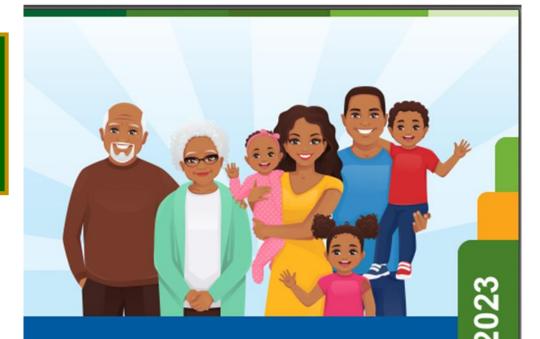
## Vertical Transmission Prevention

Mother-to-child transmission will be known as vertical transmission



Guideline for Vertical Transmission Prevention of Communicable Infections

South African National Department of Health

Draft 3 May 2023





# Overview of Recommended Interventions to for Vertical Transmission Prevention

#### Strategy 1

Minimize infant exposure to the virus by

Maternal VL suppression

Strategy 2

Infant post-exposure prophylaxis

If these steps fail / are suboptimal, we need to identify infected children as soon as possible by providing:

**Early Infant Diagnosis** 

**Antiretroviral therapy** 

Cotrimoxazole Prevention Therapy (CPT)

At the same time we need to promote and protect breastfeeding

**HIV-free Survival** 

Normal growth and development

# Considerations for Vertical Prevention Transmission: overview

Still central theme of maternal VL suppression, especially postnatally

## Similarities with adult and adolescent section

- Focus on optimised regimens (DTG benefits also applicable to WOCP)
- Principles of switching and management of confirmed virological failure also apply

#### **Differences**

- Timing of the repeat VL in the VL management algorithm
- Specific changes to tighten the definition of higher risk for the HIV-exposed infant
- Specific changes related to cotrimoxazole prophylaxis

# VTP: Optimising care for a mother living with HIV to minimise vertical transmission

## Part 1: Implementing optimized regimens

#### **Definition**

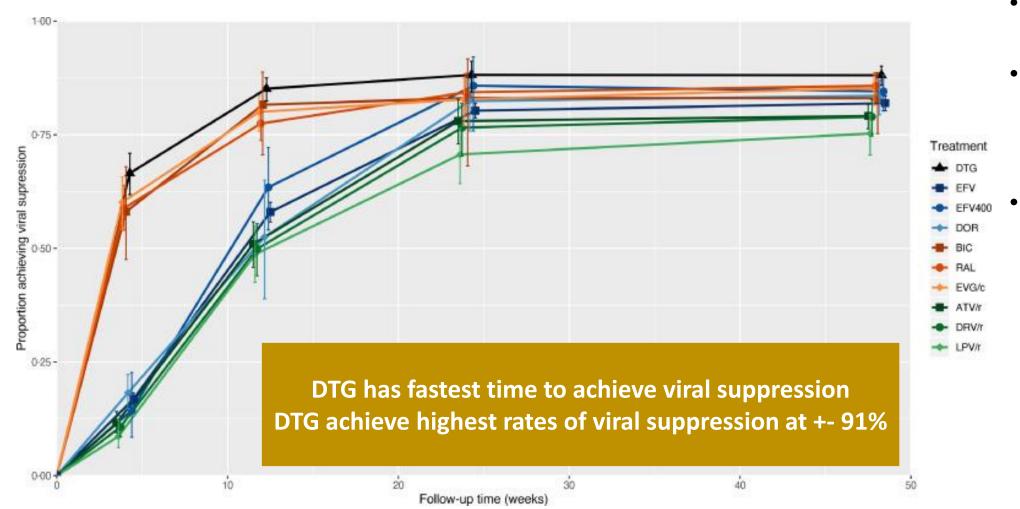
On an Optimised ART Regimen PLHIV can receive the best-available ART in the most efficient and cost-effective manner possible

#### An optimized regimen using DTG:

- simplifies regimens with reduced pill burden and dosing frequency
- enhances tolerability
- reduces toxicity
- reduces potential drug-drug interactions
- maintains viral suppression without jeopardizing future treatment options through the development of drug resistance

TLD is the regimen of choice in all pregnant and breastfeeding women, and also in those wanting to conceive

## Optimised regimens: Benefits of Dolutegravir



- DTG was protective of drug-resistance
- DTG led to fewer discontinuations due to better tolerance
- Can be used in TB-HIV co-infected persons and pregnant women.

No additional risk of NTDs!!

## Optimised regimens: Recycling of TDF in second-line regimens

#### **NADIA** trial conclusions:

DTG in combination with NRTIs was as effective as DRV/r (a protease inhibitor) including in those with extensive NRTI resistance in whom no NRTIs were predicted to have activity.

TDF was superior to AZT as second-line therapy.

- TDF may safely be reused in 2nd-line therapy following 1st-line failure with TDFcontaining regimens.
- TDF to replace AZT for patients on second-line ART. Benefits of TDF:
  - Better viral suppression than AZT
  - Better tolerated than AZT
  - Less intense initial monitoring
  - Once daily (vs twice daily) and available as a fixed-dose combination (TLD)
  - Cheaper
  - Greater harmonisation with first-line TDF-based regimens would likely improve 2nd-line drug stock challenges.

## A paradigm shift

In the new ART era of dolutegravir, TLD used as a

First-line regimen

Second-line regimen

Part of Third-line regimens

→ need to rethink our terminology related to "1st and 2nd-line"

TLD 1

Clients on a DTG-containing regimen, who have never failed a previous regimen (old "1st line" terminology)

TLD 2

Clients on a DTG-containing regimen, who have failed a previous regimen (old "2nd line" terminology)

#### Dolutegravir and neural tube defects

- •In May 2018, a safety signal was raised.
  - -DTG (0.7%) vs EFV (0,1%)
- At the IAS conference in Mexico in July 2019, new data was released:
  - -DTG (0.3%), vs EFV ART (0.1%).
- Evidence from Tsepamo study released at AIDS 2020 virtual conference in July 2020:

#### No statistically significant difference

in NTD prevalence between dolutegravir and any non-dolutegravir antiretrovirals from conception

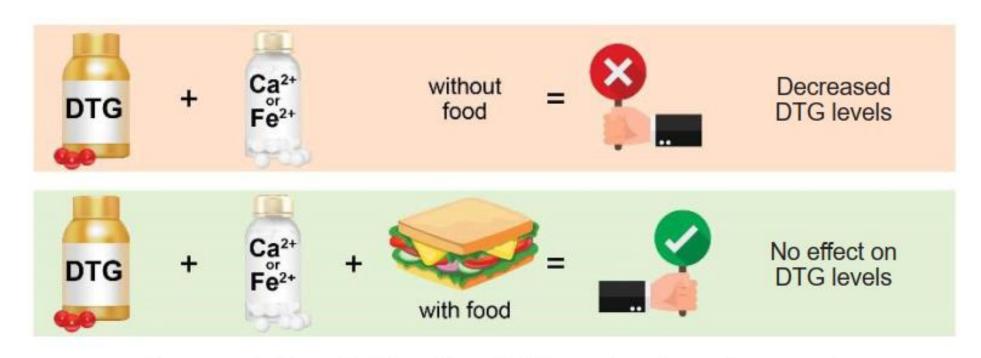
(0.09% difference; 95%CI -0.03%, 0.30%).

## Dolutegravir and the risk of NTDs

Many women and HCWs will still have concerns regarding dolutegravir and the risk of NTDs

- Provide reassurance
- There is no statistically significant difference in NTD prevalence between dolutegravir and any non-dolutegravir antiretrovirals from conception
- Inform them that the benefits of DTG far outweigh the risks, and DTG is now the recommended regimen in all men and WOCP
- If she is switching from TEE to TLD, inform her of the new side-effects that may be experienced when switching to a new drug
- Also explain about potential drug interactions with calcium iron, and antacids

### Drug interactions between DTG and the polyvalent cations



However, Calcium (Ca2+) and Iron (Fe2+) must be taken 4 hours apart



# VL Monitoring and management

- Timing of the repeat
   VL in the VL
   management
   algorithm is different
- Principles of switching and management of confirmed virological failure also apply

#### VL Non-Suppression Algorithm for Pregnant and Breastfeeding Women on TLD

VL unsuppressed (VL > 50 c/ml) in a pregnant or breastfeeding woman

#### Do a thorough assessment of the cause of an elevated VL



as per ABCDE on page xx

#### Implement interventions to re-suppress the VL.

Switch to TLD if indicated (See "Switching existing clients to DTG-containing regimens" on page xx of the 2023 ART Clinical Guideline)
Start, re-start, or extend **high-risk infant prophylaxis** if breastfeeding, and intensify breastfeeding support.

