MANAGEMENT OF HIV IN PREGNANCY

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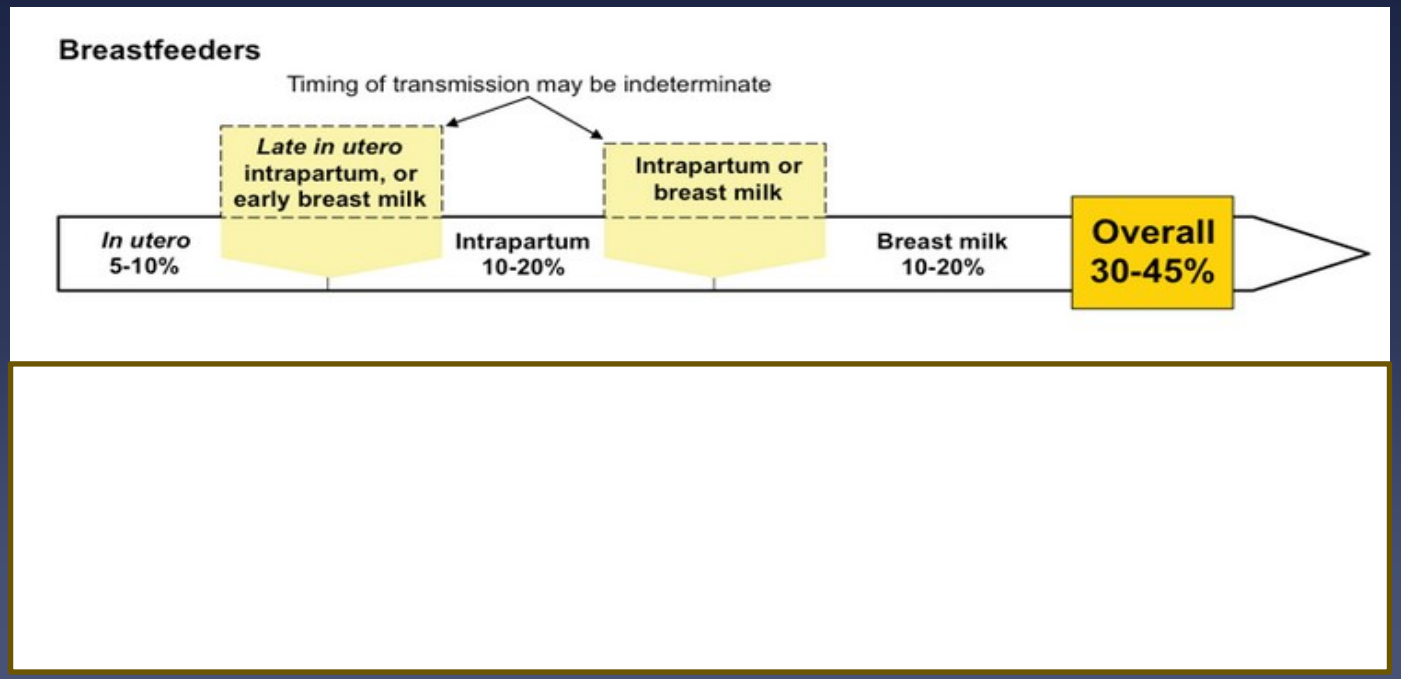
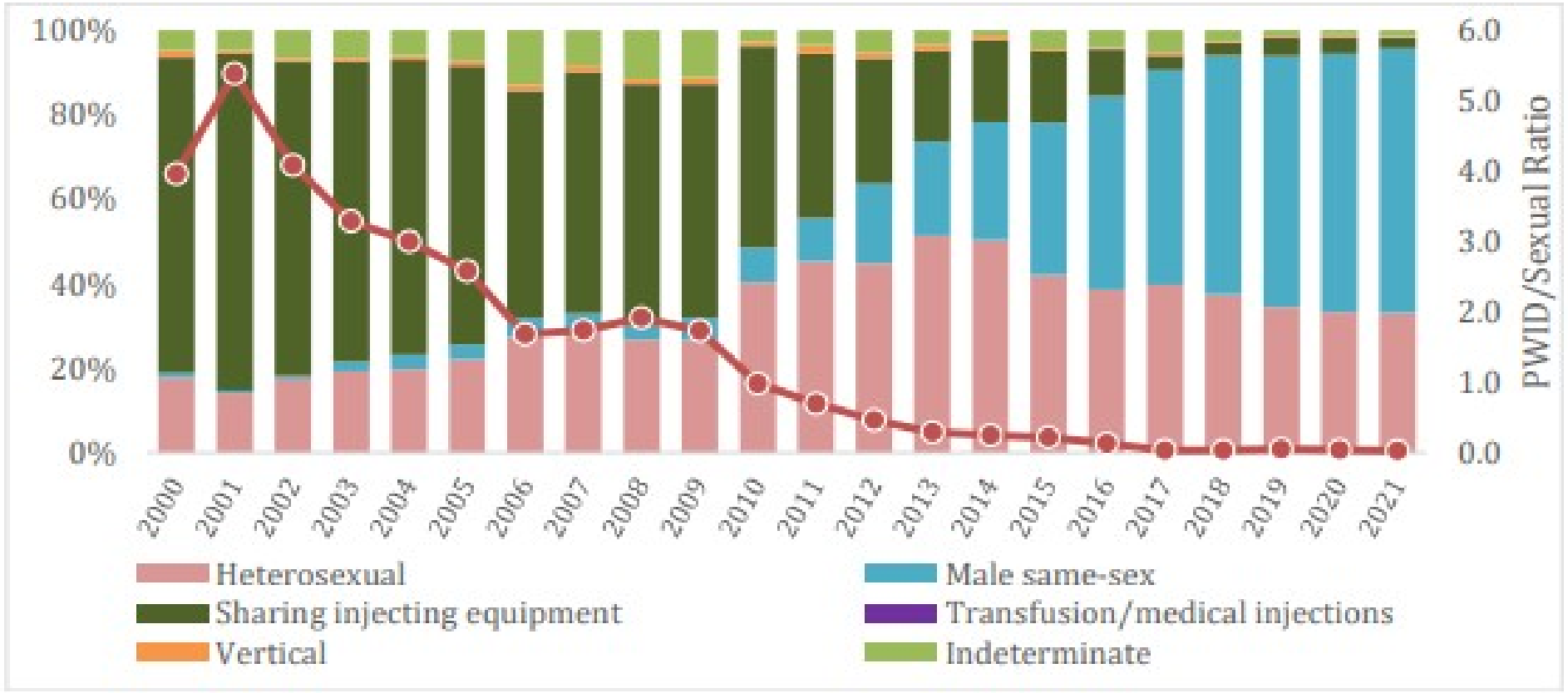
WHAT IS THE RISK OF ACQUIRING HIV ?

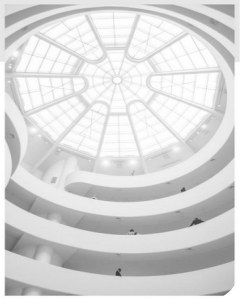


In the absence of intervention , transmission rate of HIV infection from mother to child is 15- 45%

Figure 7: Trend of HIV infection by mode of transmission, Malaysia 2000 – 2021



More than three quarter of HIV new infections were reported among people aged 20 to 39 years old in year 2021 (Figure 8).



