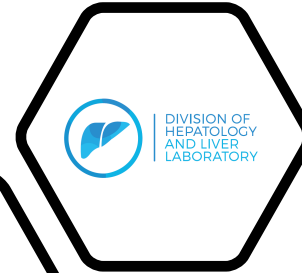


# The cradle of Viral Hepatitis epidemiology: Mother To Child Transmission

Mark W. Sonderup

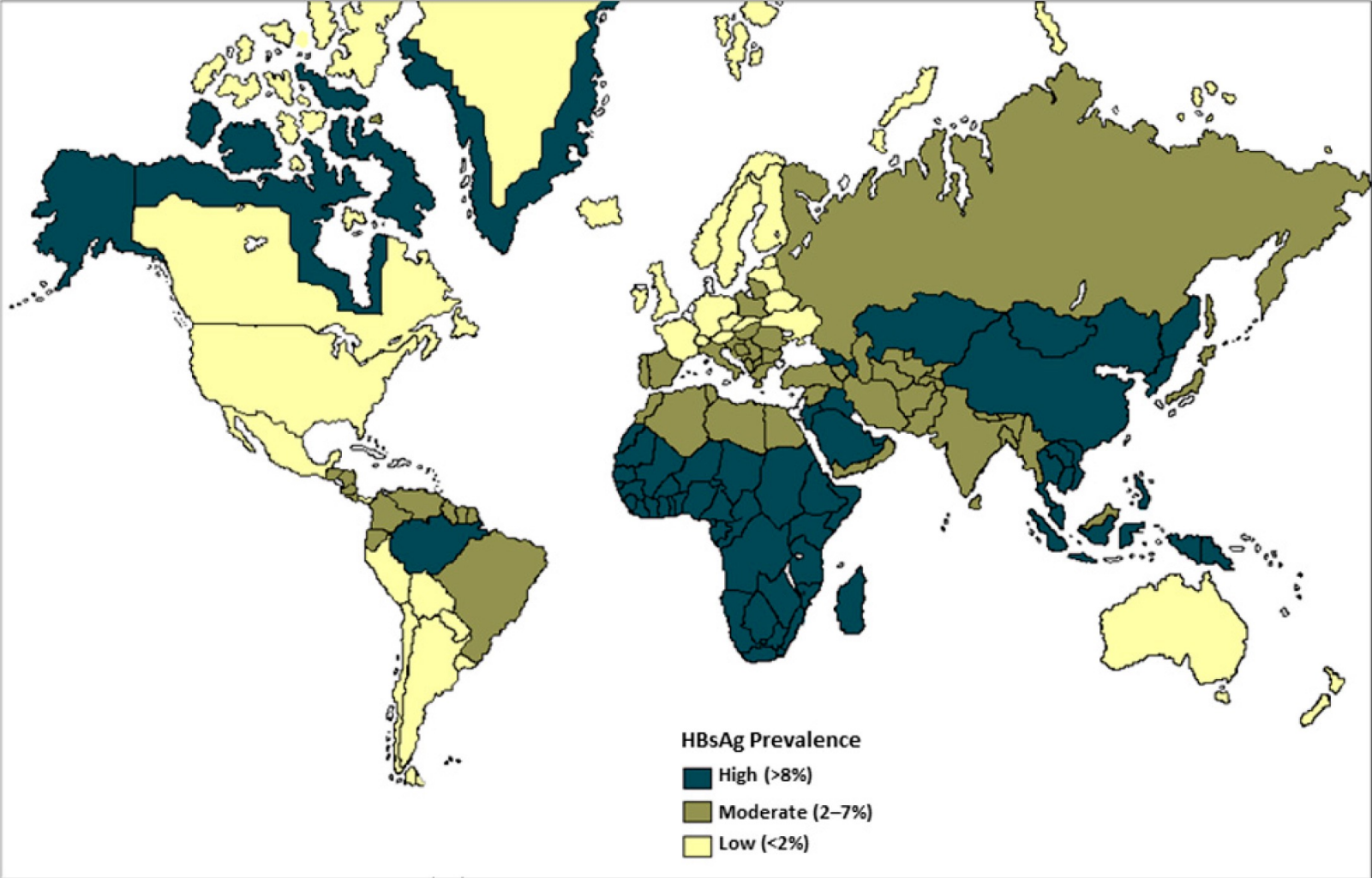
Division of Hepatology

University of Cape Town and Groote Schuur Hospital



# Global prevalence of chronic HBV – 258 million

2022 Global prevalence 3.2% (95% UI 2.7–4.0)



**WHO AFRO 5.4%**  
**(UI 4.4 to 6.8)**  
**= 65 million**

# WHO AFRICA REGION – VIRAL HEPATITIS



Source: WHO, 2021

## Hepatitis B

- **New infections**
  - 990 000 [660 000–1 600 000]
- **Deaths**
  - 80 000 [47 000–110 000]

## Hepatitis C

- **New infections**
  - 210 000 [150 000–370 000]
- **Deaths**
  - 45 000 [23 000–72 000]