Recommend **condom use and contraception** as appropriate, and partner testing

VL < 50 c/mL Repeat as per VL Monitoring schedule on page 20 Repeat VL after 4-6 weeks 1

Result of repeat VL is unsuppressed 2 (VL > 50 c/ml)

Re-assess and resolve adherence issues! 3

(See also page xx)

On TLD for at least 2 years, and two or more VLs ≥ 1000 c/mL (taken two or more years after starting TLD regimen) and Adherence > 80% <sup>5</sup>

Go to the algorithm for

"Management of confirmed
virological failure on TLD"

on page xx of the ART Clinical Guideline

On TLD less than 2 years <sup>4</sup>
or adherence still suboptimal <sup>5</sup>,
or persistent low-level viraemia<sup>6</sup>

Repeat VL in 3 months' time

(or at delivery if > 28 weeks gestation)
Intensify efforts to
resolve adherence issues 7

## **Electronic Gate Keeping (EGK) Codes**

#### **EGK codes serve three functions:**

1

Prevent sample rejection

Allow individual patients to be traced using the NHLS RfA reports

3

Monitor VL suppression rates at a program level





## EGK code Job Aid



**EGK authorisation codes** for HIV Viral Load testing

in pregnant and breastfeeding women

**Two special EGK approval codes** must be provided with EVERY HIV VL requested during pregnancy and breastfeeding.

#### The electronic gatekeeping (eGK) codes will:

prevent HIV VL tests from being cancelled by gatekeeping

ACILITY NAME

COLLECTION DATE

LINICIAN / HCW NAME

C#PMTCT

 facilitate HIV VL monitoring of the pregnant and breastfeeding women



## Pregnancy-related EGK approval codes

C#PMTCT To be used during pregnancy and breastfeeding

C#DELIVERY To be used during labour

Please spell the eGK codes correctly

#### **NHLS Requisition Form**

Fill in the eGK code in 'eGK approval code' if present on the form or, on forms where this is not provided, clearly state in an available space such as below the 'HPCSA/SANC number' as indicated







# NHLS Results for Action (RfA) Report

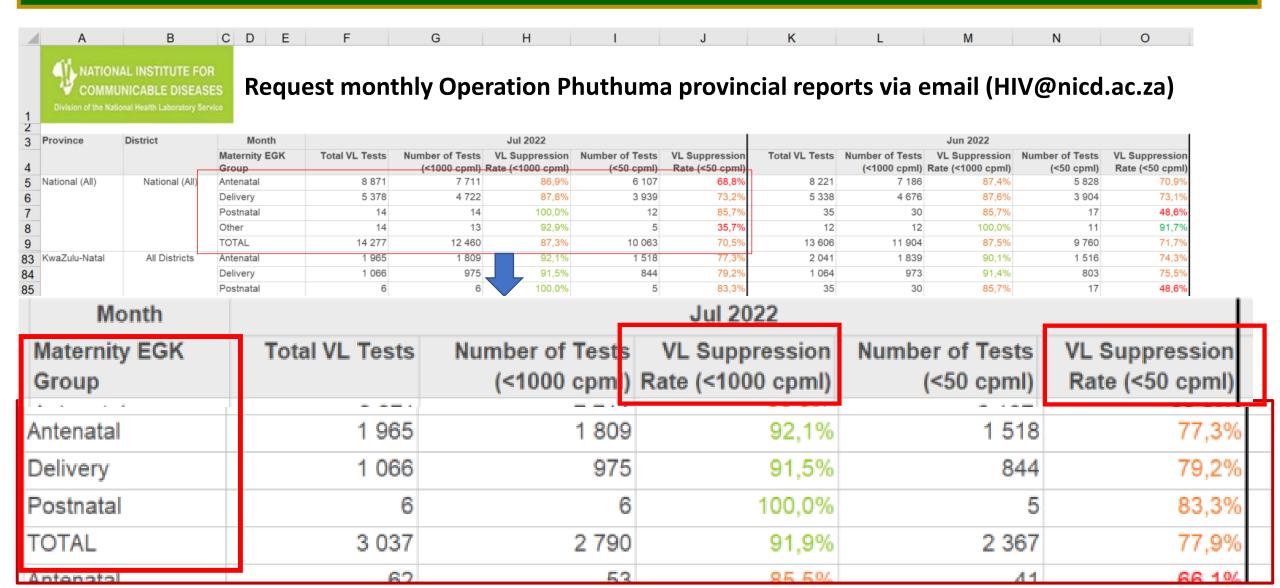
VL results >1000 cpml are highlighted in red.

VL results between 50-999 cpml are highlighted yellow.

The "Maternity EGK Group" column indicates the EGK code classification: antenatal, delivery, postnatal or other.

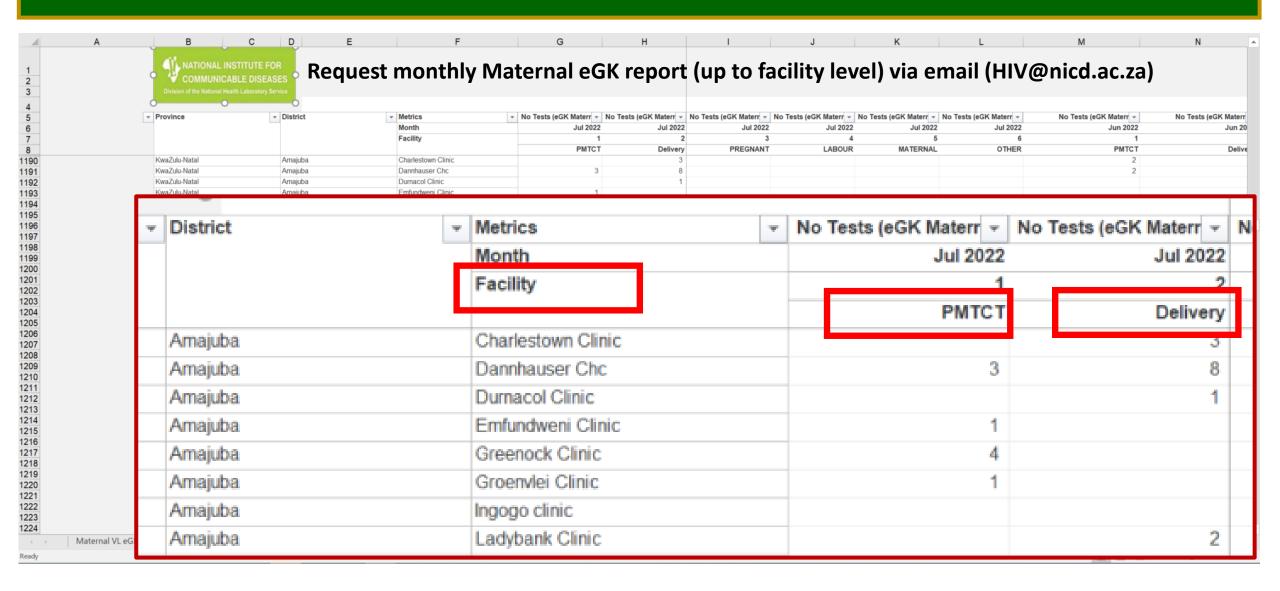
																			T-4-11
Province	District	Sub District	Facility	Ward	Folder No	Patient Surname	Patient Name	Patient DOB	Sex	Patient Address	Patient Tel No	Patient Age	Taken Date	Reviewed Date		CDW Patient Identifier	HIV VL Result (Detected VL)	Maternity EGK Group	Total No. of Previous Consecutive VL >1000
KwaZulu-Natal	eThekwini Metro	eThekwini	Bluff Clinic	Not Applicable	xxxxxxxx	xxxxxxx	xxxxxxx	DD-MMM-YY	F	xxx xxxxxxxxxx	xxxxxxxxxx	32 years 11 months 5 days	DD-MMM-YY	07-FEB-2021	xxxxxxxxxx	xxxxxxxx	1010		1
KwaZulu-Natal	eThekwini Metro	eThekwini	Addington Hospital	Ikusasa Clinic	xxxxxxx	xxxxxxx	XXXXXXXXX	DD-MMM-YY	М	XXX XXXXXXX XXXXXXX XXXXXXX	xxxxxxxxxx	70 years 9 months 23 days	DD-MMM-YY	07-FEB-2021	xxxxxxxxxx	-1	1006		
KwaZulu-Natal	eThekwini Metro	eThekwini	Ntuzuma Clinic	Anti- retroviral Clinic	xxxxxxx	xxxxxxx	xxxxxxx	DD-MMM-YY	М	xx xx	xxxxxxxxxx	50 years 2 months	DD-MMM-YY	06-FEB-2021	xxxxxxxxxx	xxxxxxxx	1003		
KwaZulu-Natal	eThekwini Metro	eThekwini	Waterfall Clinic	Ward Not Stated	xxxxxxx	xxxxxxx	xxxxxxx	DD-MMM-YY	F	XXX XXXXXXX XXXXXXX		32 years 8 days	DD-MMM-YY	02-FEB-2021	xxxxxxxxxx	xxxxxxx	950	Antenatal	
KwaZulu-Natal	eThekwini Metro	eThekwini	Overport Clinic	Not Applicable	xxxxxxx	xxxxxxx	xxxxxxx	DD-MMM-YY	F			31 years 10 months 1 day	DD-MMM-YY	04-FEB-2021	xxxxxxxxx	xxxxxxx	947		
KwaZulu-Natal	eThekwini Metro	eThekwini	Mfume Clinic	Not Applicable	xxxxxxx	xxxxxxx	xxxxxxx	DD-MMM-YY	М	XXX XXXXXXX XXXXXXX XXXXXXX		31 years 4 months 29 days	DD-MMM-YY	02-FEB-2021	xxxxxxxxxx	xxxxxxxx	943		
KwaZulu-Natal	eThekwini Metro	eThekwini	Glen Earle Clinic	Ward Not Stated	xxxxxxx	xxxxxxx	xxxxxxx	DD-MMM-YY	F	XXX XXXXXXX XXXXXXX XXXXXXX	xxxxxxxxxx	33 years 1 month 3 days	DD-MMM-YY	01-FEB-2021	xxxxxxxxxx	xxxxxxx	940	Delivery	
KwaZulu-Natal	eThekwini Metro	eThekwini	Goodwins Clinic	Anti- retroviral Clinic	xxxxxxx	xxxxxxx	xxxxxxx	DD-MMM-YY	F	xxx		25 years 4 months	DD-MMM-YY	04-FEB-2021	xxxxxxxxx	xxxxxxx	940		
KwaZulu-Natal	eThekwini Metro	eThekwini	Halley Stott Clinic	Not Applicable	xxxxxxx	xxxxxxx	xxxxxxx	DD-MMM-YY	F			37 years 2 months 14 days	DD-MMM-YY	02-FEB-2021	xxxxxxxxx	xxxxxxx	940		
KwaZulu-Natal	eThekwini Metro	eThekwini	Goodwins Clinic	Anti- retroviral Clinic	xxxxxxx	xxxxxxx	xxxxxxx	DD-MMM-YY	F	xxx		35 years 10 months 16 days		04-FEB-2021	xxxxxxxxx	xxxxxxx	906		
KwaZulu-Natal	eThekwini Metro	eThekwini	Tongaat CHC	Unknown	xxxxxxx	xxxxxxx	xxxxxxx	DD-MMM-YY	F			44 years 10 months 1 day		07-FEB-2021	xxxxxxxxx	xxxxxxx	898		
KwaZulu-Natal	eThekwini Metro	eThekwini	Lancers Road Clinic	Not Applicable	xxxxxxx	xxxxxxx	xxxxxxx	DD-MMM-YY	F			29 years 10 months 11 days	DD-MMM-YY	06-FEB-2021	xxxxxxxxx	xxxxxxx	897		
KwaZulu-Natal	eThekwini Metro	eThekwini	Prince Mshiyeni Hospital	Ward D3	xxxxxxxx	xxxxxxx	XXXXXXXXX	DD-MMM-YY	М			64 years 4 months	DD-MMM-YY	05-FEB-2021	xxxxxxxxxxx	xxxxxxxx	896		][
< →	Terms & Cor	nditions C	over Page	VL Results	for Actio	on Prev	ious VL>1	000	<b>(+)</b>							: 4			<b>•</b>