PMTCT PROGRAM IN MALASIA

- Antenatal HIV screening initiated in 1997

- Malaysia has started PMTCT services since 1998

  - Zidovudine monotherapy after 14 weeks POG and Caeserean section (ACTG Protocol 076)

- Feb 2008 , Management of HIV infection in pregnant women were published

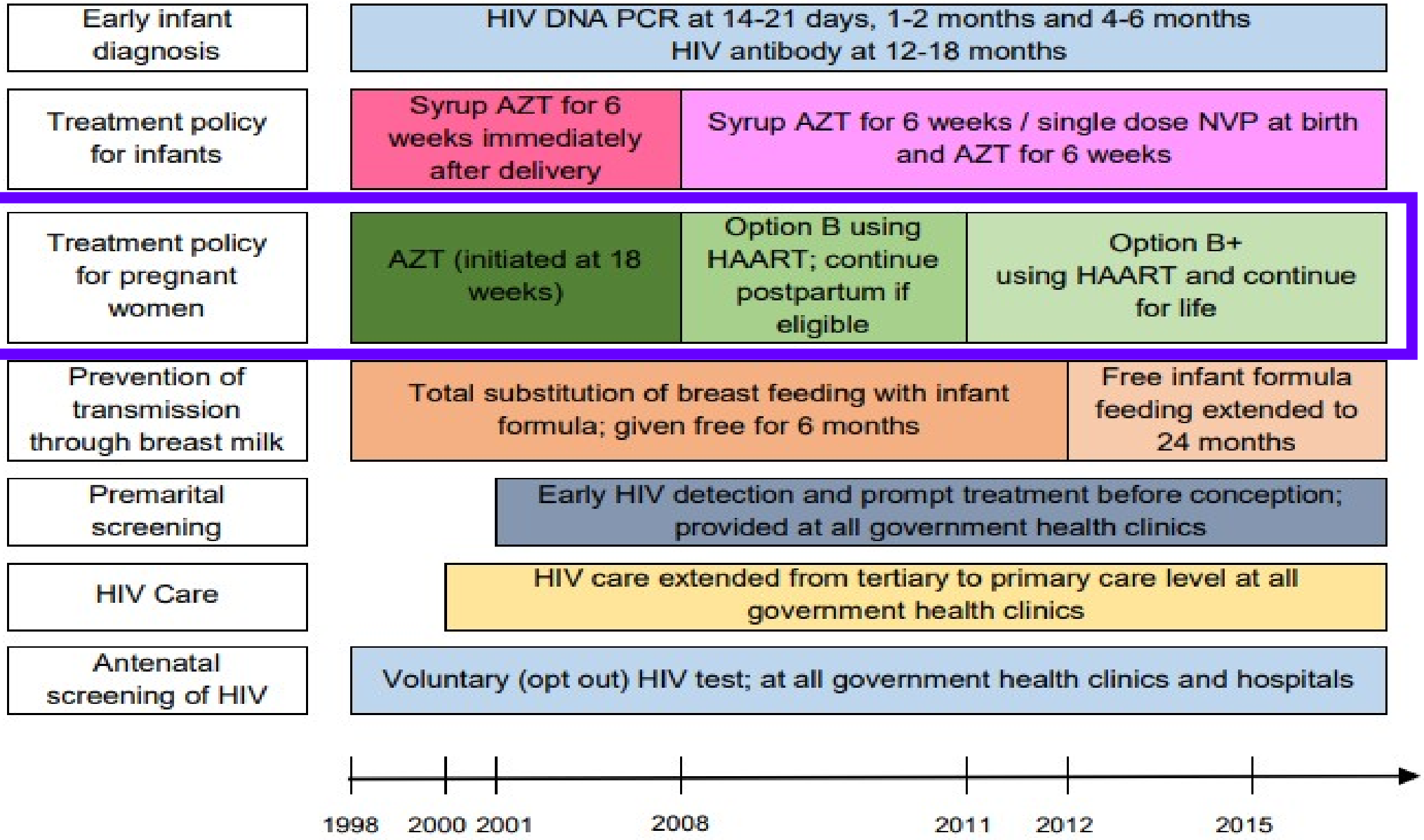
PROTOCOL 076

(PACTG) 076 Zidovudine (ZDV) Regimen

Time of ZDV administration	Regimen
Antepartum	Oral administration of 100 mg ZDV five times daily, initiated at 14-34 weeks' gestation and continued throughout the pregnancy.
Intrapartum	During labor,intravenous administration of ZDV in a 1-hour initial dose of 2 mg/kg body weight,followed by a continuous infusion of 1 mg/kg body weight/hour until delivery.
Postpartum	Oral administration of ZDV to the newborn (ZDV syrup at 2 mg/kg body weight/dose every 6 hours) for the first 6 weeks of life,beginning at 8-12 hours after birth. (Note: intravenous dosage for infants who can not tolerate oral intake is 1.5 mg/kg body weight intravenously every 6 hours.)

- Randomized, double blinded, placebo controlled study 1991-1993.
- 13-34 weeks gestation with CD4>200
- Reduction of MTCT in up to two thirds

Figure 14. Timeline of PMTCT programme, Malaysia 1998-2015



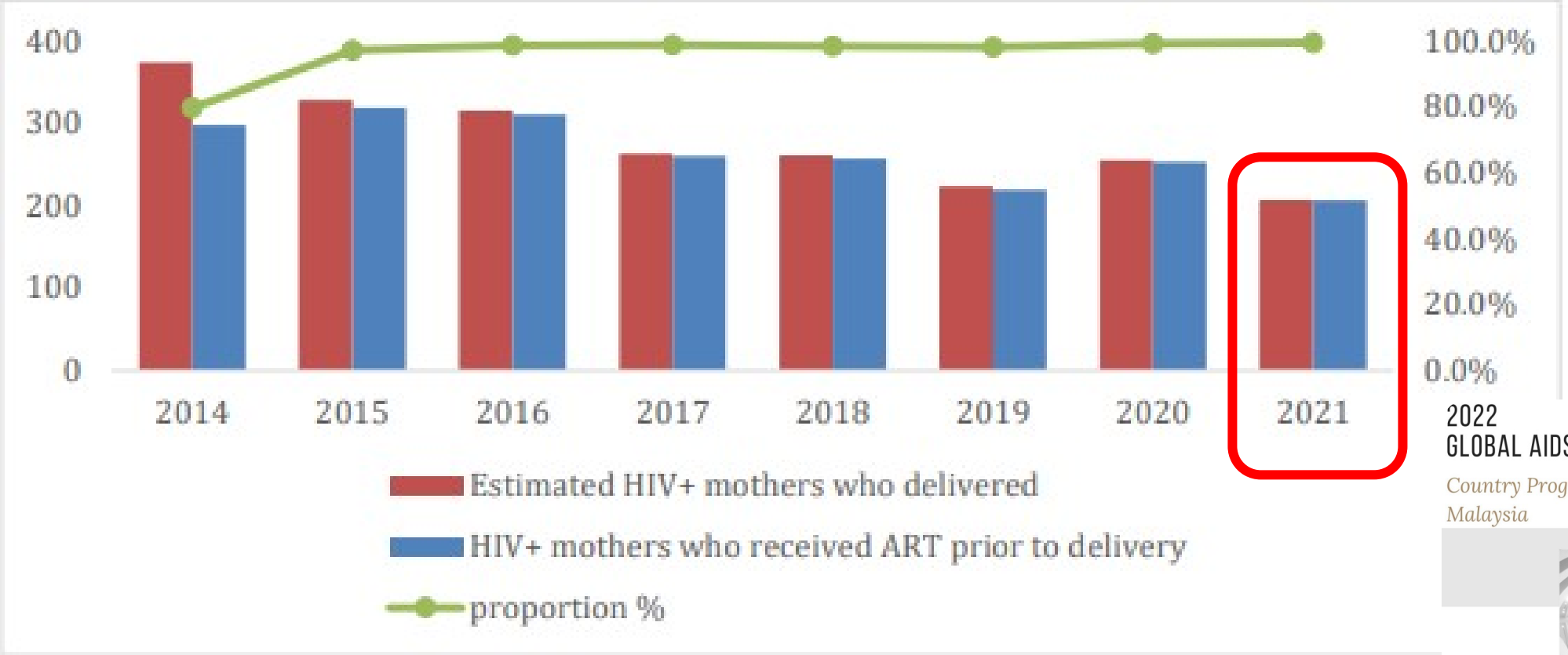
JUNE 2021

2022

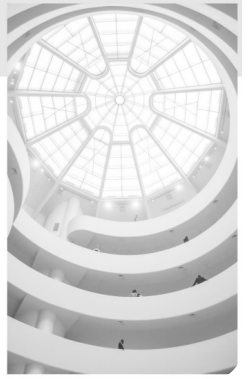
EMPHASIZE now…

- **Antenatal care** (instead of intrapartum care)
- Mother's psychosocial well being
- Management of co-infections

Figure 17 Percentage of pregnant women living with HIV who received antiretroviral medicine to reduce the risk of mother-to-child transmission of HIV



Source: Spectrum file Malaysia AEM-Spectrum 2022



- Treatment for PMTCT is **not** 100% effective, elimination of transmission is defined as a **reduction of transmission to such a low level that it no longer constitutes a public health problem**.

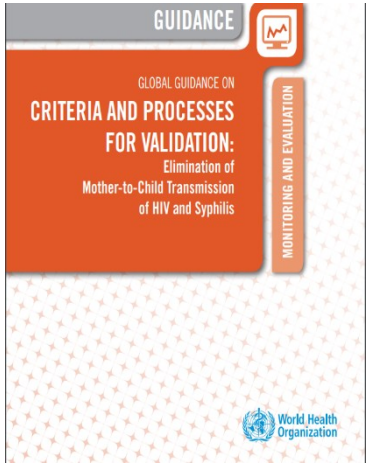
Impact Indicators – must be met for at least 1 year:

- fewer than 50 new paediatric HIV infections due mother-to-child transmission of HIV per 100 000 live births;
- HIV mother-to-child transmission rate of less than 5% in breastfeeding populations, less than 2% in non-breastfeeding populations; and
- fewer than 50 new cases of mother-to-child transmission of syphilis per 100 000 live births.

