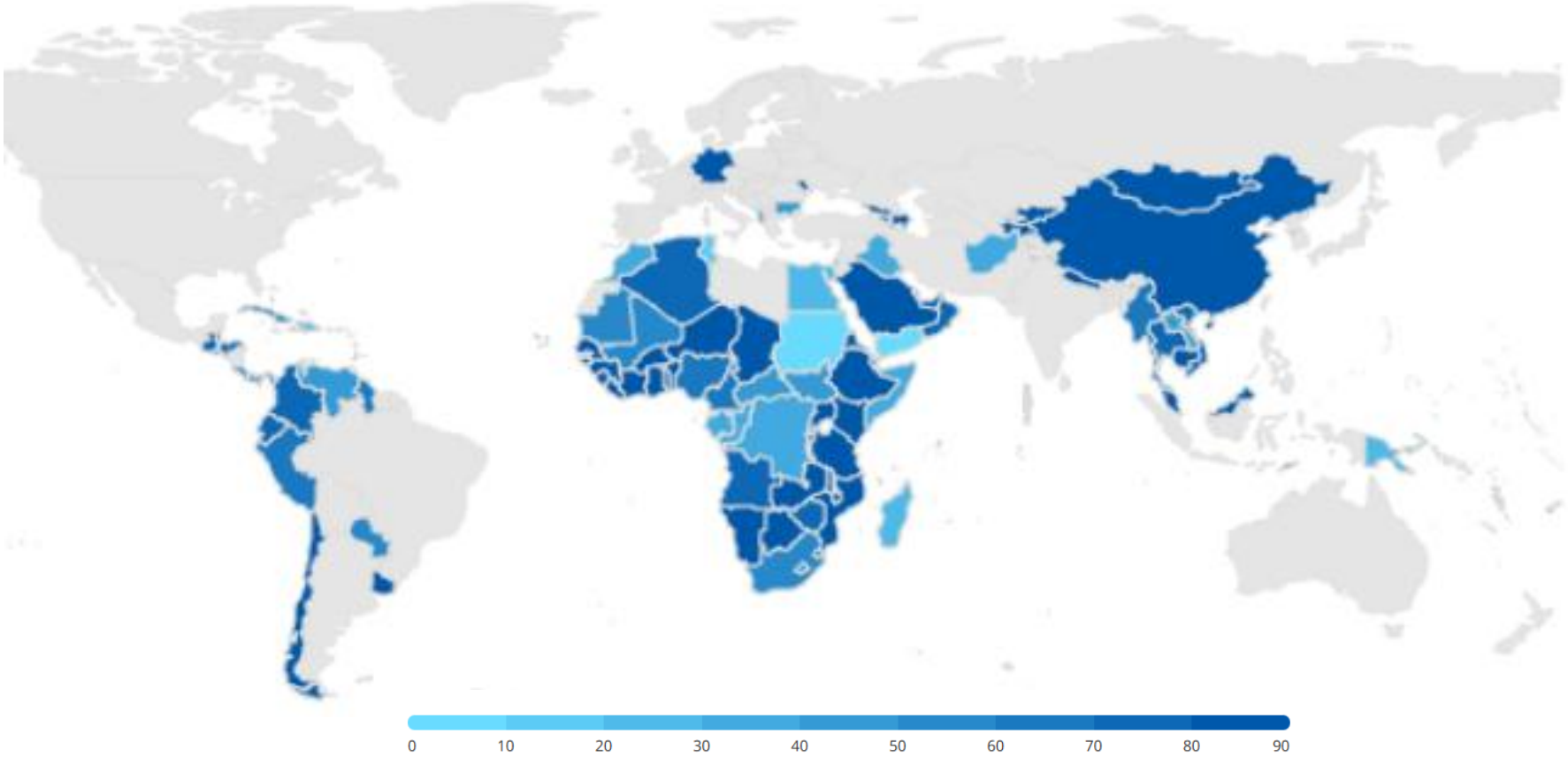
% of pregnant women in antenatal care who were tested for HIV or already knew their HIV positive status, 2024



Why did vertical transmissions occur in 2024?