## Operation Phuthuma report – District level VLS rates





## Monthly Maternal eGK report (facility level)



## Interpretation

- Now that you know how many VLs had EGK codes per facility
- You need to determine

## How many VLs should have had EGK codes??

- 1. DHIS data provides the denominator for VL EGK codes in ANC
  - Antenatal already on ART at 1st visit
  - Antenatal start on ART
  - 2. DHIS data provides the denominator for VL EGK codes at delivery
    - Live births to HIV-positive women

# VTP: Optimising Care for the HIV Exposed Infant to minimise vertical transmission

## 2019 GL definition of "high-risk" for an HEI



#### South African 2019 PMTCT GL

- Maternal delivery VL > 1000 c/ml
- If no delivery VL result available at discharge
  - Review VL in the last 12 weeks of antenatal care
  - High-risk if
    - VL > **1000** c/ml, or
    - No VL in last 12 weeks



#### **WHO Guidelines**

- Review VL in the last 4 weeks of antenatal care
- High-risk if
  - VL > 1000 c/ml, or
  - no VL in last 4 weeks
  - Mother on ART for < 4 weeks prior to delivery

## Tightening the definition of higher-risk

Delivery VL will determine the final risk profile of the HIV exposed Infant

Higher-risk until proven low-risk

#### **Need to consider**

- VL threshold where the delivery VL is known
- When delivery VL is not known, at discharge from labour ward

# Tightening the definition of higher-risk: Where the delivery VL result is known

**Change 1: VL threshold for defining higher risk** 

VL > 1000 c/ml

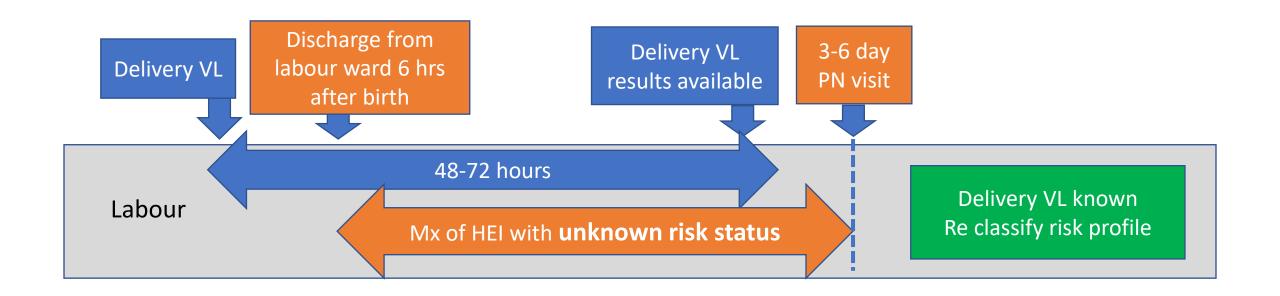
to

VL > 50 c/ml

## Tightening the definition of high-risk: When delivery VL is not known, at discharge from labour ward

Delivery VL will determine the final risk profile of the HIV exposed Infant

#### Higher-risk until proven low-risk



## Considerations for defining "higher-risk"

- ANC 1<sup>st</sup> booking before 20 weeks gestation rate = 70%
- ANC on ART at 1<sup>st</sup> booking > 75%

For most women NO VL done in last 4 wks



- Maternal Delivery VL> 1000 c/ml
- Review VL in the last
   12 weeks of antenatal
   care

84% HEI will be high-risk



- Maternal VL > 1000 c/ml
- Review VL in the last 4 weeks of antenatal care

94% HEI will be high-risk



- Maternal Delivery VL> 1000 c/ml
- Simplify decision

All HEI will be high-risk until proven low-risk by delivery VL results at 3-6 day visit

# Tightening the definition of high-risk: Where the delivery VL result is not known

## **Change 2: Universal Dual Prophylaxis**



#### 2023 VTP Guideline

Dual prophylaxis will be given to all HEI at birth until proven low-risk by delivery VL results at 3-6 day visit

## Pros and Cons of Universal Dual Prophylaxis

- Simplicity in a blanket approach
- If mothers do not return at 3-6 day visit, at least babies are covered while VL remains unknown
- UDP may strengthen implementation of delivery VL and 3-6 day PN visit
- There is AZT "wastage" for the 6 % additional HEIs who will get dual prophylaxis while their status is unknown, but this is a minimal cost when compared to potential gains from the changes

## Changes for the VTP programme –HIV-exposed Infant

Summary: Tightening the definition of "high-risk" for transmission

- All babies will receive Dual prophylaxis at birth (NVP & AZT) until the results of the delivery VL are known
- Once delivery is VL known, the threshold for defining "higher-risk" has been moved from VL > 1000 c/ml
   to VL > 50 c/ml

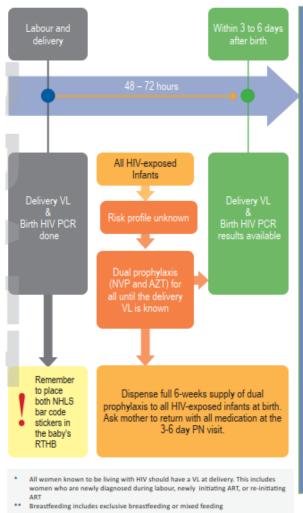
566 HIV infections prevented



Cost-saving of R11,3 million



## 3 pages in the VTP Guideline



	Maternal Delivery VL *	Classification	Prophylaxis	Comment
	Delivery VL< 50 copies/mL regardless of feeding choice	Low risk	Change to low-risk prophylaxis • Stop AZT • NVP daily for six weeks.	Affirm and encourage good adherence.     Repeat maternal VL 6 monthly during breastfeeding.     Do all routine HIV tests for HIV-exposed infants as indicated on "HIV Testing For The HIV-Exposed Infant" on page 27.
Reclassify risk profile	Delivery VL ≥ 50 copies/mL in a breastfeeding mother**	Higher risk	Continue dual prophylaxis:  • AZT twice daily for six weeks.  • NVP daily for a minimum of 12 weeks.	Do an ABCDE assessment and intervention as a matter of urgency to achieve a suppressed VL in the mother as soon as possible. Follow the "VL Non-Suppression Algorithm" on page 22. Stop infant NVP only after confirmation of maternal VL being less than 50 c/mL, or until four weeks after cessation of all breastfeeding. Do all routine HIV tests for HIV-exposed infants as indicated on "HIV Testing For The HIV-Exposed Infant" on page 27.
	Delivery VL ≥ 50 copies/mL in a mother who is exclusively formula- feeding her infant from birth	Higher risk	Continue dual prophylaxis:  AZT twice daily for six weeks.  NVP daily for six weeks.	Do an ABCDE assessment and intervention as a matter of urgency to achieve a suppressed VL in the mother as soon as possible. Follow the "VL Non-Suppression Algorithm" on page 22. Do all routine HIV tests for HIV-exposed infants as indicated on "HIV Testing For The HIV-Exposed Infant" on page 27.
	Birth PCR positive	HIV infected	Con with a 2nd PCR o	and AZT prophylaxis. Initiate ART.  Ifirm the positive result  In a new sample. Start cotrimoxazole  therapy (CPT) at 6 weeks of age.