Process Indicators – must be met for at least 2 years:

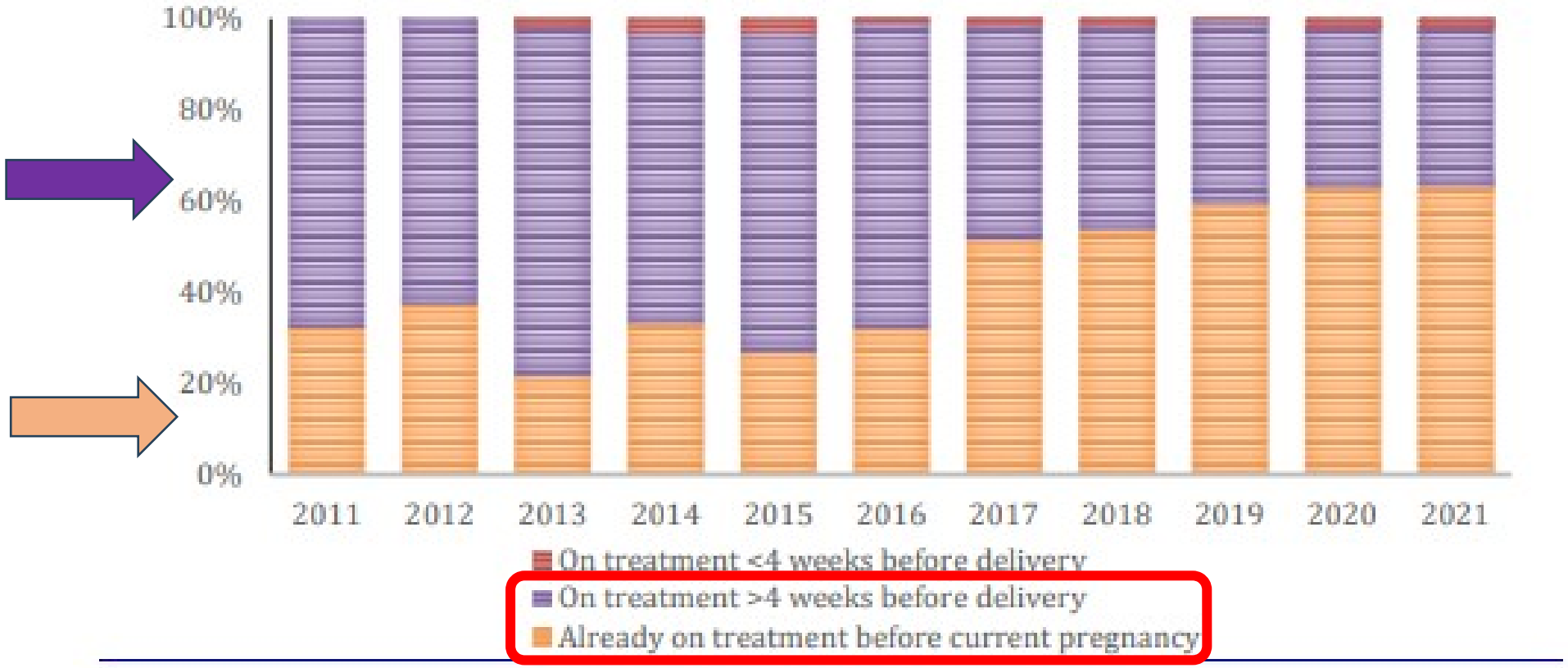
- ≥95% of pregnant women receive at least one antenatal visit;
- ≥95% of pregnant women are tested for HIV and syphilis; and
- ≥95% of infected pregnant women receive adequate treatment.

A country that is "validated" has met the internationally set targets at a specific point in time. They are required to maintain ongoing programmes after validation.

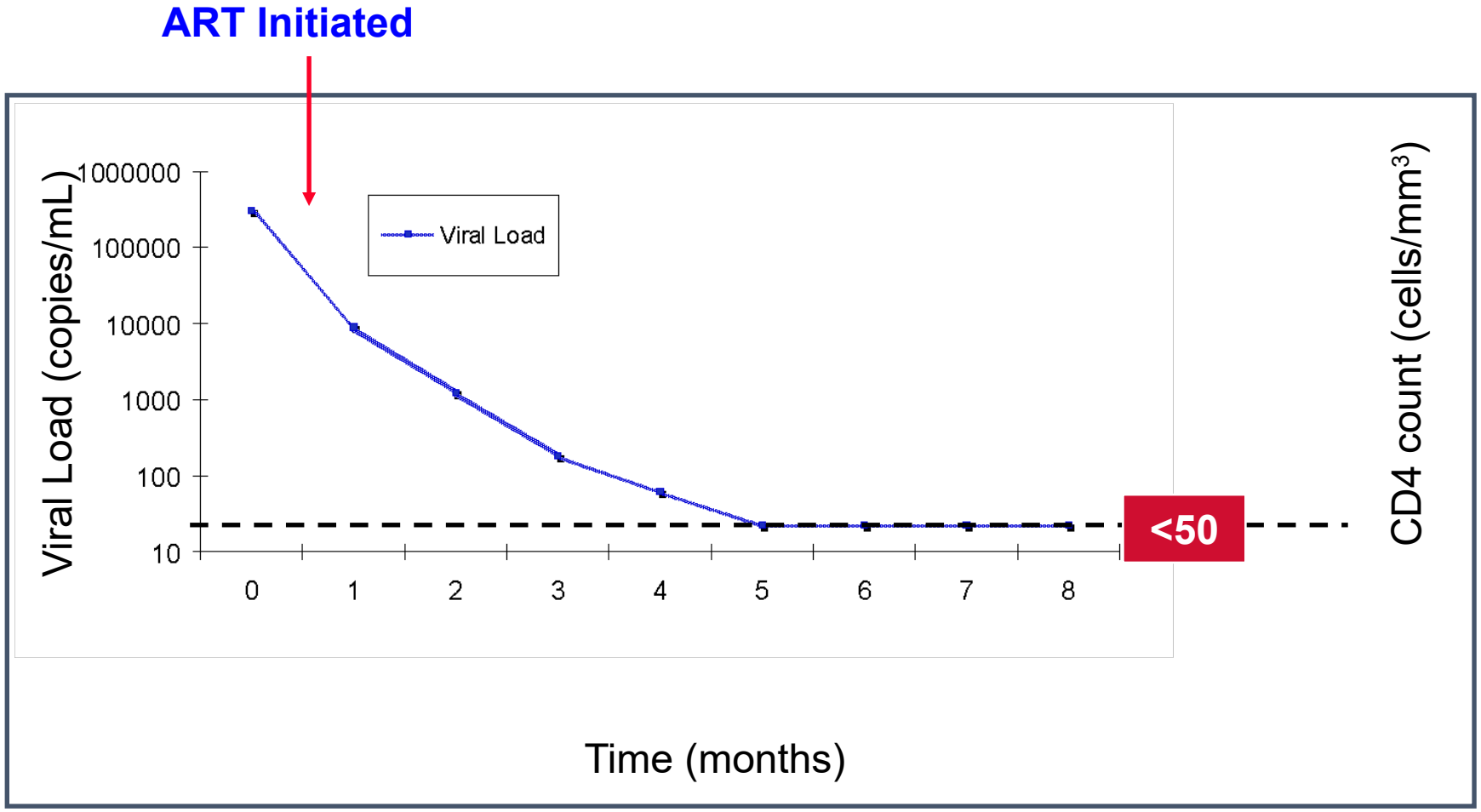


- Largest proportion of HIV-infected mothers attending antenatal care are already on ARV.

Figure 18 Percentage of pregnant women living with HIV who received antiretroviral medicine to reduce the risk of mother-to-child transmission of HIV



Antiretroviral Therapy: Optimal Response



- Pre-pregnancy ARV increases the likelihood of mothers being virally suppressed throughout pregnancy and birth, hence minimizing the risk of vertical transmission

Our challenges …

- Women of childbearing age
- HIV in pregnancy: ART naïve or stable on ART
- Can my patient be allowed for SVD?
- Postnatal care
- Approach to pregnant women with positive HIV partners

How do we go about it?