Possible reasons:

HIV not diagnosed (e.g. due to lack of access to antenatal care and testing)

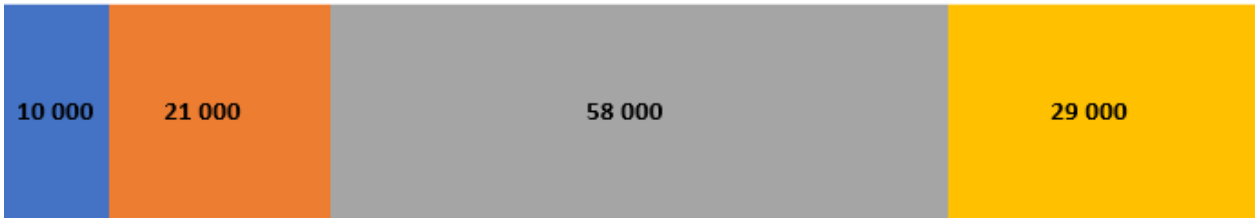
HIV diagnosed but lost to care before ART can start

49%
No maternal ART in pregnancy or whilst BF

84%

ART coverage in pregnant and BF women, 2024

Number of new child HIV infections



UNAIDS

https://aidsinfo.unaids.org/

Why did vertical transmissions occur in 2024?

18%: mother had been on ART but stopped during pregnancy or BF

Poor retention in HIV care can be linked to a range of personal and structural barriers
- Stigma
- Travel time / costs
- Childcare / household duties / work
- Experience of negative HCP attitudes

9%: mother on ART but not virally suppressed

Adherence challenges
Drug resistance
Lack of viral load monitoring

UNAIDS

Why did vertical transmissions occur in 2024?

25%
Mother acquired HIV in pregnancy or whilst BF

UNAIDS

Models of care / differentiated care

- Work is ongoing to understand more about best models of care for people on ART in pregnancy and postpartum to support treatment and retention in care
- This will vary based on contextual factors
- Examples include
  - Integration with maternal and child health, with services co-located and co-scheduled
  - Differentiated service delivery models (client-centred approaches)
    - Community-based adherence clubs for maternal ART
    - Mentor mothers (facility based, community-based, phone-based)
    - Peer group interventions
    - Community health workers

Circumstances associated with recent cases of vertical transmissions in the US, UK and Spain*

- No or late entry to prenatal care
- Diagnosis late in pregnancy
- Undetected seroconversion in pregnancy or postnatally
- Engagement and/or adherence issues
- Preterm delivery

* VT rate in Spanish national cohort was 0.72% (0% - 1.54%) for 2020-2022

Illán Ramos et al Anales de Pediatría 2024, Griffith et al Pediatrics 2024, ISOSS 2025 https://www.ucl.ac.uk/integrated-screening-outcomes-surveillance/