#### DOSING CHARTS FOR PROPHYLAXIS FOR THE HIV-EXPOSED INFANT

#### Summary of infant prophylaxis regimens

**PROPHYLAXIS** 

FOR

푦

**HIV-EXPOS** 

ш

INFANT

A

BIRTH

	Risk Profile	NVP	AZT
At birth	Low-risk, whether breastfed or formula-fed	6 weeks	Stop AZT
(following maternal delivery	Higher-risk and breastled ##	minimum of 12 weeks	6 weeks
VL review)	Higher-risk and exclusively formula fed	6 weeks	6 weeks
During breast/seeding	Higher-risk during breas#eeding	minimum of 12 weeks	6 weeks

#### Dosing charts for infant HIV prophylaxis in infants > 2000 gm

ı	bosing charts for infant the prophylaxis in finants 2 2000 gm												
	NVP and AZT dosing table for prophylaxis at birth and during breastfeeding (see also Management of an Unsuppressed VL during Breastfeeding on page xx)												
Birth-6 weeks 6 weeks -													
		2.0 – 2.49 kg	≥2.5 kg	6 months	6 – 9 months	9 – 24 months							
	NVP (Daily)	1 mL (10 mg) daily	1.5 mL (15 mg) daily	2 mL (20 mg) daily	3 mL (30 mg) daily	4 mL (40 mg) daily							
	AZT 1 mL (10 mg) 1.5 mL (15 mg) twice 6 mL (60 mg) twice Children >6 months of age requiring AZT (Twice daily) twice daily grophylaxis should use treatment doses.												

Source: Paediatric Hospital Level EML 2022

#### Dosing charts for infant HIV prophylaxis in preterm infants < 2000 gm

Nevirapine, oral, daily										
First 2 weeks after birth (mg of NVP)	After first 2 weeks after birth (mg of NVP)									
1 mg	2 mg									
1.5 mg	3 mg									
2 mg	4 mg									
3 mg	5 mg									
3.5 mg	6 mg									
	First 2 weeks after birth (mg of NVP)  1 mg  1.5 mg  2 mg  3 mg									

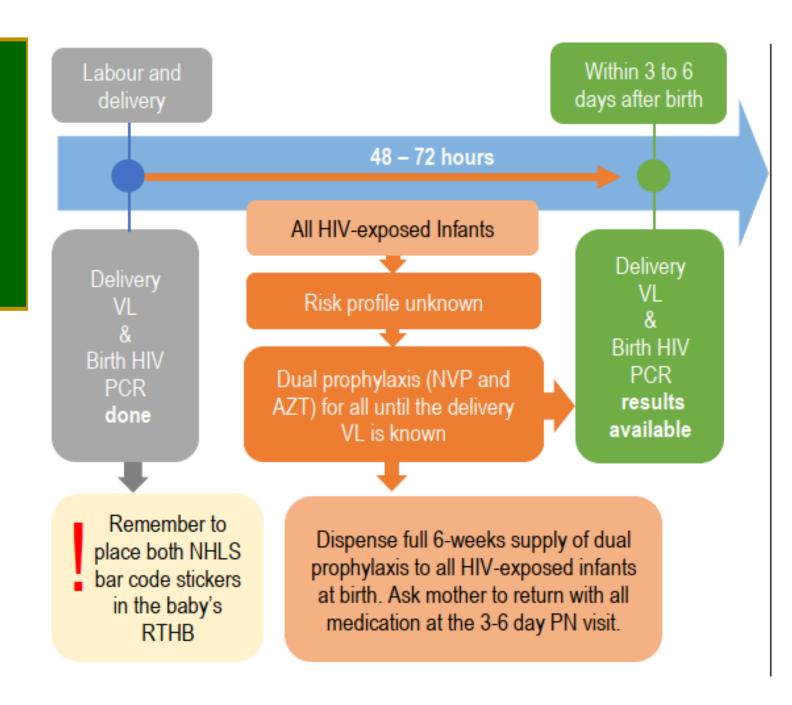
If the infant at the time of discharge is severely underweight-for-age (3 5D or 3 z-scores below the mean), give NVP according to weight (i.e. 4 mg/kg/dose daily) until in the normal weight-for-age range.

Zidovudine, oral, twice daily										
Gestational age at birth	First 2 weeks after birth	2-4 weeks after birth	4–6 weeks after birth	>6 weeks after birth						
30–35 weeks	2 mg/kg	3 mg/kg	4	mg/kg						
<30 weeks	2 mg	kg	3 mg/kg	4 mg/kg						

#### Dosing chart for intravenous (IV) AZT prophylaxis

Gestational Age	Approximate birth weight	AZT IV dosing for the first 14 days (If unable to tolerate oral agents)
≥35 weeks ≥ 2.5 kg		3 mg/kg body weight IV every 12 hours
<35 weeks	< 2.5 kg	1.5 mg/kg body weight IV every12 hours

# Prophylaxis for the HIV-exposed infant at birth (1)



## Prophylaxis for the HIVexposed infant at birth (2)

	Maternal Delivery VL *	Classification	Prophylaxis	Comment
	Delivery VL< 50 copies/mL regardless of feeding choice	Low risk	Change to low-risk prophylaxis • Stop AZT • NVP daily for six weeks.	Affirm and encourage good adherence.     Repeat maternal VL 6 monthly during breastfeeding.     Do all routine HIV tests for HIV-exposed infants as indicated on "HIV Testing For The HIV-Exposed Infant" on page 27.
Reclassify risk profile	Delivery VL ≥ 50 copies/mL in a breastfeeding mother**	Higher risk	Continue dual prophylaxis:  AZT twice daily for six weeks.  NVP daily for a minimum of 12 weeks.	Do an ABCDE assessment and intervention as a matter of urgency to achieve a suppressed VL in the mother as soon as possible. Follow the "VL Non-Suppression Algorithm" on page 22.  Stop infant NVP only after confirmation of maternal VL being less than 50 c/mL, or until four weeks after cessation of all breastfeeding.  Do all routine HIV tests for HIV-exposed infants as indicated on "HIV Testing For The HIV-Exposed Infant" on page 27.
	Delivery VL ≥ 50 copies/mL in a mother who is exclusively formula- feeding her infant from birth	Higher risk	Continue dual prophylaxis:  • AZT twice daily for six weeks.  • NVP daily for six weeks.	Do an ABCDE assessment and intervention as a matter of urgency to achieve a suppressed VL in the mother as soon as possible. Follow the "VL Non-Suppression Algorithm" on page 22.      Do all routine HIV tests for HIV-exposed infants as indicated on "HIV Testing For The HIV-Exposed Infant" on page 27.
	Birth PCR positive	HIV infected	Con with a 2nd PCR o	and AZT prophylaxis. Initiate ART. firm the positive result n a new sample. Start cotrimoxazole therapy (CPT) at 6 weeks of age.

## **Cotrimoxazole Prophylaxis**

Change 3: CPT will no longer be given to for HEI infants

- CPT for confirmed HIV-infected infants and children (unchanged)
- No CPT for HIV-exposed infants who are uninfected, regardless of the mother's VL or breastfeeding status

## Clinical Evidence Informing CPT Guidelines

#### Current guidelines based on the 2004 CHAP study, in the context of

- no maternal ART,
- no infant prophylaxis (HIV),
- no paediatric ART,
- CPT showed benefit in those HIV-positive children with very low CD4 counts

#### Recent evidence for Botswana and South African studies

- No benefit for mortality or morbidity for HEIs
- Potential harm
  - SA study CTX associated with microbiome dysbiosis and increase in resistance genes
  - Botswana study showed CTX prophylaxis increased resistance to CTX AND Amoxicillin (1st line pneumonia treatment)

Lockman et al. 2017; Daniels et al. 2019

## Cotrimoxazole Prophylaxis Therapy for HEIs

### In context of tighter definition and management of high-risk HEIs

No CPT for HIV-exposed infants

who are uninfected, regardless of the mother's VL or breastfeeding status

### Focus should be on preventing HIV infection

- Achieving and maintaining maternal VL suppression
- keeping HIV-exposed infants in care with
- PCR testing as per guidelines, and
- ART initiation in the small proportion of children who do become HIV infected, with
- CPT for confirmed HIV-infected infants and children (unchanged)

## Integration of clinical and service delivery components





Toolkit

Who decides which tool is used where??