ANTENATAL HIV SCREENING

- How do we provide HIV screening ?

- In which group of patients should we do a repeat HIV test and when?

PMTCT : HIV screening in pregnant women

2.0 GARIS PANDUAN PENGUKUHAN PROGRAM PENCEGAHAN JANGKITAN HIV DARI IBU-KE-ANAK

2.1 SARINGAN HIV UNTUK IBU MENGANDUNG

2.1.1 Pendidikan Kesihatan

- Sebelum saringan dilakukan, setiap ibu mengandung perlu diberi maklumat yang mengenai transmisi jangkitan HIV, tujuan ujian, kebaikan ujian dan implikasi jang kepada ibu dan anak dalam kandungan. Ianya boleh dilakukan secara berse (berkumpulan atau bersendirian) serta memberi masa yang mencukupi untu membaca dan memahami brosur kesihatan yang disediakan oleh klinik masing-m Panduan maklumat mengenai HIV untuk disampaikan kepada ibu mengandung a seperti di **Lampiran 1**.

Lampiran 1

Soalan lazim dan maklumat mengenai HIV untuk ibu mengandung
FAQ and information on HIV for pregnant mother

1. **Apa itu HIV?**
   What is HIV?

   HIV adalah sejenis virus yang dipanggil retrovirus yang menyebabkan sistem ketahanan tubuh menjadi lemah sehingga sukar untuk melawan jangkitan kuman. Sekiranya anda mempunyai virus ini di dalam badan, anda didapati positif untuk HIV.
   HIV is a type of virus called a retrovirus that prevents the body's immune system from working properly and makes it hard to fight off infections. If you have the virus, this is known as being HIV positive.

2. **Bagaimana HIV menular?**
   How is HIV spread?

   HIV boleh menjangkiti dari seorang kepada seorang lain melalui pertukaran cecair tubuh termasuk darah, air mani, cecair faraj dan susu ibu. Ibu positif HIV boleh menularkan virus kepada bayi melalui uri ketika mengandung, semasa kelahiran dan melalui susu ibu.
   HIV can be passed from one person to another through the exchange of body fluids including blood, semen, vaginal fluids and breast milk. A HIV positive mother can pass the virus to her baby through the placenta while pregnant, during birth and through breast milk.

3. **Bagaimana HIV boleh dikesan semasa mengandung?**
   How can HIV be detected during pregnancy?

   Semua ibu mengandung akan dipelawa untuk ujian saringan HIV ketika datang untuk pemeriksaan kandungan kali pertama dan doktor akan menyarankan ujian ulangan pada 28-32 minggu jika ibu berisiko tinggi. Ujian ini selamat untuk ibu dan janin dalam kandungan.
   All pregnant mothers are offered a screening test for HIV during early pregnany check up with re-screening recommendation at 28-32 weeks for high risk mother. The test is safe for the mother and the fetus.

PMTCT : HIV screening in pregnant women

2.1.2 Persetujuan

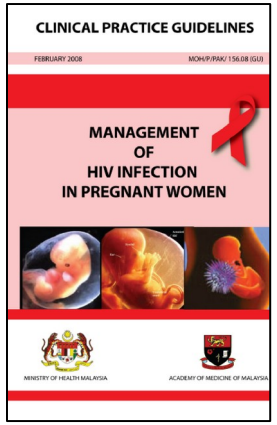
- Persetujuan ujian saringan perlu diperolehi samada secara bertulis atau *verbal (informed consent)* dan dikemaskini di dalam buku rekod/kad kesihatan ibu. Walau bagaimanapun, ibu berhak untuk menolak ujian saringan HIV (*opt-out*) dan kaunseling secara berasingan perlu diberikan kepada ibu oleh Pegawai Perubatan / Pakar Kesihatan Keluarga/ Pakar O&G.

3.2 Recruitment strategy

In a systematic review carried out by The US Preventive Services Task Force it was noted that the acceptance rates for voluntary HIV testing among more than 174,000 pregnant women ranged from 23% to 100%. The HIV test rates during pregnancy appear to be higher using "opt-out" testing policies.[9,Level 1]

In order to ensure better coverage, intrapartum testing should be offered to women who have not been screened. [19,Level 8]

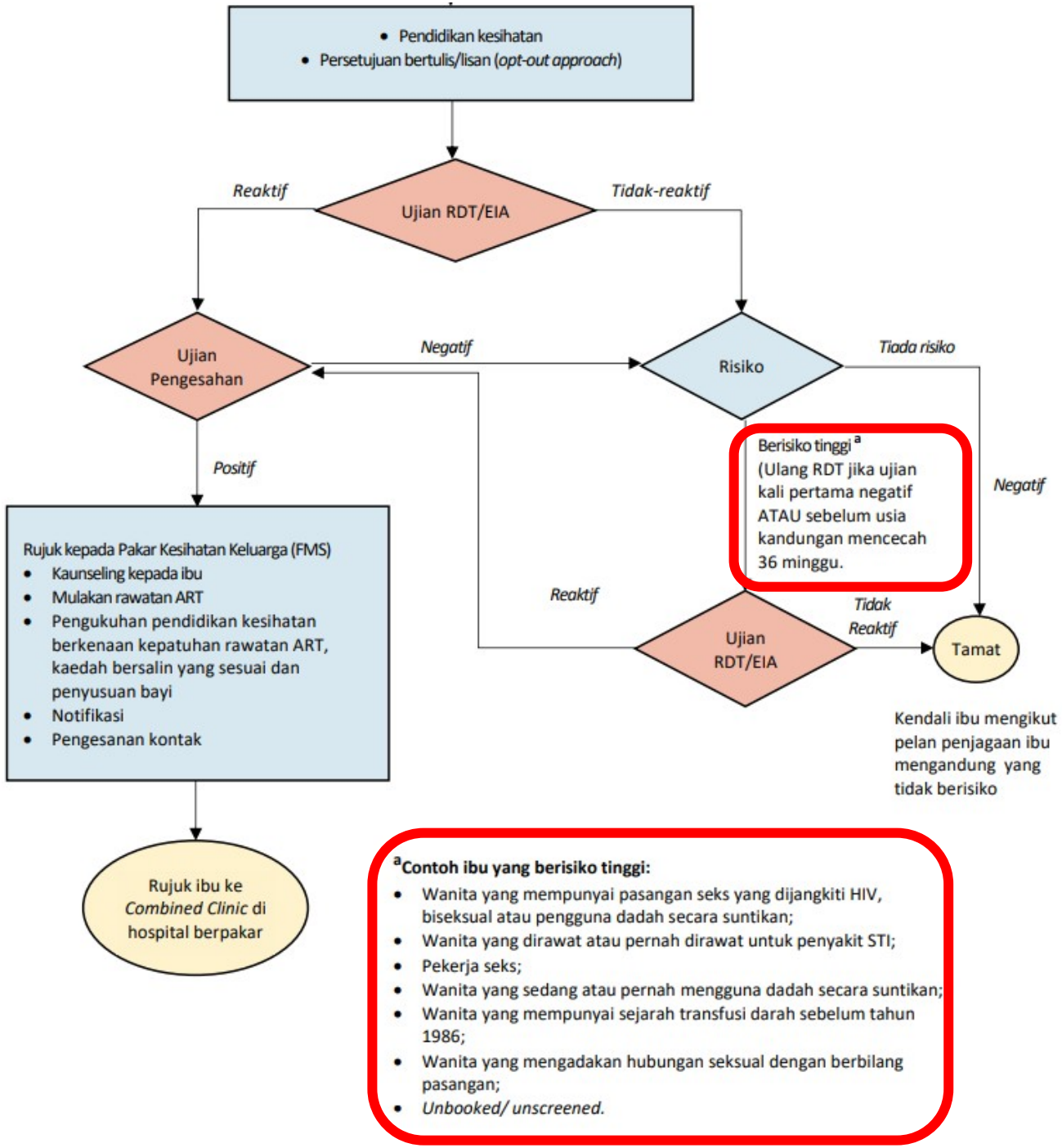
Opt-out screening is defined as performing a HIV test after notifying the patient that the test will be done; consent is inferred unless the patient declines.[20,Level 9]



ANTENATAL HIV SCREENING

✔ How do provide HIV screening ?

- **In which group of patient should we do a repeat HIV test and when?**



In Johor additional testing is done at 28 weeks and 36 weeks

Case Study : PLHIV prenatal counselling.

HIV diagnosed 2018 . On ARV since 2018 (Nadir CD4 = 198).