# Modes of Transmission HBV - summary

Vertical



90% Chronicity

Horizontal

Children



30-60% Chronicity

Adults

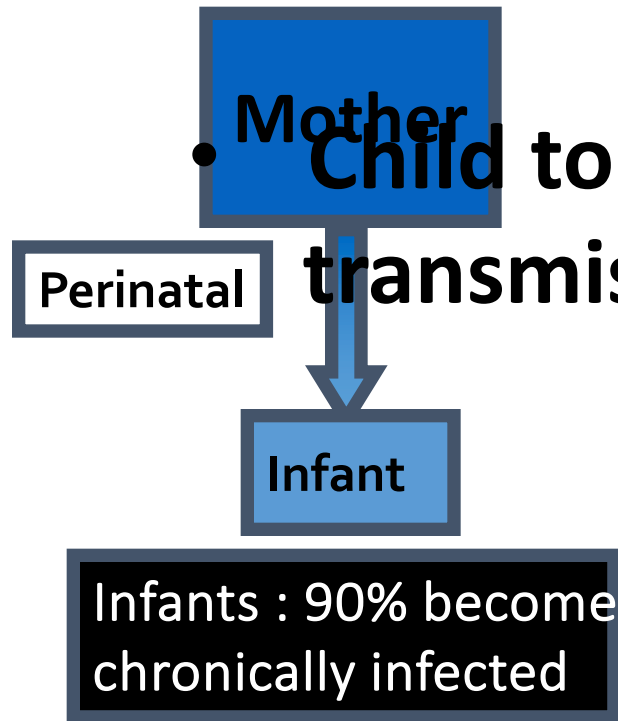


< 5-10% chronicity

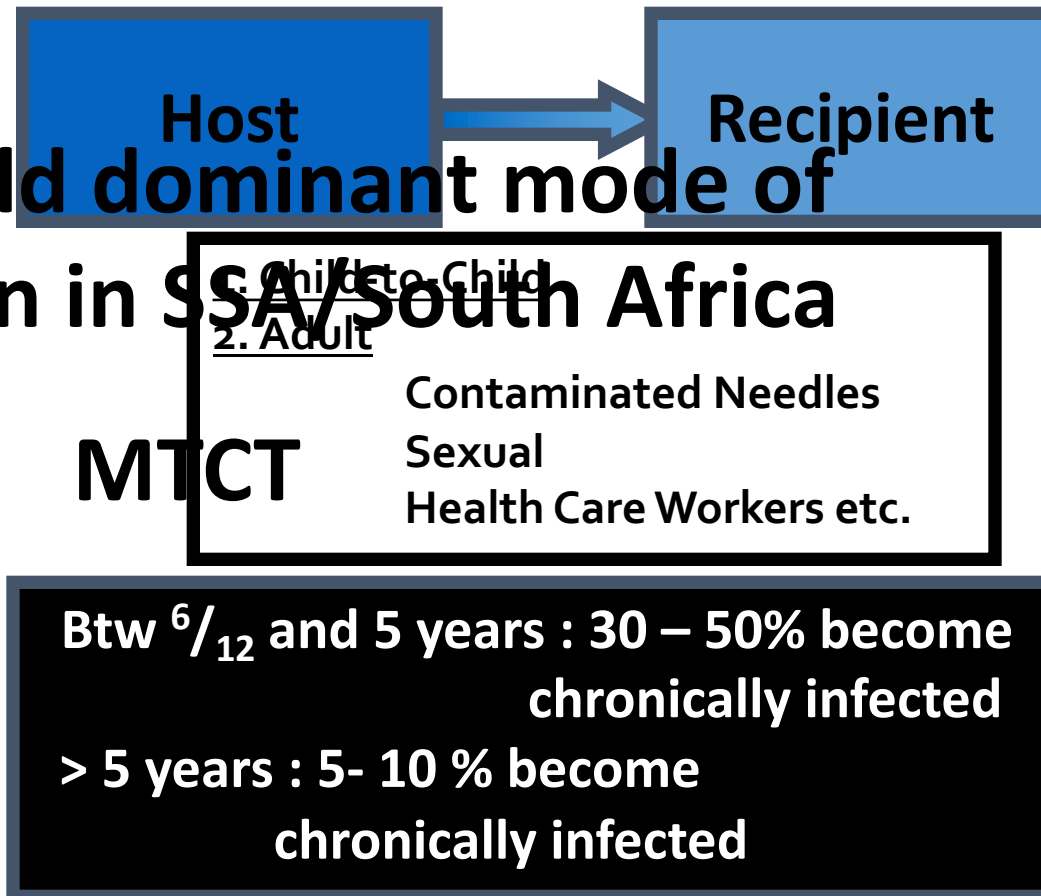
Sexual, needle stick, PWID etc

# Epidemiology and Transmission of HBV

## Vertical Transmission

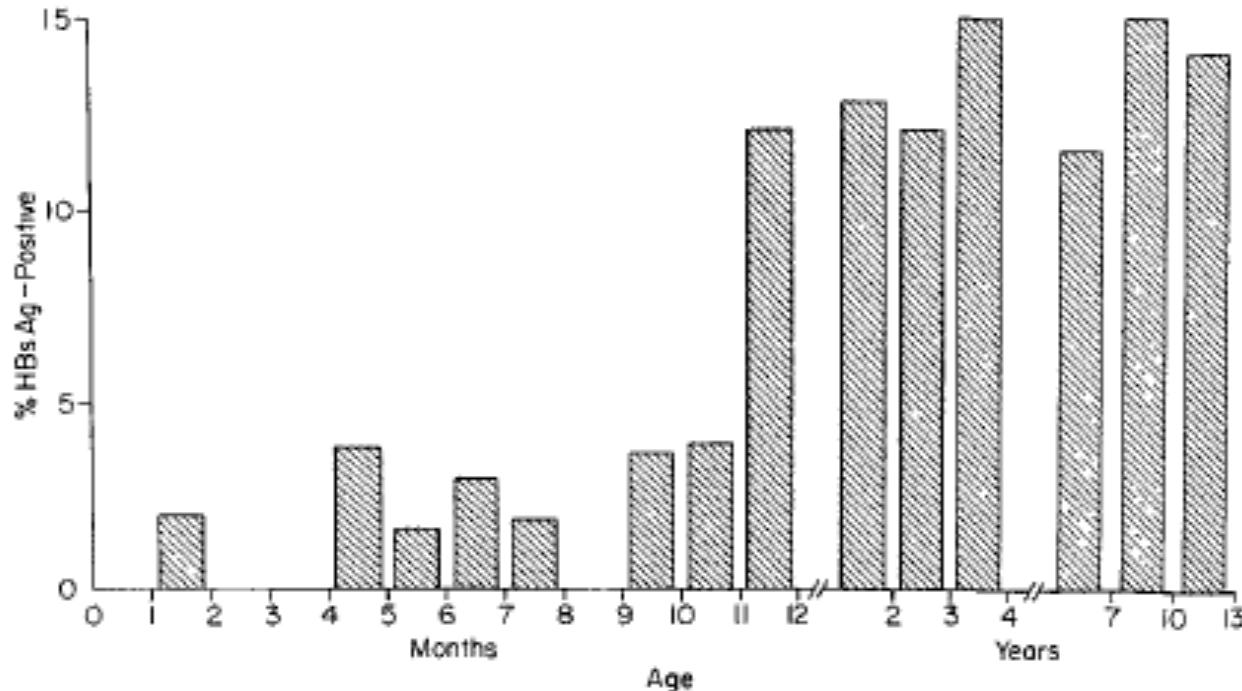