→ The clinician

#### 1. Tools for Clinical Management

Optimised regimens using TLD

Monitoring on ART

Preventing and managing STIs, NCDs and OIs with TPT and CPT

#### 2. Tools for Differentiated Care (DMOC SOPs)

**New patient** 

SOP 1 FTIC

**Stable patient** 

SOP 5 RPCs SOP 6 Switch in RPCs Non-stable patient

SOP 2 EAC

SOP 7 Trace

SOP 8 Re-engagement

**SOP 3 Disclosure** 

**SOP 4 MMD** 

#### 3. Tools for the Provision of Integrated Care

Visit schedules to align EPI visits with paeds ART, maternal ART, maternal contraception, maternal PrEP, TB treatment and ART

## Specific table aligning to infant EPI schedule: HIV exposed infant and mother ART visits and mother's FP visits

	Age group	Age of child	Routine visits as per RTHB	ART Dispensing cycle (DC)	Follow-up for the HIV-exposed baby	ART Follow-up for mother	Immunisations	Feeding advice
	Neonate	1# week of life	3-6 days postnatal (PN) visit for mother and baby	1	Follow-up results of birth PCR* and mother's delivery VL if birth PCR negative, re-classify the risk profile of the HEI:     Delivery VL < 50 c/mL (low-risk)     Stop AZT and continue NVP daily for six weeks     Delivery VL ≥ 50 c/mL (higher-risk)     Continue AZT twice daily for six weeks     Continue NVP daily for minimum of 12 weeks     Check adherence to NVP and AZT dispensed at delivery	Follow-up results of mother's delivery VL     Delivery VL ≥ 50 c/mL: manage as per "Viral Load Monitoring Schedule" on page 20.     Check ART supply: The mother should have been provided with 2 months ART at discharge from labour ward which will last her until 6 week PN visit     Adherence check-in for mother     Provide breastfeeding support and routine PN care		x
		6 weeks	6 weeks	2*	Ensure that birth PCR and mother's VL results were checked, recorded and acted upon correctly     If low-risk, stop NVP     If higher-risk, stop AZT and dispense NVP for additional 6 weeks	Postnatal clip review and adherence check-in. c/mL, repeat VL at this visit     Provide     Prov     Same as EPI	х	اِ
		10 weeks	10 weeks	3	Do 10 week HIV-PCR * If higher-risk, check result of repeat maternal VL done at 6 weeks visit.  If VL < 50 c/mL, advise to stop NVP after 12 weeks  If VL still ≥ 50 c/mL, dispense and continue NVP until the breastfeeding mother's VL is confirmed to be < 50 c/mL	• It as p. 22 • If mother or NET-EN (It repeat injection this visit***	х	
	2-6 months (monthly follow-up)	14 weeks	14 weeks 14 weeks		Check that 10 week HIV-PCR results were checked, recorded and acted upon correctly	<ul> <li>Adherence check-in for mother</li> <li>Provide breastfeeding support.</li> <li>Provide ART for 3 DCs (3MMD) for mother</li> </ul>	х	
	Tollow up,	18 weeks	4 months	5				
		22 weeks	5 months	6				
		26 weeks	6 months	7	<ul> <li>Do 6-month HIV-PCR test *</li> <li>Review results of PCR and VL in 1 week using NHLS RfA reports. If mother's VL ≥ 50c/mL, restart/extend infant prophylaxis if still breastfeeding. Go to "Management of a High Maternal Viral Load after Delivery" on page 24.</li> </ul>	<ul> <li>Clinical review and '6-month' VL.</li> <li>Provide breastfeeding support and discuss the introduction of complementary feeding at age 6 months</li> <li>Script for and provide ART for 3DCs at a time (3MMD)</li> <li>Review results of VL and PCR in 1 week using NHLS RfA reports. If VL ≥ 50c/mL, manage mother as per the "VL Non-Suppression</li> </ul>	х	

#### Key points to note (pg 40-41):

Deworming

**EPI** 

Oral Health

- Align HIV exposed infant clinical follow-up and HIV testing schedule with EPI schedule
- Aim to provide all care at same service OR AT LEAST SAME return date schedule and same facility

# Specific table aligning to infant EPI schedule: HIV exposed infant and mother ART visits and mother's FP visits

Age group	Age of child	Routine visits as per RTHB	ART Dispensing cycle (DC)	Follow-up for the HIV-exposed baby	ART Follow-up for mother	Immunisations	Feeding advice	Growth monitoring	Development	Head circumference	Vit A	Deworming	Oral Health	TB Screen	Mother's Family planing (FP)
Neonate	1st week of life	3-6 days postnatal (PN) visit for mother and baby	1	Follow-up results of birth PCR* and mother's delivery VL If birth PCR negative, re-classify the risk profile of the HEI:     Delivery VL < 50 c/mL (low-risk)     Stop AZT and continue NVP daily for six weeks     Delivery VL ≥ 50 c/mL (higher-risk)     Continue AZT twice daily for six weeks     Continue NVP daily for minimum of 12 weeks     Check adherence to NVP and AZT dispensed at delivery	Follow-up results of mother's delivery VL     Delivery VL ≥ 50 c/mL: manage as per "Viral Load Monitoring Schedule" on page 20.     Check ART supply: The mother should have been provided with 2 months ART at discharge from labour ward which will last her until 6 week PN visit     Adherence check-in for mother     Provide breastfeeding support and routine PN care		x	Sar	ma	<b>EF</b>				х	x**
	6 weeks	6 weeks	2*	Ensure that birth PCR and mother's VL results were checked, recorded and acted upon correctly     If low-risk, stop NVP     If higher-risk, stop AZT and dispense NVP for additional 6 weeks	<ul> <li>Postnatal clinical review and adherence check-in.     If delivery VL ≥ 50 c/mL, repeat VL at this visit</li> <li>Provide breastfeeding support.</li> <li>Provide ART for 2 DCs (2MMD) for mother*</li> </ul>	х				dule				x	
	10 weeks	10 weeks	3	Do 10 week HIV-PCR  If higher-risk, check result of repeat maternal VL done at 6 weeks visit.  If VL < 50 c/mL, advise to stop NVP after 12 weeks  If VL still ≥ 50 c/mL, dispense and continue NVP until the breastfeeding mother's VL is confirmed to be < 50 c/mL	If VL repeated at 6 weeks, review results. Manage as per "VL Non-Suppression Algorithm" on page 22  If mother received either DMPA (Depo Provera®) or NET-EN (Nur Isterate®) after delivery, give repeat injection at this visit***	х	x	х						х	х
2-6 months (monthly follow-up)	14 weeks	14 weeks	4	Check that 10 week HIV-PCR results were checked, recorded and acted upon correctly	Adherence check-in for mother     Provide breastfeeding support.     Provide ART for 3 DCs (3MMD) for mother					as E dule			_	¥	
ioliow-up)	18 weeks	4 months	5				(ι	ınle	ss l	NET.	-EN	)		х	
	22 weeks	5 months	6				х	х						х	
	26 weeks	6 months	7	<ul> <li>Do 6-month HIV-PCR test *</li> <li>Review results of PCR and VL in 1 week using NHLS RfA reports. If mother's VL ≥ 50c/mL, restart/extend infant prophylaxis if still breastfeeding. Go to "Management of a High Maternal Viral Load after Delivery" on page 24.</li> </ul>	<ul> <li>Clinical review and '6-month' VL.</li> <li>Provide breastfeeding support and discuss the introduction of complementary feeding at age 6 months</li> <li>Script for and provide ART for 3DCs at a time (3MMD)</li> <li>Review results of VL and PCR in 1 week using NHLS RfA reports. If VL ≥ 50c/mL, manage mother as per the "VL Non-Suppression Algorithm" on page 22</li> </ul>	х	x	x	х		х			х	х

Mother ART clinical follow-up AND contraception aligned with EPI schedule

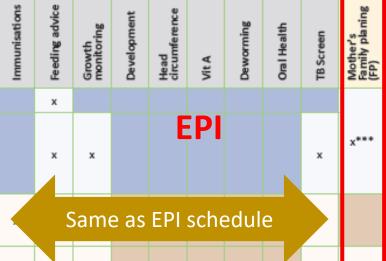
2-month supply at birth

#### **NEW:**

- 2-month supply again at 6 wks\*
- 3-month supply at 14 wks, 6 months and 3-monthly to align with VL