Tenofovir + Emtricitabine + Efavirenz
Latest CD4 = 400 . Viral load suppressed.

‘Doctor, I would like to have a baby .’

Question : How would you manage this patient ?

A. Inform her that she cannot have children

B. Stop ARV because patient is Efavirenz. Restart after patient is pregnant after 14 weeks .

C. Continue ARV and encourage patient to conceive

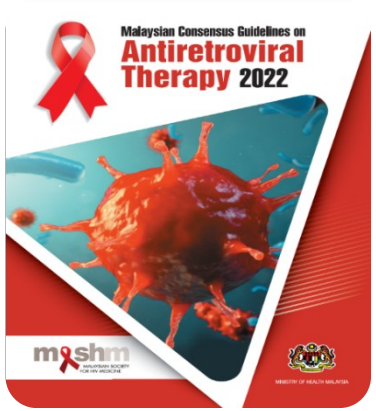
D. Call ID to ask if patient can have sex and make baby

PLHIV Stable on ARV who wishes to get pregnant

7.2 Women Who are Stable on ART before Pregnancy

In general, the existing ART is to be continued throughout pregnancy and after delivery, unless taking a regimen that is contraindicated in pregnancy (eg. Tenofovir Alafenamide)[4]. Consultation with an ID physician is strongly recommended if the current regimen is contraindicated in pregnancy and if the patient is experiencing virological failure. Special effort must be made to determine the current CD4 and viral load during the early stages of pregnancy, preferably the first trimester.

UPDATE!

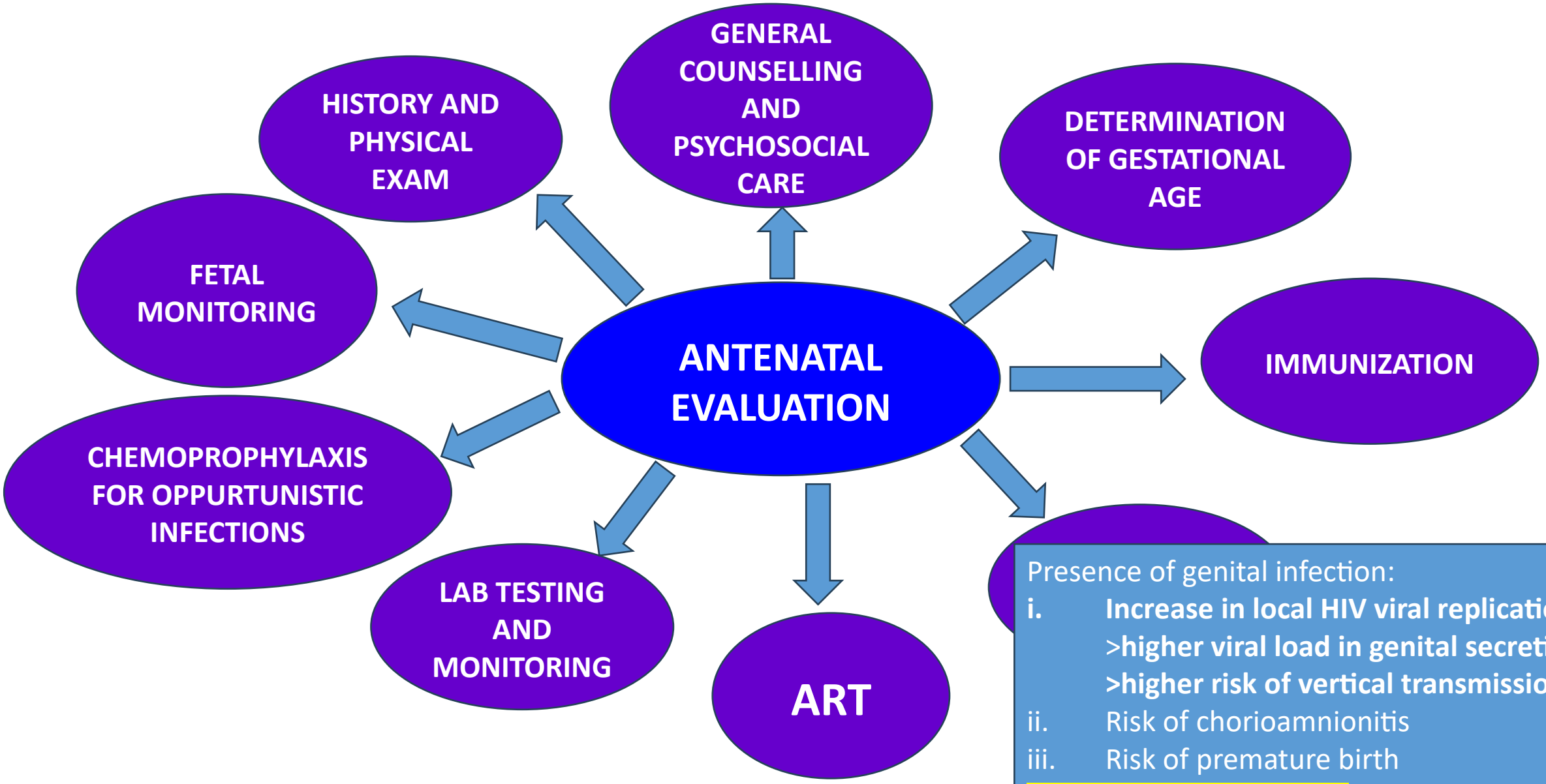


Case scenario :

Madam K

- 28yr old lady . Married. Primigravida
- Came for booking-> self-tested UPT positive
- HIV confirmation test-> **POSITIVE**
- Syphilis screening->negative
- TAS parameters correspond to 10 weeks
- Clinically no opportunistic sign on examination

How would you manage this patient ?



Presence of genital infection:

i. **Increase in local HIV viral replications->higher viral load in genital secretions->higher risk of vertical transmission**
ii. Risk of chorioamnionitis
iii. Risk of premature birth

Do not forget the partner

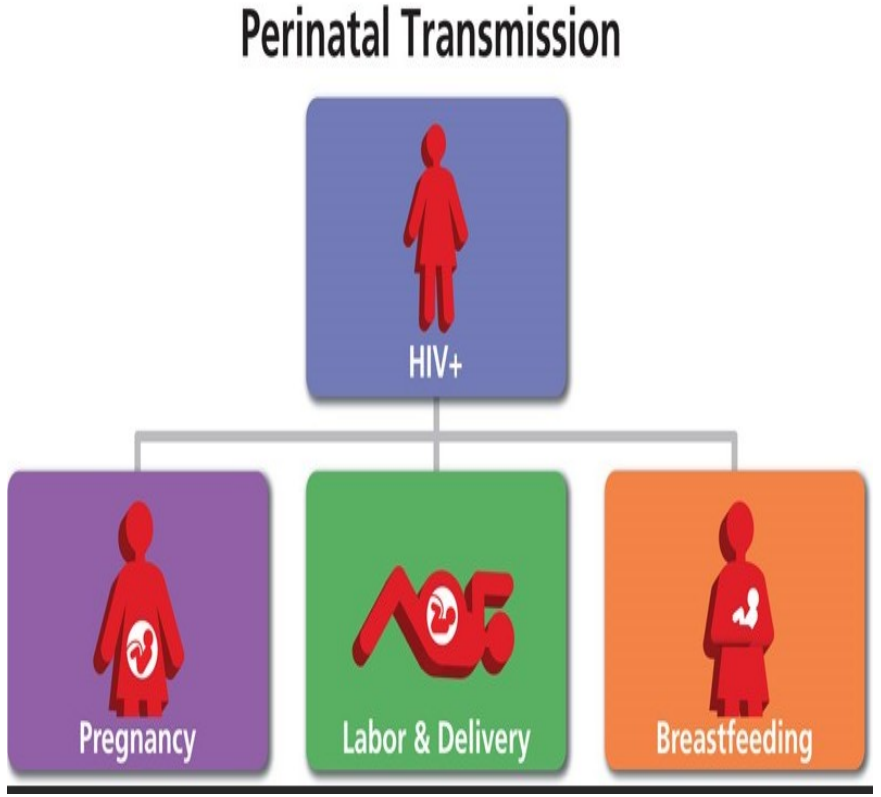
GENERAL COUNSELLING TO A NEWLY DIAGNOSED HIV

- Explain nature of the disease
- Explain how vertical transmission occurs:

i. Transplacental maternal-fetal micro transfusion

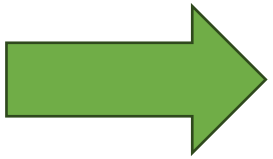
ii. Exposure of virus in the cervicovaginal secretions and blood during delivery

iii. Breastfeeding



PSYCHOSOCIAL CARE

- Anxiety(GAD)
- DEPRESSIVE symptoms (WHOOLEY)
- **STIGMA**



- REASURANCE OF CONFIDENTIALITY
- MULTIPLE TCA->HOW TO HELP?
- TRAINED SUPPORT WORKERS
- COMING UP WITH POSSIBLE ‘REASONS’

Newly diagnosed HIV during antenatal screening

- Lifelong ART should be started immediately regardless of CD4 count.
- Women should be counselled regarding :
  - the benefits of ART in prolonging life expectancy and reducing serious AIDS and non-AIDS events,
  - ART should be continued lifelong, **even after delivery**..