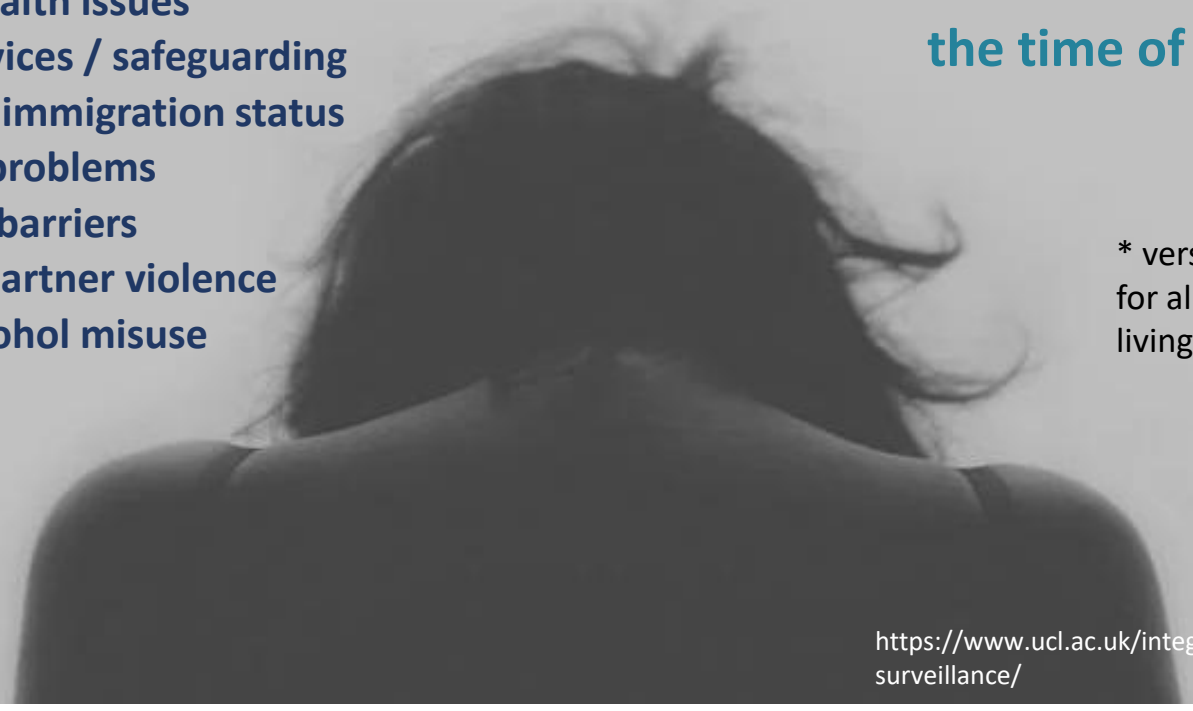
New vertical HIV infections and complex social factors, England, 2014-2024

- **27% Housing issues**
- **24% Mental health issues**
- **24% Social services / safeguarding**
- **16% Uncertain immigration status**
- **12% Financial problems**
- **12% Language barriers**
- **10% Intimate partner violence**
- **8% Drug or alcohol misuse**

Issues may overlap

In 57% of 51 pregnancies where VT occurred, complex social factors were reported at the time of pregnancy*

* versus 38% reported for all pregnant women living with HIV



https://www.ucl.ac.uk/integrated-screening-outcomes-surveillance/

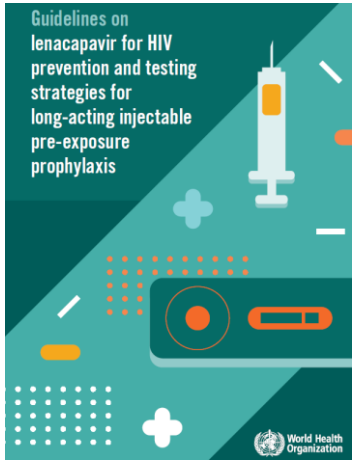
The future?

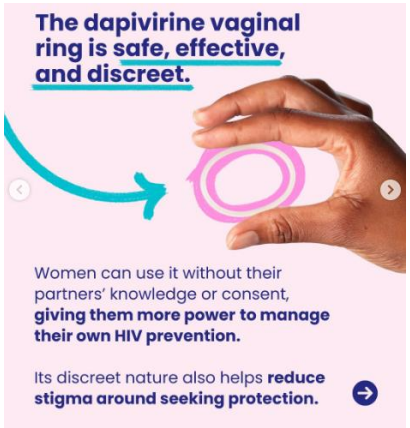
- Long acting ART for mother and/or infant
- Role of broadly neutralising antibodies ?
- Case for extended PNP during breast feeding ?
- Case for PEP after breastmilk exposure ?
- Maternal pre-exposure prophylaxis in pregnancy and BF
- Everyone doing the same across Europe ? NO

Expanding the prevention ‘toolbox’

- PrEP is a key component of combination HIV prevention
- Toolbox includes - **oral PrEP** (TDF/FTC or TAF/FTC), **long-acting injectables** (Cabotegravir, Lenacapavir), **Dapivirine vaginal ring** (DVR)
- WHO guidelines now recommend Lenacapavir (twice yearly injectable) as an additional PrEP option
  - nearly 100% effective
  - Addresses adherence barriers to oral PrEP

- **Pregnancy**:
  - CAB-LA: open label extension on safety in pregnancy showed outcomes consistent with expected background rates