## Horizontal Transmission



# Hepatitis B virus in children – role of perinatal and horizontal transmission

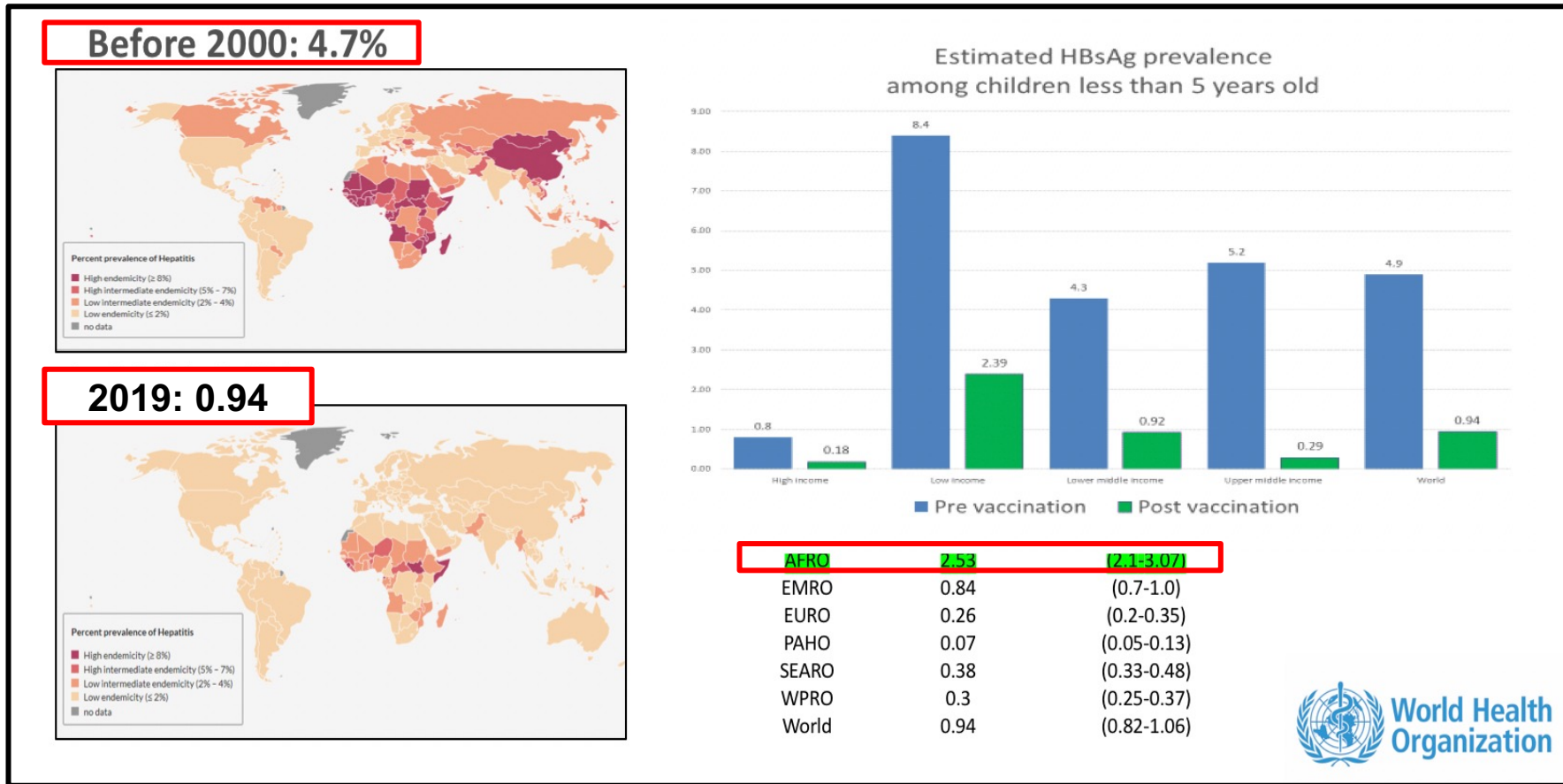
HBsAg: 17% of adult males and 11% of Mothers in Ovamboland, Namibia



- 1% of children <6 months were HBsAg +
- 13% of children >1 year were HBsAg +
- 27% of HBsAg + Moms had HBsAg + children
- HBsAg neg Moms → 6% were HBsAg +
- 63% of mothers HBeAg + had HBsAg + children
- 37% of HBsAg + children had HBsAg + mothers