## Specific table aligning to EPI schedule Mother's PrEP and FP visits

Age group	Age of child	Routine visits as per RTHB	PrEP Dispensing cycle (DC)	PrEP Follow-up for mother	Immunisations	
Delivery			1	<ul> <li>Provide 3 months* of PrEP (3MMD) which will last until 10 week PN visit</li> </ul>		
Neonate	1st week of life	3-6 days postnatal (PN) visit for mother and baby		<ul> <li>Provide HIV test to mother (if not tested in labour)</li> <li>Check PrEP supply: The mother should have been provided with 3 months* of PrEP at delivery which will last her until 10 week PN visit</li> <li>PrEP adherence check-in for mother</li> <li>Provide breastfeeding support and routine post natal care</li> </ul>		
	6 weeks	6 weeks	2*	Postnatal clinical review     Provide breastfeeding support     PrEP adherence check-in	<	
	10 weeks	10 weeks	3	<ul> <li>Postnatal and PrEP clinical review and PrEP adherence check-in</li> <li>Provide breastfeeding support.</li> <li>Provide HIV test and STI screen to mother</li> <li>Provide PrEP for 3 PrEP DCs (3MMD) for mother**</li> <li>If mother received either DMPA (Depo Provera<sup>o</sup>) or NET-EN (Nur Isterate<sup>o</sup>) after delivery, give repeat injection at this visit****</li> </ul>		
2-6 months	14 weeks	14 weeks	4	Postnatal clinical review     Provide breastfeeding support     PrEP adherence check-in		
	18 weeks	4 months	5			
	22 weeks	5 months	6			
	26 weeks	6 months	7	<ul> <li>PrEP clinical review</li> <li>Provide breastfeeding support.</li> <li>HIV test and STI screen for mother</li> <li>Script for and provide PrEP for 3DCs at a time (3MMD)</li> </ul>		



NEW: Annexure 4 (pg 49-50)

Align to infant EPI schedule:

- Mother's PrEP visits including PrEP related HIV and STI monitoring
- Contraception visits

# Specific table aligning to EPI schedule Mother's PrEP and FP visits

Age group	Age of child	Routine visits as per RTHB	PrEP Dispensing cycle (DC)	PrEP Follow-up for mother	Immunisations	Feeding advice	Growth monitoring	Development	Head circumference	Vit A	Deworming	Oral Health	TB Screen	Mother's Family planing (FP)
Delivery			1	<ul> <li>Provide 3 months* of PrEP (3MMD) which will last until 10 week PN visit</li> </ul>		х								
Neonate	1st week of life	3-6 days postnatal (PN) visit for mother and baby		Provide HIV test to mother (if not tested in Jahour)  Check PrEP supply: The mother should have been provided with 3 months* of PrEP at delivery which will last her until 10 week PN visit  Prep agnerence check-in for modier  Provide breastfeeding support and routine post natal care		x	x		E	PI			х	x***
	6 weeks	6 weeks	2*	Postnatal clinical review     Provide breastfeeding support     PrEP adherence check-in	x	x	x						х	
2-6 months	10 weeks	10 weeks	3	Postnatal and PrEP clinical review and PrEP adherence check-in Provide breastfeeding support. Provide HIV test and STI screen to mother Provide PrEP for 3 PrEP DCs (3MMD) for mother** If mother received either DMPA (Depo Provera®) or NET-EN (Nur Isterate®) after delivery, give repeat injection at this visit****	х	х	x						х	x
	14 weeks	14 weeks	4	Postnatal clinical review     Utilizes 3-monthly combined PrEP clinical	х	x	x	х	x				х	
	18 weeks	4 months	5	reviews and drug refills from birth		х	x						х	
	22 weeks	5 months	6	Where mother on PrEP at delivery, mother		х	х						х	
20	26 weeks	6 months	7	must leave maternity unit with 3-months of PrEP supply on hand			x	х		x			x	x

# VTP: Optimising care for a mother living with syphilis to minimise vertical transmission

### Resurgence of Congenital Syphilis case in SA

- Syphilis remains a significant cause of preventable perinatal death in SA.
- 2019 prevalence of syphilis is estimated at 2.6% (95% CI: 2.4%–2.9%)
- 30% increase in prevalence between 2015 and 2019
- Maternal syphilis screening coverage at first antenatal visit was 96.4% at national level.
- However, despite good antenatal attendance and early maternal syphilis testing, there has been a resurgence of congenital syphilis cases in many provinces in South Africa
- Adverse pregnancy outcomes occur in up to 80% of syphilis seropositive, untreated pregnant women
- South Africa has committed to dual elimination of both HIV and syphilis

### Modifiable factors for congenital syphilis

Testing and f/up

n=20 (38%)

Booking test not traced

n=12

Booking test not treated

n=3

No booking test done

*n*=5

- Related to the timing of testing n=37%
  - Seroconvert during pregnancy: *n*=16
  - Maternal treatment inadequate *n*=3

• Drug stock-outs n=2

Maternal factors: N = 16 (30%)

• Unbooked: n=10

Defaulted follow-up n=4

• Late booker n=2

Quality of care related to testing and f/up of test result is improved

38% of CS cases could be prevented

If testing was more frequent

37% of cases could be prevented

### **Syphilis**

PPIP Analysis of the modifiable factors in 52 cases of congenital syphilis in KZN revealed:

If quality of care related to testing and f/up of test results is improved

38% of CS cases could be prevented

If testing was more frequent 37% of cases could be prevented

Total preventable 38% + 37% = 75%

Rapid testing

To facilitate immediate results and treatment

More frequent testing

To identify seroconversion later in pregnancy

Change 1: Use of single and dual syphilis rapid tests

Change 2: Alignment of HIV and syphilis testing schedule

### Frequency of syphilis testing

- A pregnant woman should be screened and tested for syphilis at her 1st/booking visit in antenatal care. If she tests negative, syphilis testing should be repeated:
  - Scheduled antenatal visits, at approximately 4-weekly intervals, e.g., for BANC+ clients, this could be at 20, 26, 30, 34, and 38 weeks gestation
  - During her labour/delivery admission
  - At the time of diagnosis of an intrauterine death
  - At any time, if the mother has clinical symptoms or signs suggestive of syphilis
- Syphilis testing should be aligned with the HIV testing schedule:
  - If a woman tests positive for HIV, but tests negative for syphilis, repeat syphilis testing should continue at the intervals described above.
  - If a woman tests positive for syphilis but tests negative for HIV, repeat HIV testing should continue at recommended intervals

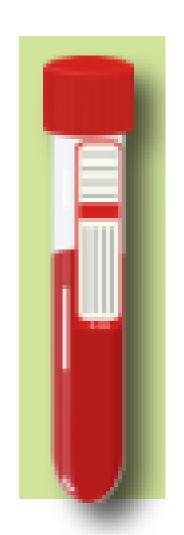
### Types of syphilis tests and their uses: Rapid tests

- Specific (or treponemal) test for syphilis
- Remain positive for life, even if the infection has been treated.
- Positive rapid tests should be confirmed using an RPR test.
  - The RPR will determine if the positive rapid result indicates a current active infection or an earlier infection, and
  - the baseline titre allows the response to treatment to be monitored
- Once a woman has tested positive using a rapid test, a rapid test should no longer be used for routine screening to identify new infections at subsequent visits.
  - A rapid test cannot differentiate between a new and previous infection.
  - An RPR should then be used as the screening test to identify new infections



### Types of syphilis tests and their uses: RPR

- Non-specific (or non-treponemal) tests
- Done in a laboratory.
- RPR titres change in response to treatment or disease progression.
- Used to confirm a positive rapid tests
  - The RPR will determine if the positive rapid result indicates a current active infection or an earlier infection, and
  - the baseline titre allows the response to treatment to be monitored



### Rapid Syphilis Tests

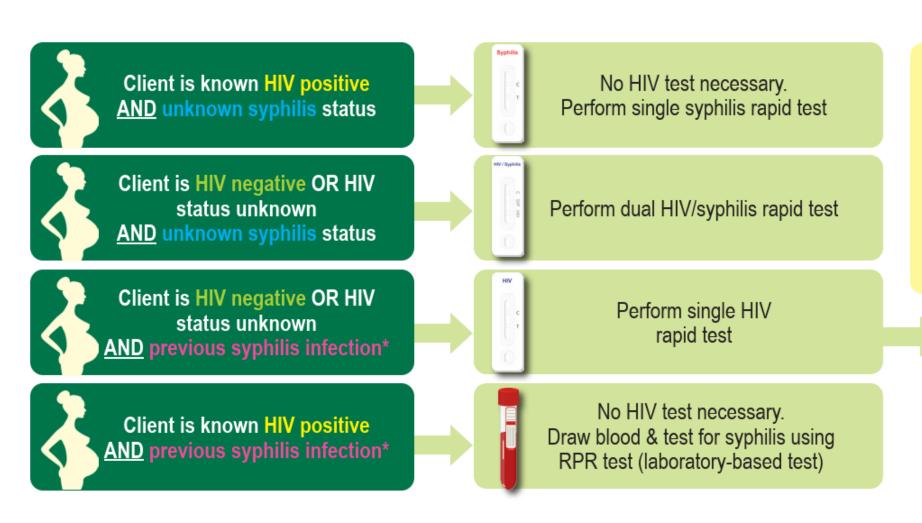
When available and appropriate, rapid testing is the preferred first-line test in pregnancy, as it allows for immediate treatment.

 Rapid syphilis tests are available as a single rapid diagnostic test (RDT) that tests only for syphilis, and a dual RDT which tests for both syphilis and HIV using the same drop of blood.