- If the women presents at 2nd or 3rd trimester, **ID** must be consulted regarding choice of ART

UPDATE!

PREGNANT WOMEN WHO ARE ART NAIVE

- **CD4 and HIV viral load** should be done at diagnosis confirmation .
- **HIV viral load** should be repeated 2 to 3months after ART initiation.
  and at 32-36weeks gestation to determine mode of delivery
- Referral to OBG team
- Delivery should be in **tertiary center**

UPDATE!

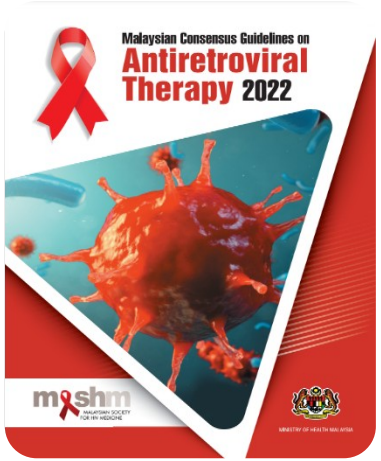
Madam K is convinced and agree to start treatment.

- What regimen should be chosen?
- How do we monitor?

What regimen should be chosen?

- ART used during pregnancy must consist of 2 NRTIs plus **either** a NNRTI **or** a boosted PI **or** integrase inhibitors.
- Updated data from Tsepamo study, DOLOMITE-NEAT ID Network study showed no significant difference in neural tube defect in infants born to women on Dolutegravir in first and second trimester.
- Dolutegravir is the drug of choice for first-line therapy by WHO even in pregnant women.

UPDATE!



What to start

Back to Madam K…

- What regimen should we start?

Table 7.1 • Choice of ART Combinations

Preferred	Alternative
TDF+FTC+EFV	AZT[#] + 3TC + EFV[a]
TDF+FTC+RAL*	AZT[#] + 3TC + NVP[b]
TDF+FTC+DTG*	TDF + FTC + NVP[b]
	TDF + FTC + LPV/RTV
*Preferred regimen for late presentation at >28 weeks	#For close monitoring of Hb if on AZT

[a] In the past EFV was considered a Category D drug and contraindicated in the first trimester of pregnancy. However, there is now good level safety evidence to recommend it as the preferred NNRTI even in the first trimester[6].

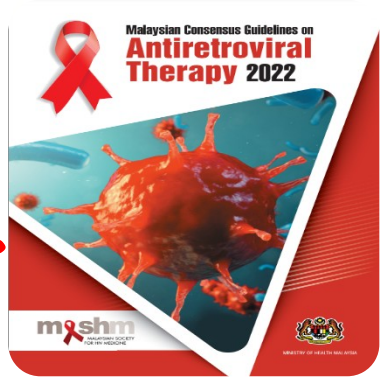
[b] NVP should be used with caution in women with CD4 > 250 cells/uL because of possible increased risk of hepatotoxicity and rash[7].

7.3 ART Used for PMTCT[4,5]

ART used during pregnancy must consist of 2 NRTIs plus either a NNRTI or a boosted PI or integrase inhibitors. The choice of agents is listed in Table 7.1.

In 2018, initial observations from the Tsepamo observational cohort identified an association between dolutegravir and an increased risk of neural tube defects (NTD) among infants born to women who had been taking it from conception. However, updated data from the study, presented in July of 2021 at the International AIDS Society Conference, showed that the prevalence of NTD was not significantly different from those on non-Dolutegravir based regimens. This was further supported by the DOLOMITE-NEAT ID Network study presented at the AIDS 2022 conference which showed no significant difference in frequency of NTD in infants born to women who had been taking Dolutegravir in the first trimester and second and third trimester. Dolutegravir still remains the drug of choice for first-line therapy by the World Health Organisation even in pregnant women based on a statement issued in July 2019.

UPDATE!



Back to our case…

- Pre ART CD4 460, Viral Load 10 354
- FBC,RP,LFT normal
- TB screening negative
- Syphilis screening negative
- Madam K was started on T Tenvir EM 1/1 OD and T Efavirenz 600mg OD at 10 weeks gestation
- Husband screening pending

- When should we review back Madam K?
- What investigations should we take?

- Review in 2 weeks
- Routine bloods->FBC,RP,LFT
- Check any side effects:

Zidovudine : anemia (2nd and 3rd trimester)
lactic acidosis
Tenofovir : renal tubular toxicity, Fanconi syndrome
Nevirapine : Transaminitis, rash
Efavirenz : CNS, transaminitis, rash

- Psychosocial->coping
- Check adherence
- Repeat viral load 2-3months after ART and at 32-36weeks gestation
- Combine care with primary care-ID-O&G team

Madam K’s pregnancy has progressed well. She is now at 33 weeks of gestation. No issues with ART. Fetal movements are good. Serial ultrasound shows normal fetal growth.
HIV viral load at 32 weeks
< 50 copies

MODE OF DELIVERY?

MODE OF DELIVERY

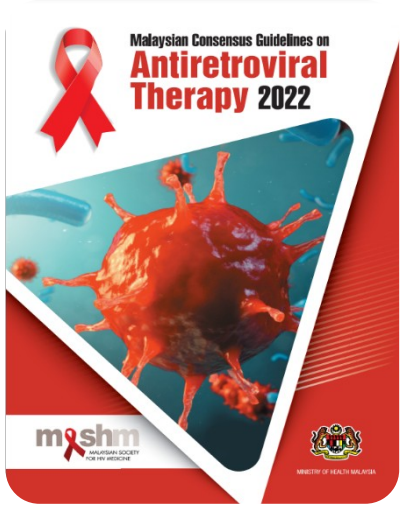
The decision between performing EL-LSCS or allowing SVD is based on:

- HIV **viral load** at 32–36 weeks of gestation
- whether the mother has **received any ART** in the pre-pregnancy or antenatal period

Table 7.2 • Mode of Delivery According to Viral Load Quantification

Viral Load at 32–36 weeks	Mode of Delivery
< 50 copies/mL	SVD
50–399 copies/mL	*PLCS recommended
> 400 copies/mL	PLCS

* Take into account the trajectory of the viral load leading up to time of delivery, length of time on ARVs, adherence issues, obstetric factors and the woman's views.



UPDATE!

HIV pregnant patient presented with Spontaneous Rupture of Membrane.
How would you approach the case?

Factors to consider when deciding the mode of delivery :

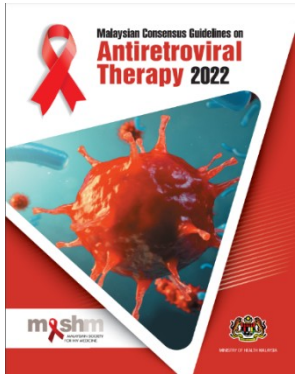
- Maternal **HIV viral load** → is it suppressed?
- **Duration** of membrane rupture. There is an increased risk of perinatal HIV transmission of 2% per hour.
- **Expedited delivery** for women with pre-labour ROM at term, either with induction of labour or Caesarean section.

Low threshold to start antibiotics if signs suggestive of chorioamnionitis are present.

PPROM < 34 weeks, intramuscular steroids given.

Multidisciplinary discussion between Obstetrician, Pediatrician and

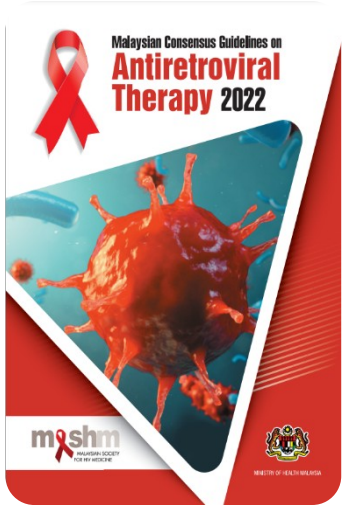
ID Physician about the timing and mode of delivery after PPROM.