**Fig 1—Prevalence of HBsAg in children between birth and 13 years.**

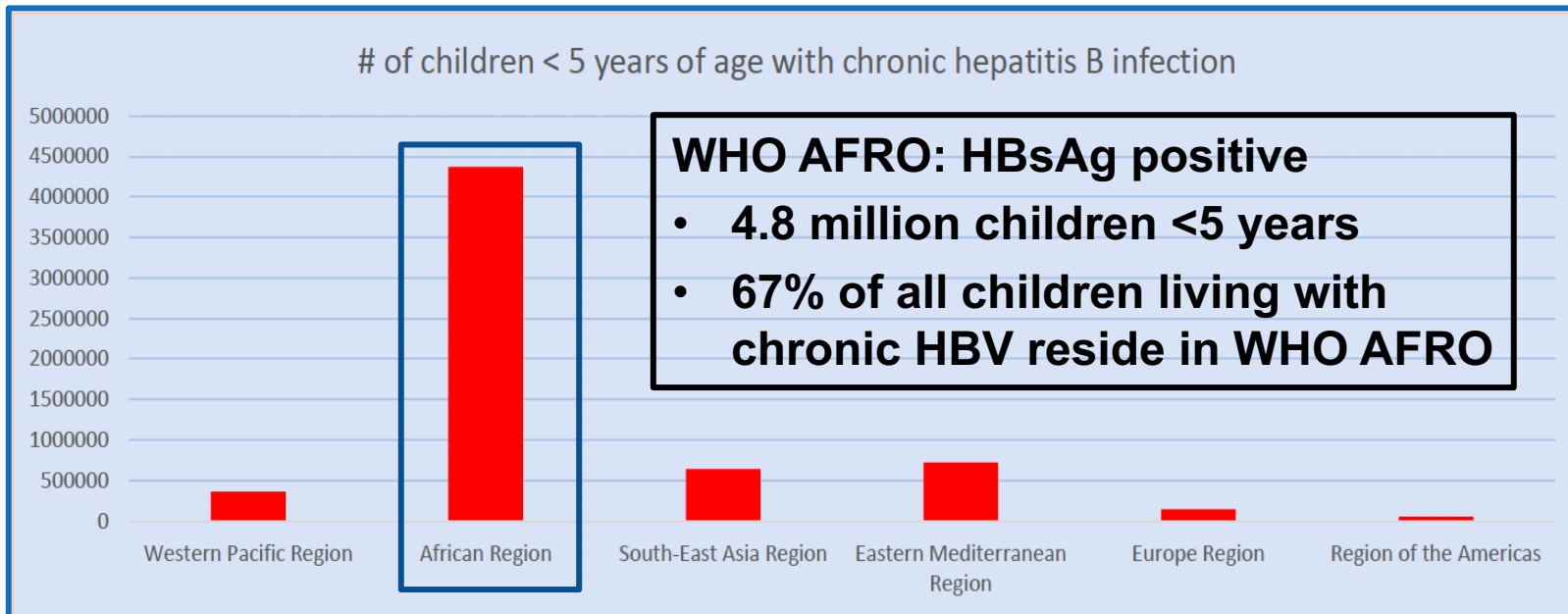
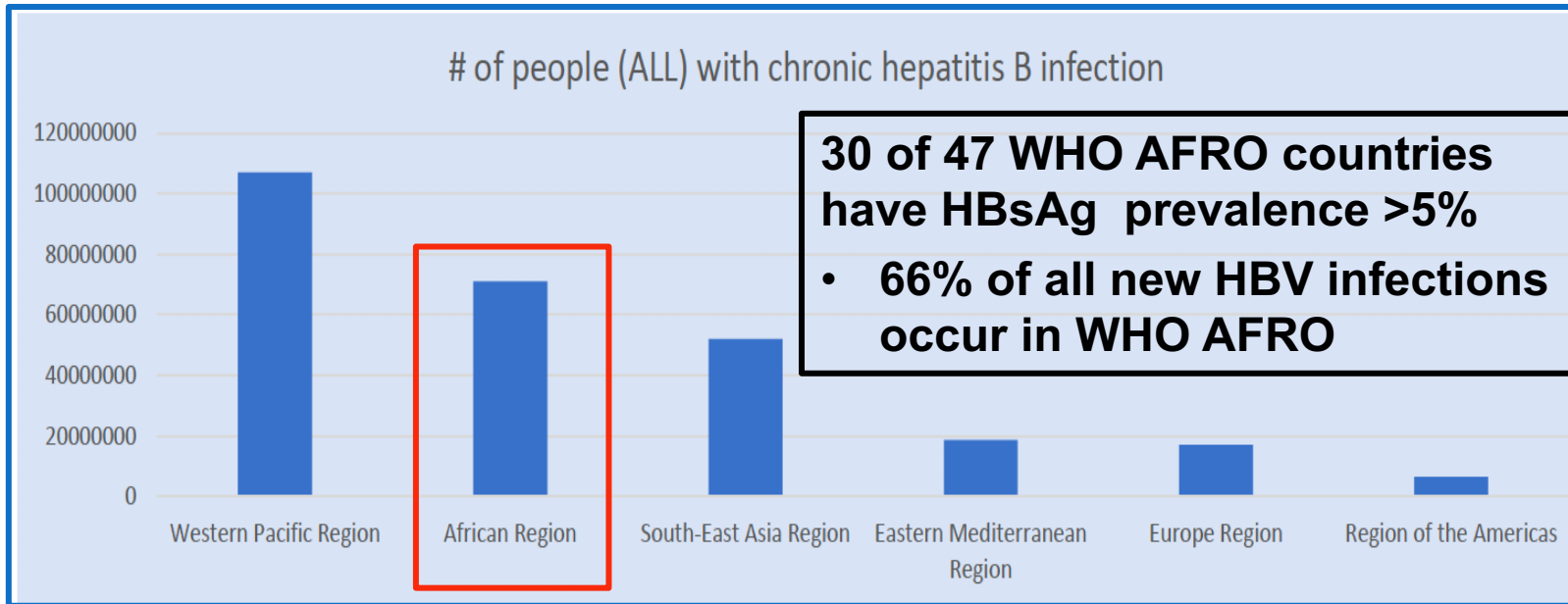
# Estimated HBsAg prevalence pre and post Universal HBV vaccination among children <5 years old