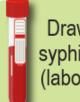
- Dual syphilis and HIV rapid tests should only be used in clients
  - Whose HIV status is negative or unknown AND
  - Who have not had a previous syphilis infection

Clients who are already known to be living with HIV should NOT be re-tested for HIV and should therefore not use a dual syphilis and HIV rapid test!

### Which test should be used when?

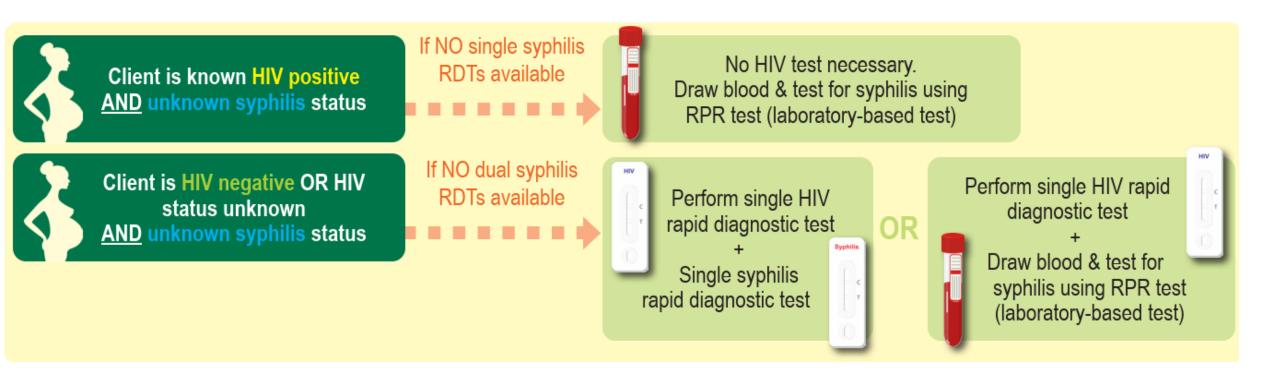


\*Previous syphilis infection: a client is said to have a previous syphilis infection if, during a previous screening the person screened positive for syphilis and through the confirmatory laboratory-based testing it indicated a past syphilis infection OR if syphilis has been diagnosed during their current pregnancy and syphilis treatment has concluded more than 3 months ago.

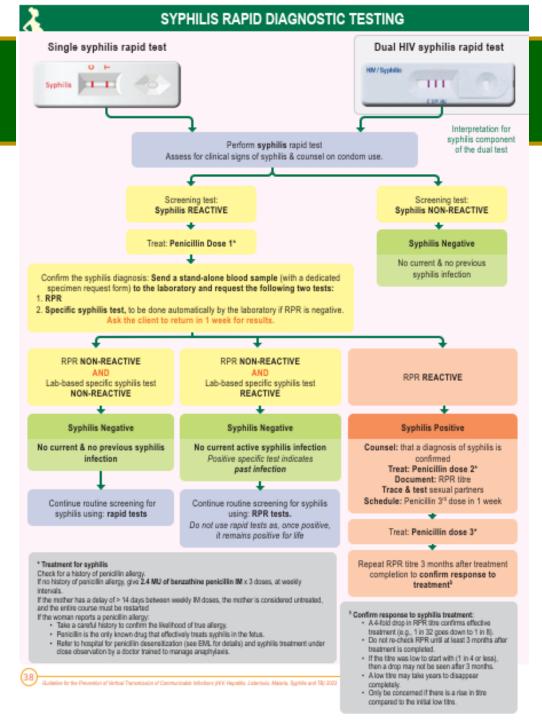


Draw blood & test for syphilis using RPR test (laboratory-based test)

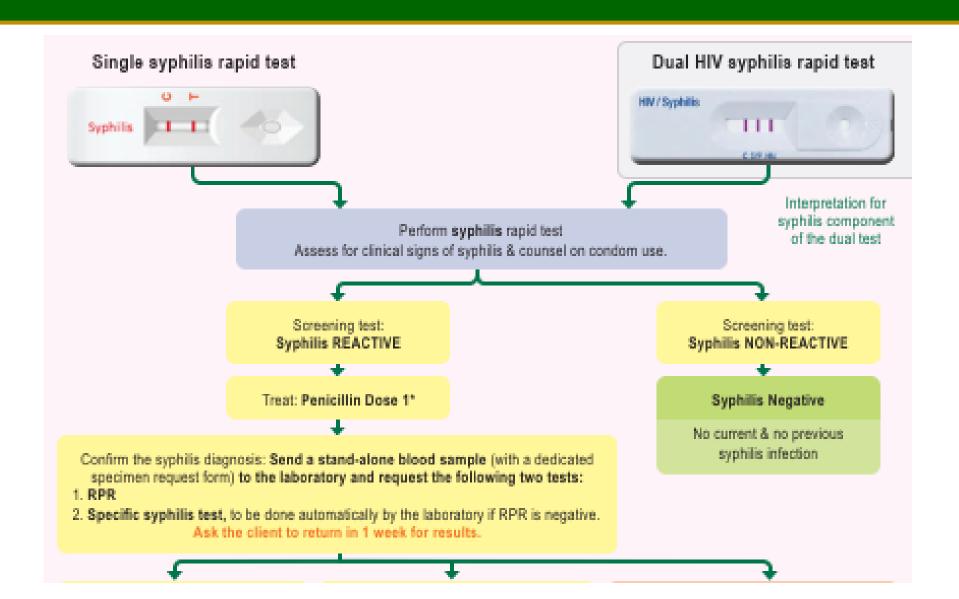
# What to do when a facility does not have syphilis rapid tests in stock



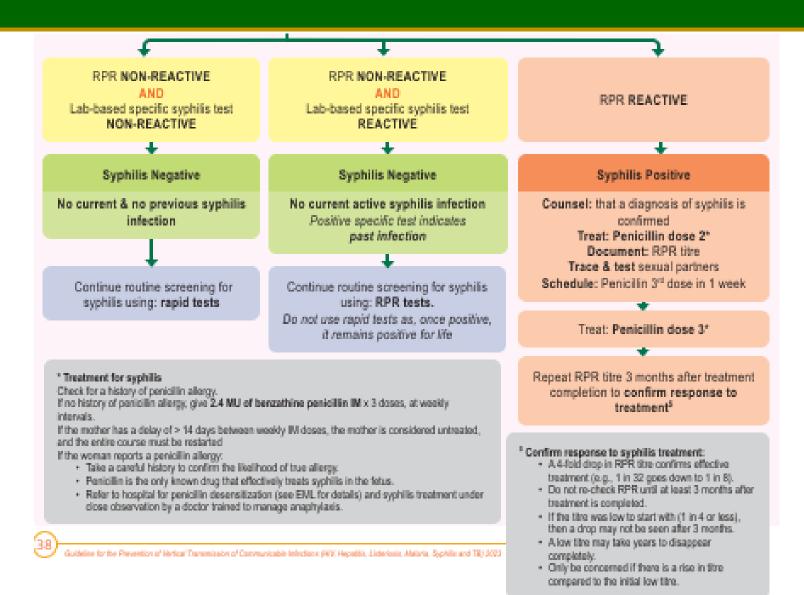
### **Syphilis**



### Syphilis Rapid Testing Algorithm (top half)



### Syphilis Rapid Testing Algorithm (bottom half)



### Confirm response to syphilis treatment:

- A 4-fold drop in RPR titre confirms effective treatment (e.g., 1 in 32 goes down to 1 in 8).
- Do not re-check RPR until at least 3 months after treatment is completed.
- If the titre was low to start with (1 in 4 or less), then a drop may not be seen after 3 months.
- A low titre may take years to disappear completely.
- Only be concerned if there is a rise in titre compared to the initial low titre.

### Treatment for syphilis

- Check for a history of penicillin allergy
  - All-over body rash, bronchospasm, hypotension/collapse, or neck/throat swelling after previously taking penicillin
- If no history of penicillin allergy, give
  - 2.4 MU of benzathine penicillin IM x 3 doses, at weekly intervals
- If the mother has a delay of > 14 days between weekly IM doses, the mother is considered untreated, and the entire course must be restarted
- If the woman reports a penicillin allergy:
  - Take a careful history to confirm the likelihood of true allergy.
  - Penicillin is the only known drug that effectively treats syphilis in the fetus.
  - Refer to hospital for penicillin desensitization (see EML for details) and syphilis treatment under close observation by a doctor trained to manage anaphylaxis.

### **RPR Algorithm**



#### LABORATORY-BASED TESTING WHEN RAPID TESTS ARE UNAVAILABLE OR INAPPROPRIATE



Send a syphilis-dedicated blood sample (with its own separate specimen request form) to the laboratory and request the following two syphilis tests:

- RPR
- 2. Specific syphilis test, to be done automatically by laboratory if RPR is 1:4 or less.

Assess for clinical signs of syphilis & counsel on condom use. Ask the client to return in 1 week for results.

RPR REACTIVE titre 1:8 or greater RPR REACTIVE titre 1:4 or less

Specific syphilis test REACTIVE

Specific syphilis test NON-REACTIVE

RPR REACTIVE titre 1:4 or less.