Intrapartum Intravenous Zidovudine Infusion

When it is indicated :

1. Women with **HIV viral load>1000 copies**
   - Current evidence showed no additional benefit in prevention of vertical transmission in pregnant women on ART with viral load ≤1000 copies/mL during late pregnancy and near delivery
2. **HIV positive women presenting to labour room with no ART therapy**



Timing to start :

- EMERGENCY LSCS->started immediately
- Planned LSCS->started 3 hours before surgery

Case scenario: Unbooked women,in labour,RTK HIV Reactive in district hospital-no specialist/ Klinik Kesihatan with no prior ART exposure.

- **No IV Zidovudine**
- **Immediately** with fixed-dose AZT and 3TC with Raltegravir/Dolutegravir as the preferred 3rd agent because it rapidly crosses the placenta.
- If Raltegravir/ Dolutegravir is not available, **NVP or EFV**
- **Give what is available**
- Inform paediatrician for ->PEP

Transfer to tertiary

What happens to the placenta…

2.2.5 Pelupusan uri

Selepas bersalin, uri tidak dibenarkan dibawa balik dan pihak hospital akan menguruskan pelupusan uri mengikut kaedah *universal precaution* yang standard.

HIV PROPHYLAXIS FOR NEWBORN

- Mother on ART with **sustained viral suppression**

->Syp Zidovudine for 4 weeks

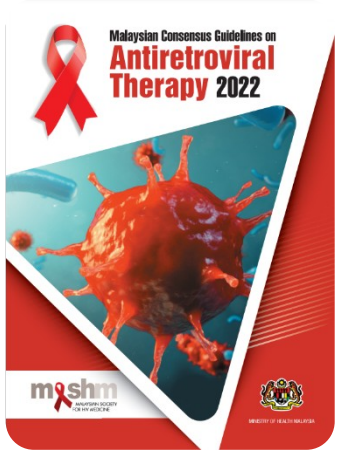
- Infants at **higher risk**:

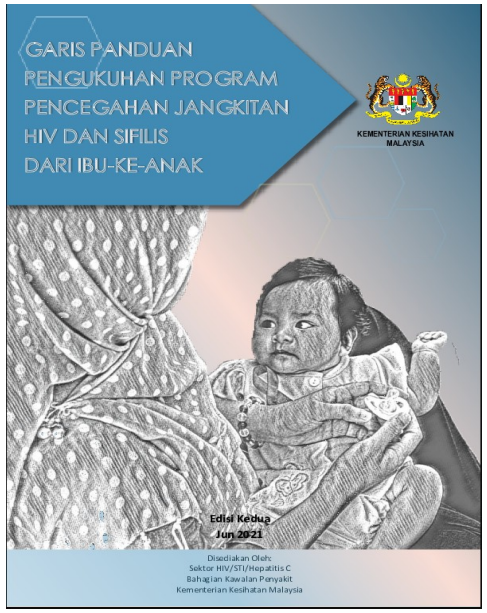
No intra/antepartum ART **OR** only intrapartum ART **OR** viral load not suppressed

->Syp Zidovudine for 6 weeks and 3 doses of Nevirapine

BREASTFEEDING

- Breast-feeding is not recommended as it is associated with risk of transmission up to 14% in those who are not virally suppressed.
- This risk reduces to 1% if the woman is virally suppressed.
- However, breast-feeding is still not encouraged in our population. For women on ART, **compliance must be stressed** if they insist on breast-feeding their baby





BUT I STILL WANT TO BREASTFEED…

- Ibu HIV positif dinasihatkan untuk menyusukan bayi dengan susu formula. Susu formula dibekalkan kepada yang layak secara percuma di fasiliti kerajaan sehingga bayi berusia 24 bulan.

- Walau bagaimanapun, sekiranya ibu masih berhasrat untuk menyusukan bayi dengan susu ibu, syarat-syarat di bawah PERLU DIPENUHI:
  i) Ibu dan bayi perlu dirujuk kepada Pakar Pediatrik sebelum dibenarkan menyusu badan.
  ii) Ibu tidak mempunyai sebarang kecederaan/ jangkitan payudara *(eg. cracked nipple, ulcer, abcess, mastitis)*.
  iii) Aras *viral load* ibu hendaklah sentiasa < 50 *copies /mL*.
  iv) Ujian HIV PCR bayi hendaklah dipantau setiap bulan sehingga berhenti menyusu badan.
  v) Penyusuan ibu hendaklah secara eksklusif. Penyusuan ibu secara campuran (*mixed feeding*) adalah tidak digalakkan kerana boleh meningkatkan risiko jangkitan kepada bayi.

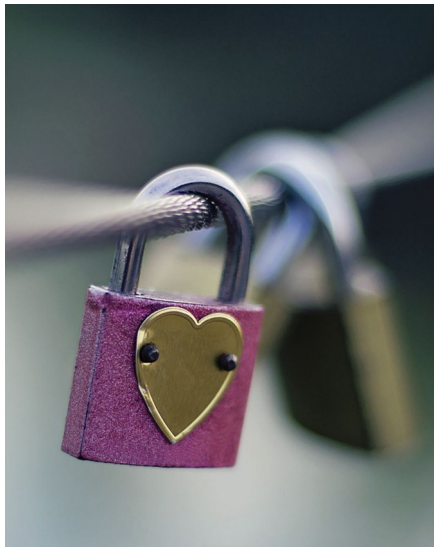
Postnatal care

- Madam K delivered a healthy baby boy via SVD at 38 weeks in a tertiary hospital. BW 3.5kg.
- Both mother and baby are doing well.
- Baby not jaundice. He is on week 2 of syrup Zidovudine.

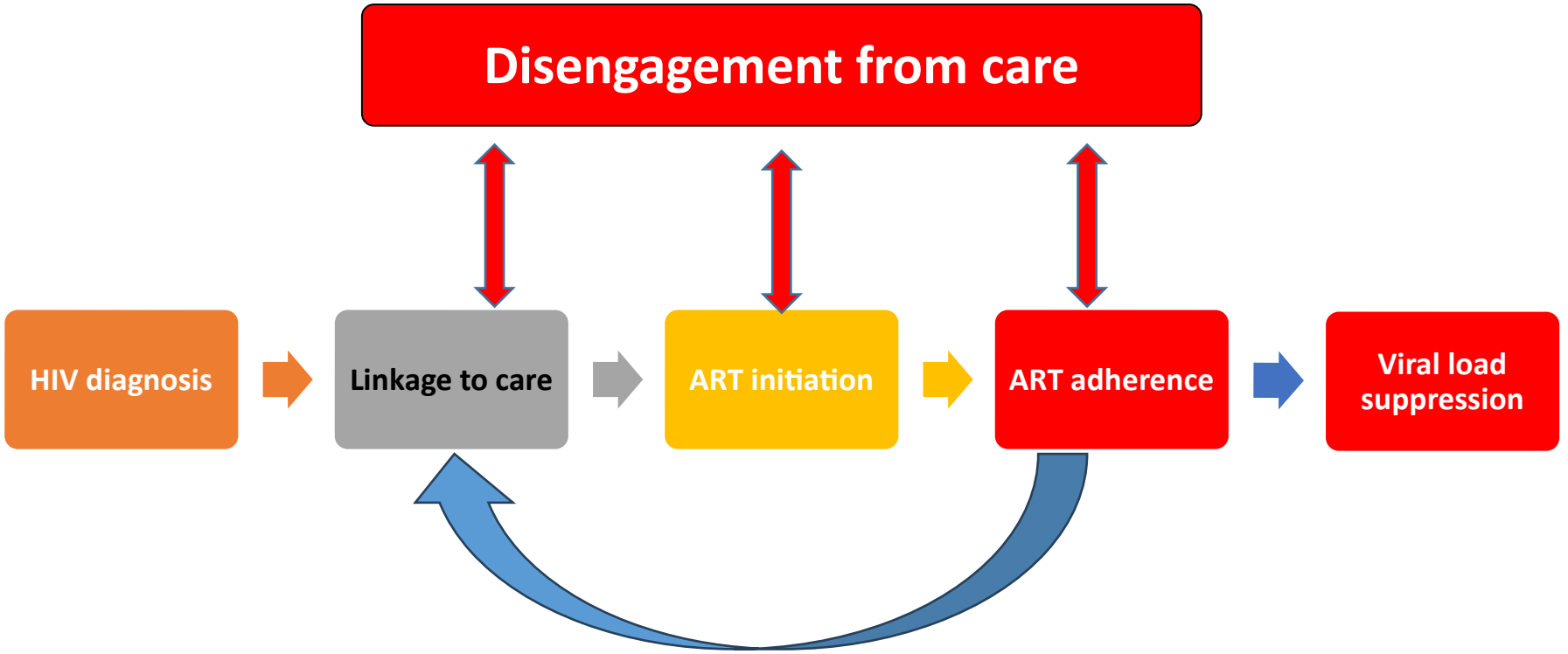
- Continuation of ART
- Breastfeeding
- **Family Planning**
- **Pap smear**