**Global: 2020 target <1.0%**

**2030 target ≤0.1%**

- **WHO AFRO <2%**
- **South Africa: 1.97% (1.63-2.33)**



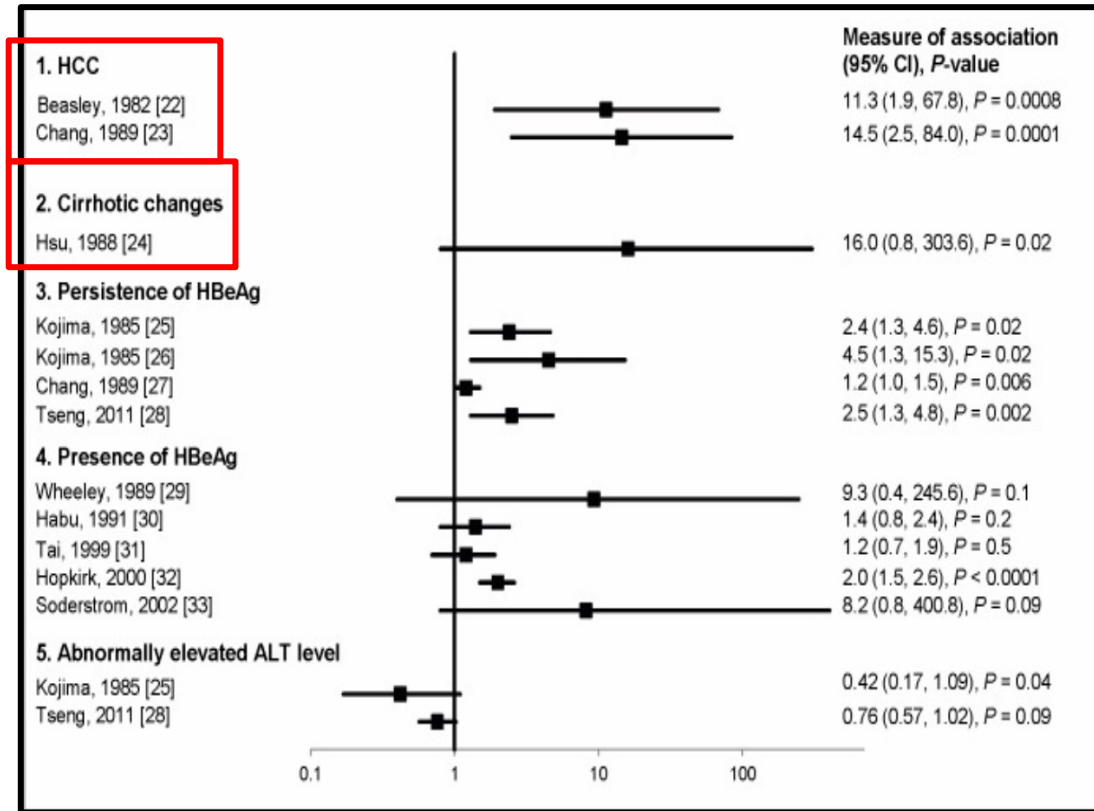


# Perinatal HBV Infection

## Systematic review:

### Earlier age at infection associated with:

- Increasing probability of chronic HBV infection
- Worse liver outcomes



## Longitudinal study in The Gambia: HBV MTCT was a risk factor for:

- Persistent high viral replication
- Significant fibrosis
- HCC

Shimakawa et al; Gut 2016;65(12):2007

Shimakawa et al; PlosOne 2013; 8(7): e69430

# Hepatitis B prevalence in South Africa

## Increase in HBsAg prevalence in rural areas

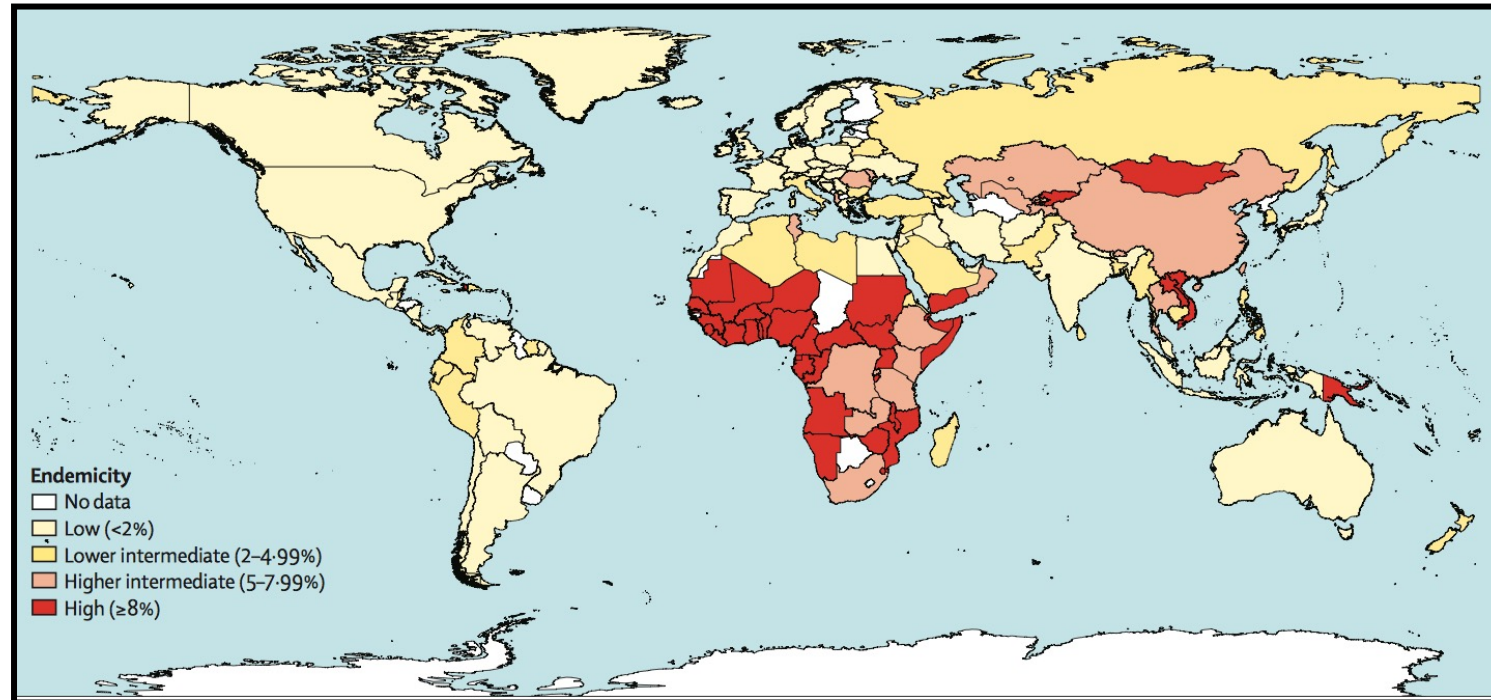
- Eastern Cape (rural) : 15.5%
- Urban areas
  - Durban 7.4%
  - Soweto 1.3%
- Male : Female - 2.6 : 1
- 94.2% men with liver cancer : previous HBV exposure
  - 56.5% HBsAg positive

# Recent data from KZN:

**Table 2**  
Seroprevalence of HBsAg and association with socio-demographic, behavioral, and clinical characteristics of 9791 participants (15–49 years of age), enrolled between June 2014 and June 2015 in rural and peri-urban KwaZulu-Natal, South Africa.