Bekker et al NEJM 2024, Delany-Moretiwe et al JIAS 2025, Fairlie et al Lancet HIV 2025

World Health Organization

https://www.who.int/tools/antiretrovirals-in-pregnancy-research-toolkit

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The global picture

Globally, there are approximately **15.7 million children** aged 0-14 years who are HIV- exposed and uninfected (‘children born HIV free’)

- 90% live in Africa - 50% in South Africa, Uganda, Nigeria, Mozambique and Tanzania
- Children who are HEU represent **>20% of the total child population** in South Africa, Eswatini, Lesotho and Botswana and **10-15%** in Zimbabwe and Namibia

❑ Around **1.2 million people living with HIV become pregnant** each year

Expanding population of children who are HIV-exposed and uninfected

Slogrove et al 2020 Lancet GH, Wedderburn et al 2025 Lancet HIV

Numerous studies have shown that children born HIV-free have distinctive health challenges

Greater risk of:

Sub-optimal birth and neonatal outcomes

(e.g., preterm, LBW, SGA)

Mortality and morbidity

Growth faltering

(e.g., stunting, underweight)

Poorer neuro-development

Increased risk of:

- Hospitalisation
- LRTIs
- Diarrhoea
- Other infections (often with more severe disease)

Evans et al Lancet 2016, Brennan et al AIDS 2016, Brennan et al JAIDS 2019, Prendergast & Evans AIDS 2023

Conclusions

- ≈ 4.5 million new HIV infections averted due to PVT of HIV to date
- But progress is uneven and global declines in new paediatric infections have stalled
- 19 countries have reached elimination targets, with one achieving triple elimination
  - Avoidable VT continues to occur, even in settings with elimination achieved
  - The COVID-19 pandemic and global health funding losses have compounded challenges in going the last mile to eliminate VT
- Innovations = opportunities
  - long-acting injectables (treatment and PreP), triple test, self testing
- Political will is key
  - >50 countries expressed interest in implementing triple elimination

Thank you for listening

Acknowledgements

Many colleagues, especially Claire Thorne, Hermione Lyall, Alasdair Bamford

RESULTS

Case series. Maternal/infant viruses linked by HIV sequencing and phylogenetic analyses.

Case	ART	VL during pregnancy	Additional factors during pregnancy?	Gestation	Mode of delivery?	Infant PEP	Infant feeding	Infant VL at birth	Infant VL at 6 weeks	Infant VL at 12 weeks
A	ART pre-conception and throughout pregnancy. ART: Tenofovir-DF, emtricitabine, efavirenz Excellent adherence reported.	At 8 weeks GA VL 380 cpm. Subsequently VL measured x6 during pregnancy and at delivery, with all VL <50 cpm	Enoxaparin for 6 weeks from 11 weeks GA; Pre-eclampsia at 38 weeks GA	38 weeks	Vaginal delivery with induction of labour <1 hour rupture of membranes	Zidovudine PEP for 2 weeks*	Exclusive formula feeding	Not detected	Not detected	17.6 x 10^6 cpm
B	ART pre-conception and throughout pregnancy. ART: Tenofovir-DF, emtricitabine, ritonavir-boosted atazanavir Excellent adherence reported.	VL measured x5 during pregnancy and at delivery. All VL <50 cpm	Iron infusion at 33 weeks GA	36 weeks	Pre-labour pre-rupture of membranes Caesarian section	Zidovudine PEP for 4 weeks*	Exclusive formula feeding	Not detected	1.4 x 10^6 cpm	

*As per contemporaneous guidelines

Abbreviations: *ART anti-retroviral therapy; cpm copies per millilitre; GA gestational age; PEP post-exposure prophylaxis; VL viral load*

Literature review.

Dolphin-2: one late transmission with HIV sequencing linking infant and maternal viruses [10].

- Efavirenz-based ART commenced week 28 GA.
- Maternal HIV VL undetectable at delivery and post-partum at weeks 6, 12, 24, 48 and 72
- Maternal breastfeeding for 48 weeks: 24 weeks exclusively then 24 weeks mixed feeding.
- Infant HIV RNA testing negative at birth and weeks 6 and 12.
- HIV RNA first detected in infant at week 72.
- Stored maternal plasma at weeks 24 and 48 – HIV RNA negative.
- Breastmilk HIV RNA negative. No mastitis reported.