Postnatal care

- Assess patient’s adherence
- Coping->new role, family members, new baby
- Reemphasize importance of ART



HIV care cascade



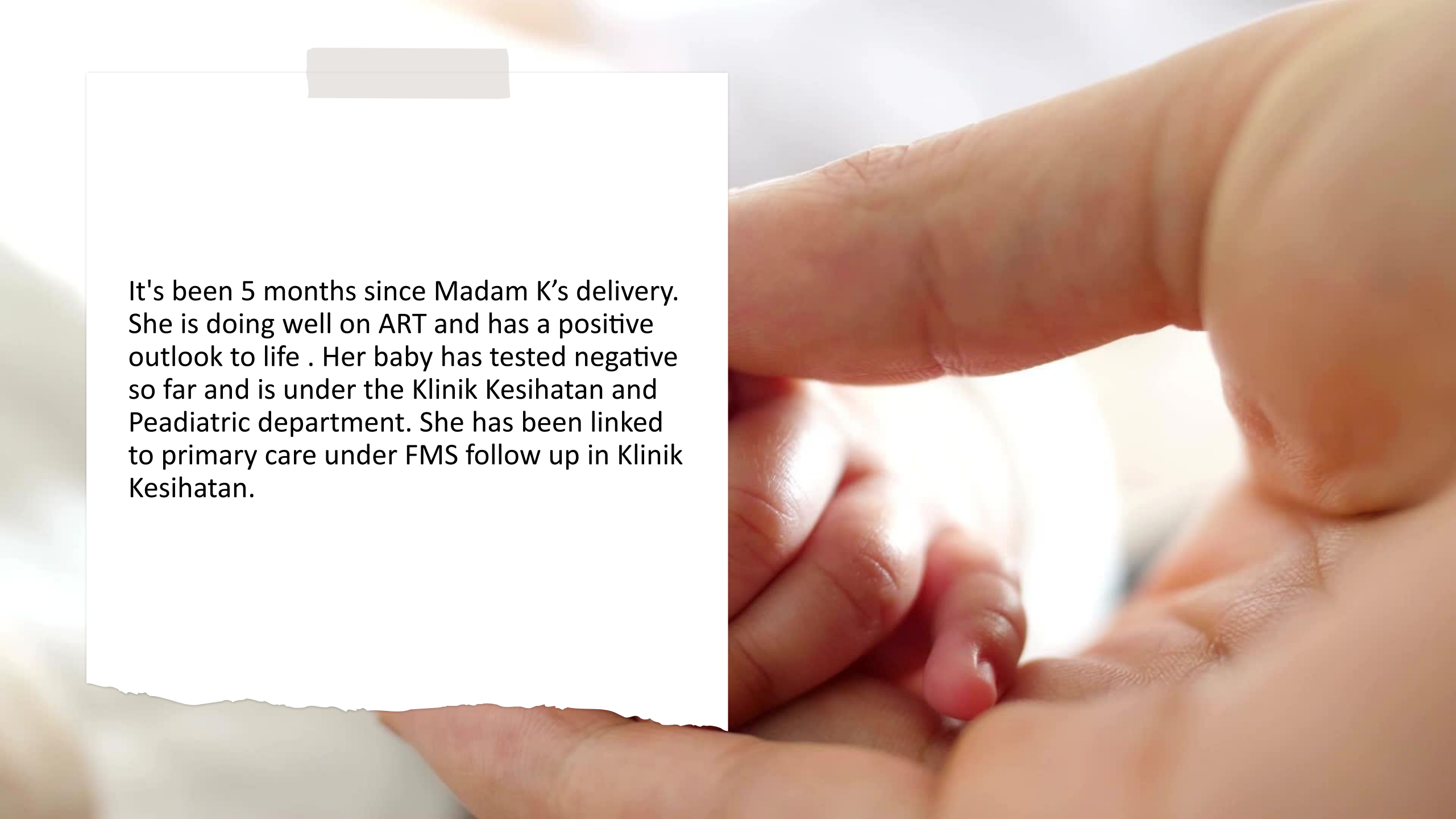
"Seek, Test, Treat & Retain"

Family planning

Ovulation may occur before 6 weeks ->mother is not breastfeeding.

Choice of contraception ->Check for Drug-Drug Interactions

It's been 5 months since Madam K’s delivery. She is doing well on ART and has a positive outlook to life . Her baby has tested negative so far and is under the Klinik Kesihatan and Peadiatric department. She has been linked to primary care under FMS follow up in Klinik Kesihatan.



“Early testing, early diagnosis and early treatment are key steps

for attaining and sustaining elimination of mother-to-child

transmission. Malaysia should be congratulated for being one of

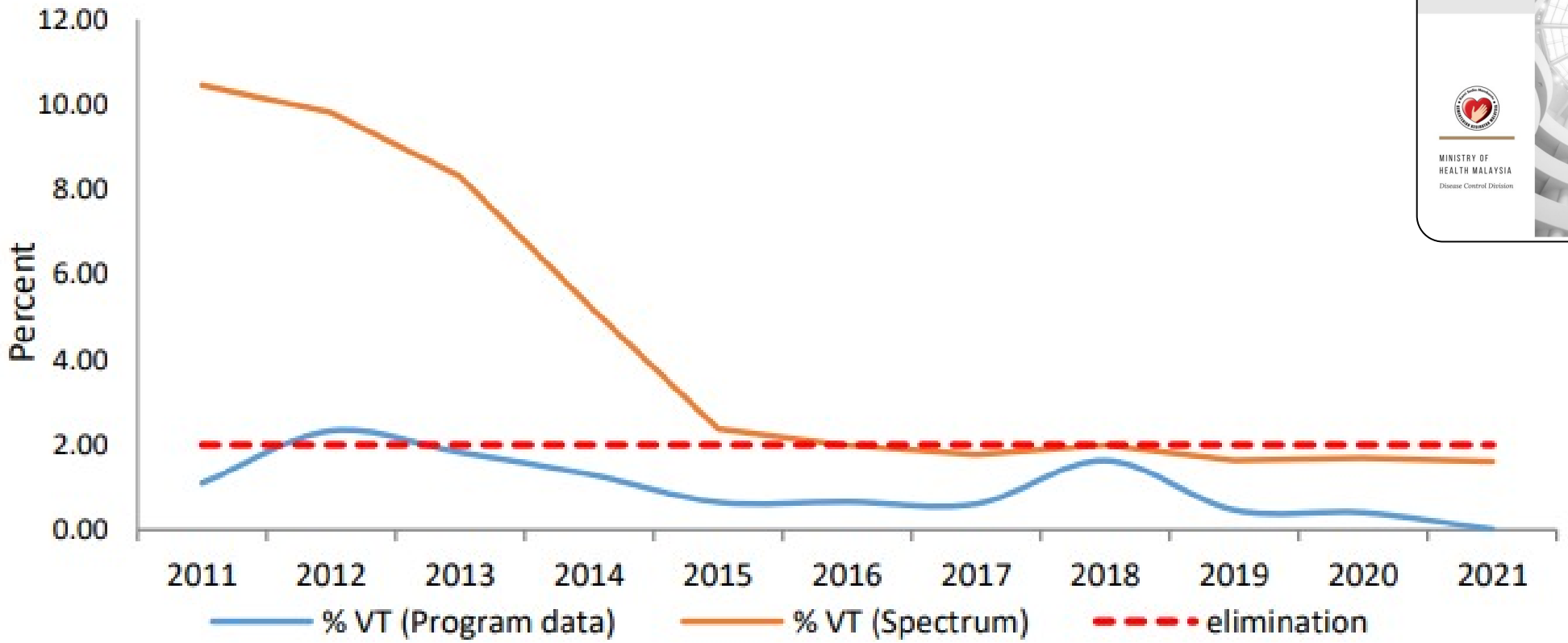
the first countries to introduce national initiatives to prevent

mother-to-child transmission of HIV and syphilis in maternal and

child health services.”

UNICEF, Regional Director

Figure 19: Vertical transmission rate of HIV, Malaysia (2011-2021)



THANK YOU