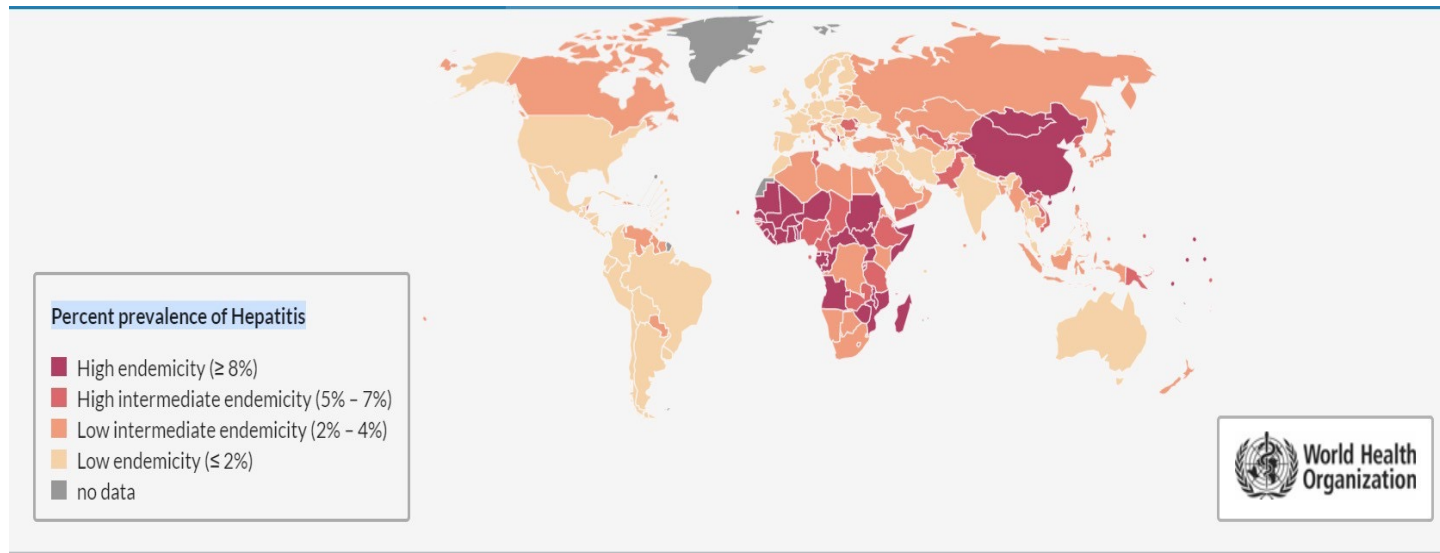
Variable	Men			Women		
	n/N	HBsAg seroprevalence Weighted % (95% CI)		n/N	HBsAg seroprevalence Weighted % (95% CI)	
Seroprevalence of HBsAg						
Overall	165/3541	<b>4.8</b>	(3.8–5.8)	196/6250	<b>3.2</b>	(2.5–3.9)
By age group in years						
15–19	7/657	1.1	(0–2.3)	8/956	0.9	(0–1.8)
20–24	26/813	3.6	(1.7–5.4)	32/1262	2.7	(1.5–3.8)
25–29	30/602	4.5	(2.4–6.6)	39/1085	3.8	(2.2–5.4)
30–34	40/459	7.8	(4.5–11)	40/831	6.0	(3.1–9)
35–39	23/404	5.6	(3.1–8.1)	27/757	2.9	(1.4–4.5)
40–44	24/319	9.6	(5–14.1)	26/660	4.1	(1.9–6.3)
45–49	15/287	6.6	(2.3–10.8)	24/699	2.5	(1.3–3.8)
		$p < 0.01^a$			$p < 0.01^a$	

# Hepatitis B in South Africa



**South Africa: HBsAg 4.5% seroprevalence**  
**2.8 million chronically infected**

# In highly endemic areas, transmission occurs primarily perinatally or in early childhood



CDA- 2021

In areas with intermediate endemicity, infection occurs in all age groups.

In areas of low hepatitis B seroprevalence, most infections occur in adults, especially among persons belonging to defined risk groups