U ≠ U

Pregnancy and Breastfeeding

The Safety of Tenofovir Exposure for Babies

- No increase in congenital abnormalities[1]
- No increase in adverse outcomes in babies exposed to TDF vs NVP over 5 years in the DART trial[2]

BUT

- TDF exposure[3] **(mainly with bPI):**
  - significantly lower neonatal bone mineral density[4]
  - Worse neonatal outcomes in TDF arm of the PROMISE Trial[5]
    - Prematurity and deaths higher in TDF vs ZDV arms
    - Results from the bone/kidney Substudy of PROMISE awaited

NEED for ongoing Pharmacovigilance

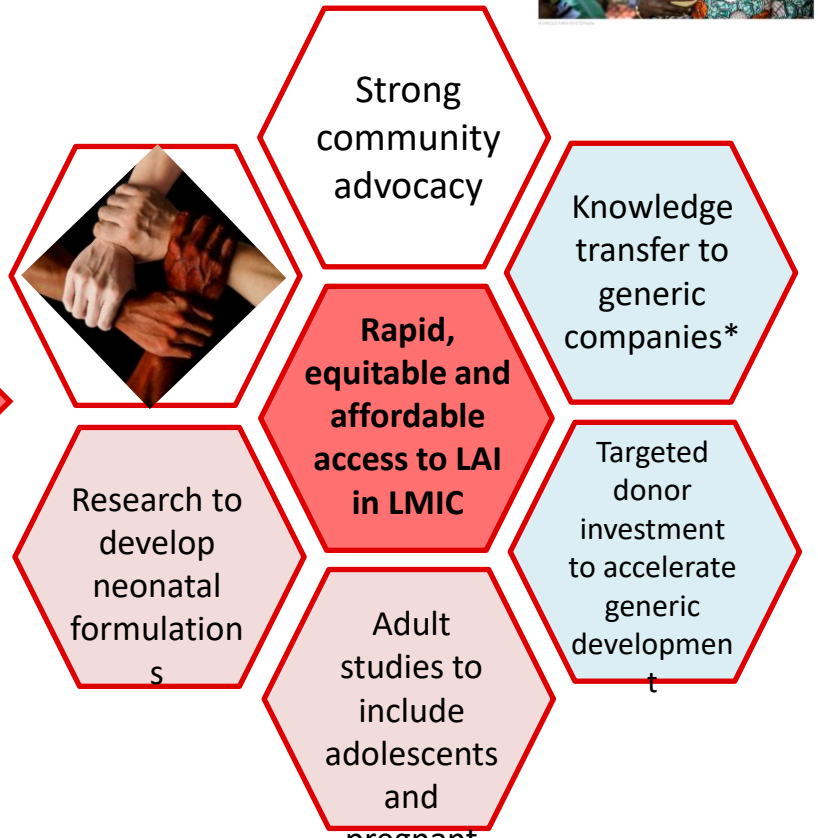
1. Pregnancy Register
2. Gibb, Plos Med 2012
3. Baheti G AIDS 2013
4. Siberry CROI 2014
5. Fowler, 31LB CROI 2015

Long-acting injectables: could be a *game changer* for *prevention* of vertical transmission

- **CABOTEGRAVIR** (2-monthly, IM) was the first INJECTABLE to show superiority over oral TDF/FTC for HIV prevention
  - Licensed for adults and adolescents ≥35kg
- **LENACAPAVIR** (6-monthly, SC) recently announced to have 100% efficacy and superiority to daily TDF/FTC for HIV prevention in cisgender women and adolescent ≥16 years (ALSO 12-MONTHLY)

Llong-acting injectables could revolutionise postnatal prophylaxis

- PrEP: for women & adolescents of reproductive age
- Postnatal Prophylaxis: for infants exposed to HIV



^Gilead. Press release. June 20, 2024

*MPP agreement is in place for CAB for prevention