#### Syphilis Negative

RPR.

NON-REACTIVE

No current syphilis infection Continue routine follow-up screening for syphilis.

#### Syphilis Positive

Counsel: that a diagnosis of syphilis is confirmed

Treat: Penicillin dose 11 Document: RPR titre Trace & test sexual partners Schedule: Penicillin 2<sup>rd</sup> dose in 1 week

Treat: Penicillin dose 2" / Schedule: Penicilin 3rd dose in 1 week

#### Treat: Penicillin dose 3\*

Repeat RPR titre 3 months after treatment completion to confirm response to treatment<sup>5</sup>

#### Confirm response to syphilis treatment:

- A.4-fold drop in RPR titre confirms effective treatment (e.g., 1 in 32 goes.
- Do not re-check RPR until at least 3 months after treatment is completed.
- If the fitre was low to start with (1 in 4 or less), then a drop may not be seen.
- Allow titre may take years to disappear completely.
- Only be concerned if there is a rise in titre compared to the initial low titre.

#### Treatment for syphilis

Check for a history of penicillin allergy. If no history of penicilin allergy, give 2.4 MU of benzathine penicillin IM x 3 doses, at weekly intervals.

If the mother has a delay of > 14 days between weekly IM doses, the mother is considered untreated, and the entire course must be restarted.

If the woman reports a penicilin allergy:

- Take a careful history to confirm the likelihood of true allergy.
- · Penicillin is the only known drug that effectively treats syphilis in the
- Refer to hospital for penicillin desensitization (see EWL for details) and syphilis treatment under close observation by a doctor trained to manage anaphylaxis.

### Congenital syphilis

- 30-40% of babies who acquire syphilis in-utero, die shortly before or after birth
- 2 considerations:
  - Babies' clinical symptoms
  - Mother's treatment status

### Syphilis symptoms in the newborn



Seizures



Jaundice Hepatomegaly



Splenomegaly



Long bone changes



Pallor Petechiae



Large, pale, greasy placenta



Growth restriction



Peeling Rash, Oedema Nonimmune fetal hydrops



Loss of eyebrows, chorioretinitis, uveitis, cataract, glaucoma



Nasal discharge ("snuffles")



Pneumonia



Myocarditis

### Definition - Inadequately or untreated mother:

#### **Inadequately treated mother**

- Mother did not complete three doses in full, or
- Mother received three doses but there was a delay of > 14 days between weekly IM doses, or
- Last dose was not more than 30 days before delivery, or
- Dose that the mother received was incorrect was incorrect

#### **Untreated mother:**

- Mother did not receive any treatment for syphilis, or
- Mother was treated for syphilis with an antibiotic that was not penicillin

### Management of the Syphilis-Exposed Baby

#### MANAGEMENT OF SYPHILIS EXPOSED BABIES

# ASYMPTOMATIC BABIES BORN TO MOTHERS WITH FULLY TREATED SYPHILIS

Mother treated with benzathine penicillin G
2.4 million IU IM weekly for 3 consecutive weeks with last dose > 30 days before delivery.

No treatment indicated. Ensure partner traced and tested. ASYMPTOMATIC BABIES
BORN TO MOTHERS
WITH INADEQUATELY
TREATED\* OR
UNTREATED SYPHILIS\*\*

#### Single dose Benzathine Penicillin G

50 000 units/kg IM.
Never give IV.
Ensure partner is traced, tested and treated (as indicated).

### SYMPTOMATIC BABIES BORN TO MOTHERS WITH SYPHILIS REGARDLESS OF TREATMENT STATUS

#### Aqueous crystalline Penicillin G

- 50 000 units/kg 12 hourly IV or IM for the first 7 days of life, then 8 hourly from day 8 of life onwards to complete 10 days of treatment
- Parenteral penicillin is drug of choice for treatment of congenital syphilis. Data are insufficient regarding use of other antimicrobial agents (e.g., ampicillin).

**Note:** If mother was fully treated & baby symptomatic – re-test mother & follow-up on reason for treatment failure; ensure partner tracing done.

If baby misses more than one day of treatment, the entire ten-day course must be restarted.

### **Babies with symptomatic syphilis**

- All babies require admission for parenteral penicillin
- If unable to admit at current level of care, refer all babies with suspected congenital syphilis infection to appropriate level of care for inpatient admission & work-up.
- Refer all symptomatic babies with complications, e.g., thrombocytopaenia, anaemia, respiratory distress, signs of liver dysfunction, & suspected meningitis to a centre with high care or intensive care unit facilities.

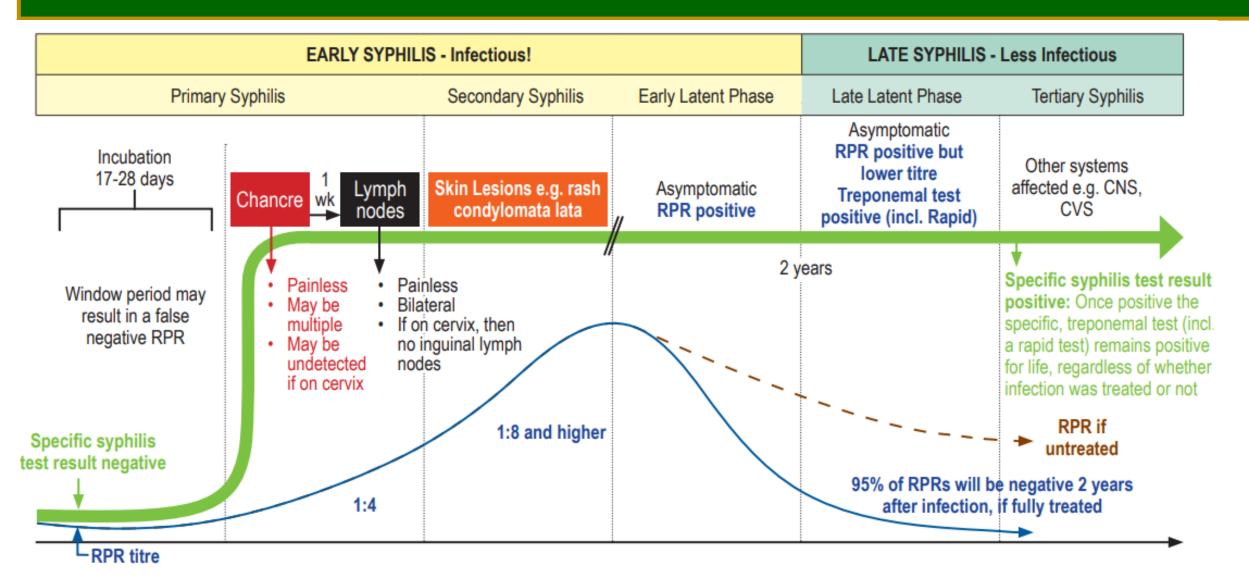
### Mandatory notification for congenital syphilis

- Category 2 Notifiable Medical Condition (NMC):
- Health care workers must notify all cases of congenital syphilis within 7 days of diagnosis.
- Test or re-test all negative mothers with stillbirths or miscarriages for syphilis at time of presentation

### Treating partners with symptoms

- Trace and test partners of women with confirmed syphilis
- Test the partner using a rapid syphilis test if available and assess for symptoms and signs of a genital ulcer or secondary syphilis.
- If the rapid test is positive, and symptoms or signs of syphilis are present, treat the partner for early syphilis using one of the following options:
  - A single immediate dose of benzathine penicillin 2.4 MU IM, if stock levels are sufficient
  - If penicillin stock levels are insufficient, give Doxycycline 100mg 12-hourly orally for 14 days

### **Syphilis Timeline**



### Treating partners without symptoms

- If the rapid test is positive and there are NO symptoms or signs of syphilis, send a confirmatory blood sample to the laboratory for an RPR. Do not wait for the results before treating the partner, but be sure to check the results 1 week later.
- Treat the partner for latent syphilis using one of the following options:
  - Benzathine penicillin 2.4 MU IM, once weekly for 3 weeks, if stock levels are sufficient
  - If penicillin stock levels are insufficient, give Doxycycline 100mg 12-hourly orally for 30 days

### Summary of changes in clinical management

- Increase access to optimised regimens (TLD) for pregnant and breastfeeding women
  - No longer any concern re NTDs
  - TLD as both first (TLD 1) and second (TLD 2) line regimens (NADIA and ARTIST trials)
  - Simplified switching from TEE to TLD not dependent on VL
- Tighten the definition of "high-risk" for HEIs
  - VL threshold for high-risk moves from 1000 to 50 c/mL
  - Dual prophylaxis for all HIV-exposed infants at birth until delivery VL is known
  - Cotrimoxazole only for confirmed HIV-infected children
- Syphilis
  - Introduction of PoC single and dual rapid tests
  - Frequency of testing aligned with HIV testing schedule
  - Notification of syphilis-related stillbirths





#### **2023 ART Clinical**

for the Management of HIV in Ac and Breastfeeding, Adolescents and Neonates

April 2023

Republic of South Africa National Department of Health

### Thank you!