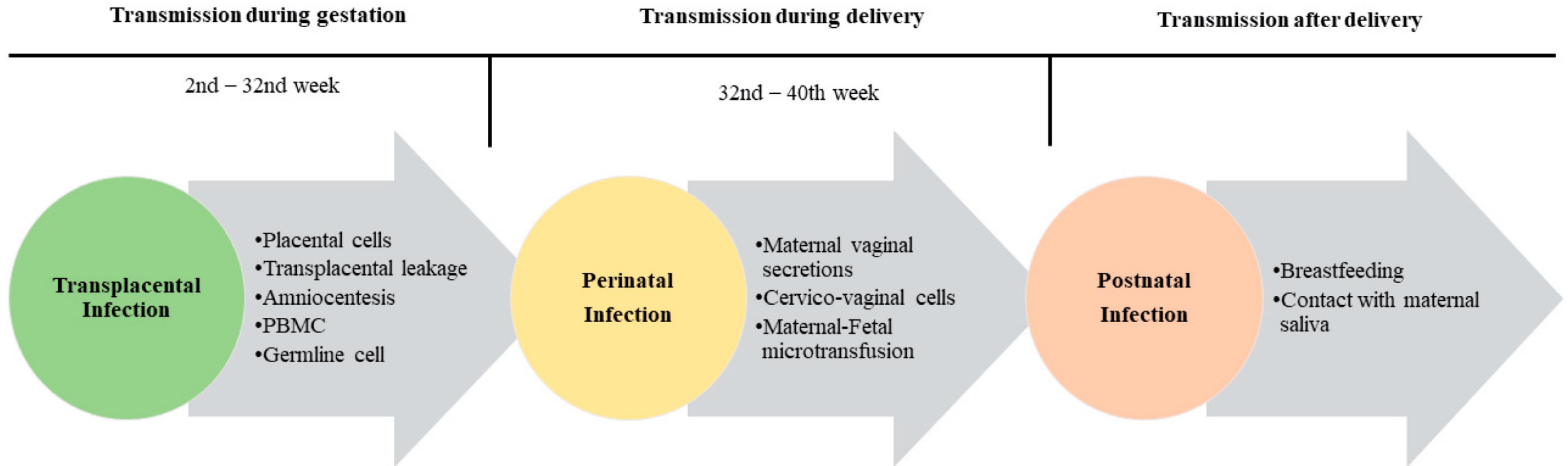
# Modes of Transmission HBV - summary

Vertical



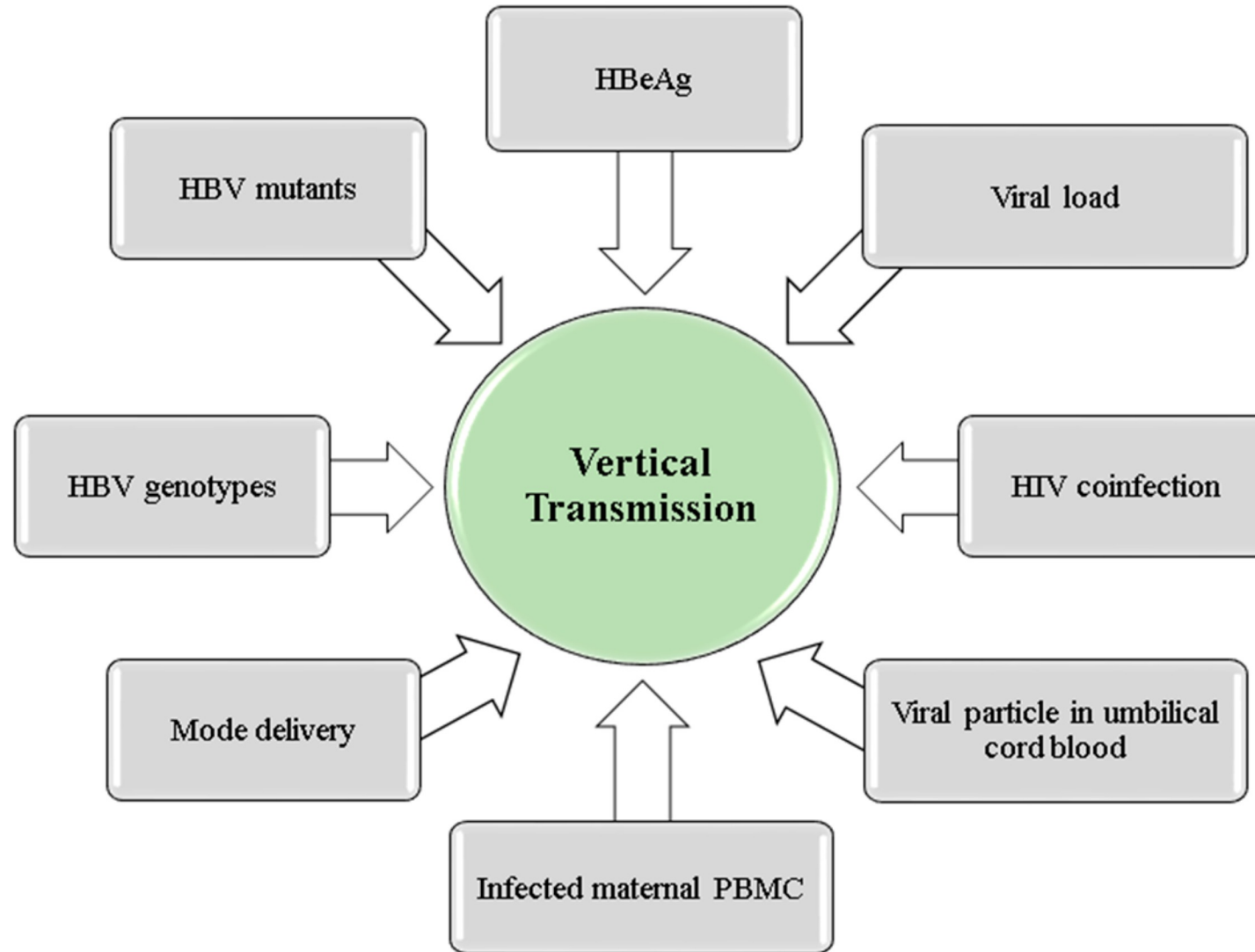
90% Chronicity

# Perinatal Transmission of HBV



1. Transplacental transmission of HBV in utero
2. Transmission during delivery
3. Postnatal transmission during care or through breast milk

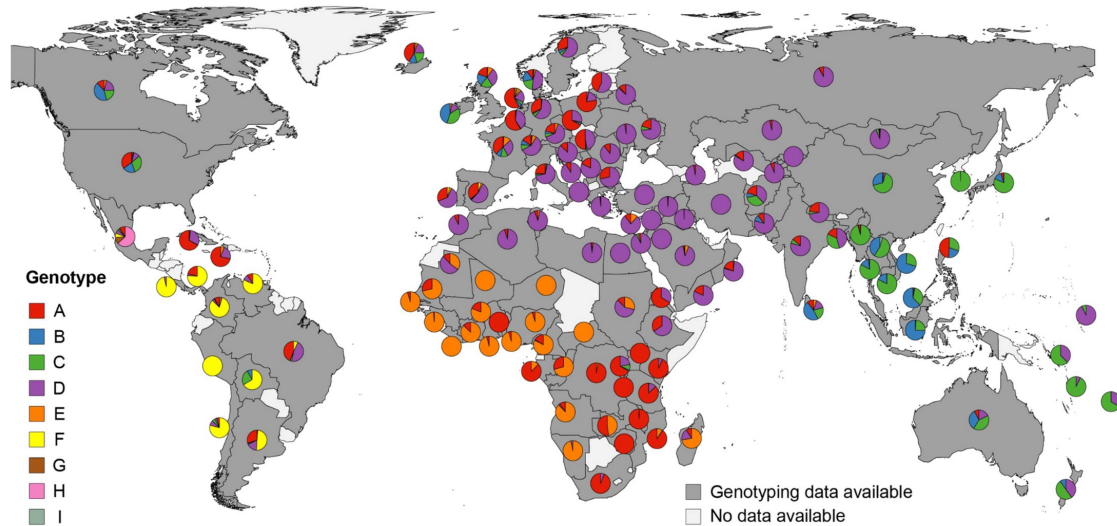
# Factors associated with HBV vertical transmission



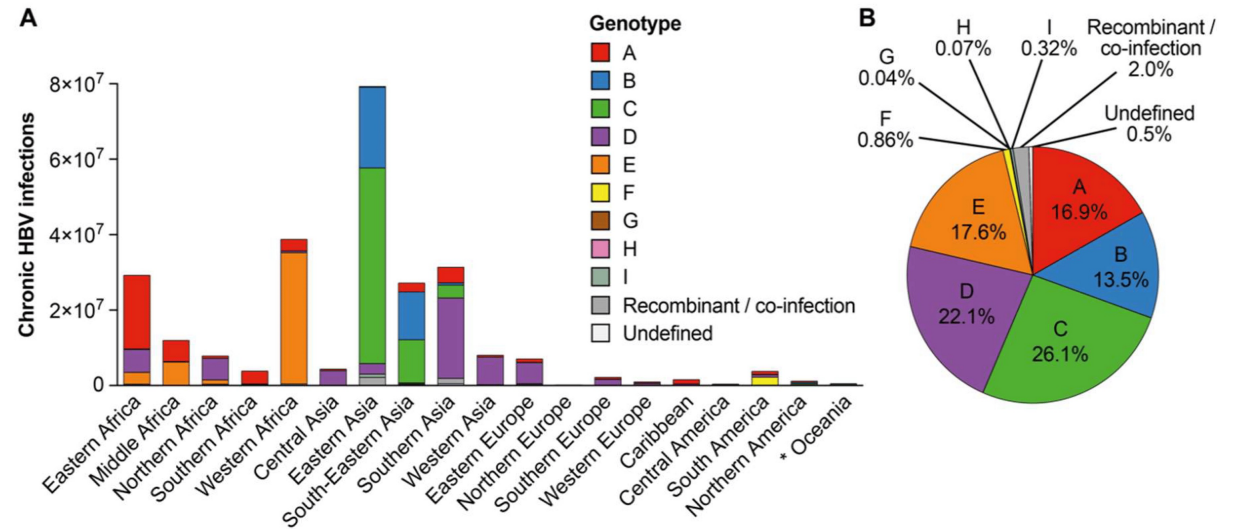


# HBV genotypes

HBV is classified into 10 genotypes (A–J) and several sub-genotypes



Distribution of HBV genotypes by country



Frequency of HBV genotype distribution

# HBV genotype and transmission risk

- ❖ Vertical transmission rate of HBV in East Asia (esp. China, 10-88%) is higher than in sub-Saharan Africa ( $\leq 8\%$ )
- ❖ Genotype B and C predominate in Asia
- ❖ Most Mothers are HBeAg+ with high viral loads
- ❖ In sub-Saharan Africa where HBV genotypes A1, D or E are prevalent, seroconversion to anti-HBe occurs earlier  $\sim 15$  years
- ❖ Most Mothers are HBeAg negative
- ❖ UNCLEAR - ? Role of Genotype in transmission risk; nature of others e.g. E, F, G and H

# Data on HBeAg sero-prevalence

## Median HBeAg prevalence in HBsAg positive pregnant women

- **West Africa:** Nigeria 28.5% Burkina Faso 21.2% Cote d'Ivoire 14.5%; Benin 11.4%
- **Central Africa:** Cameroon 12.1% Gabon 10.1%
- **Eastern Africa:** Kenya 8.8% Tanzania 12% Ethiopia 12.5% Uganda 14.9%
- **Southern Africa:** Zimbabwe 3.3% Zambia 16.1% South Africa 17.1%

## Perinatal transmission from HBeAg positive women in SSA

- **Asia:** 70-90% vs 5-30% HBeAg negative women
- **SSA: Lower rate**

# HBeAg status of pregnant women

- HBeAg + predicts for higher viral load thus greater MTCT transmission risk
- HIV infected women had a HBeAg prevalence of 37.5%  
(Durban, *Thumbiran et al 2014*)
- Soweto study found 6/14 women were HBeAg positive (Hoffmann et al 2014)
- Malawian data: HBeAg + prevalence of 38.2% in HIV infected women  
(*Chasela et al 2013*)

# HIV influences HBV transmission risk (in the absence of ART)

**Western Cape** (*9 355 pregnant women from antenatal clinics comparing HIV-positive and negative women*)

- HBsAg 3.4% (53/1 543 HIV pos) v. 2.9% (44/1 546 HIV neg)
- HBeAg 18.9% (10/53 HIV pos) v. 17.1% (7/41 HIV neg)
- HBV DNA levels were much higher in HIV positive women
  - ❖  **$9.72 \times 10^7$  IU/ml v.  $1.19 \times 10^6$  IU/ml**
- **1 in ~5 HBV-infected pregnant women, irrespective of HIV status are HBeAg+**

# HIV influences HBV transmission risk (in the absence of ART)

## KZN

- **Retrospective cross-sectional study:** July 2011 to December 2011
- 322 study samples from discarded residual dried blood spot samples following routine infant diagnosis of HIV

## 10% overall HBsAg seroprevalence

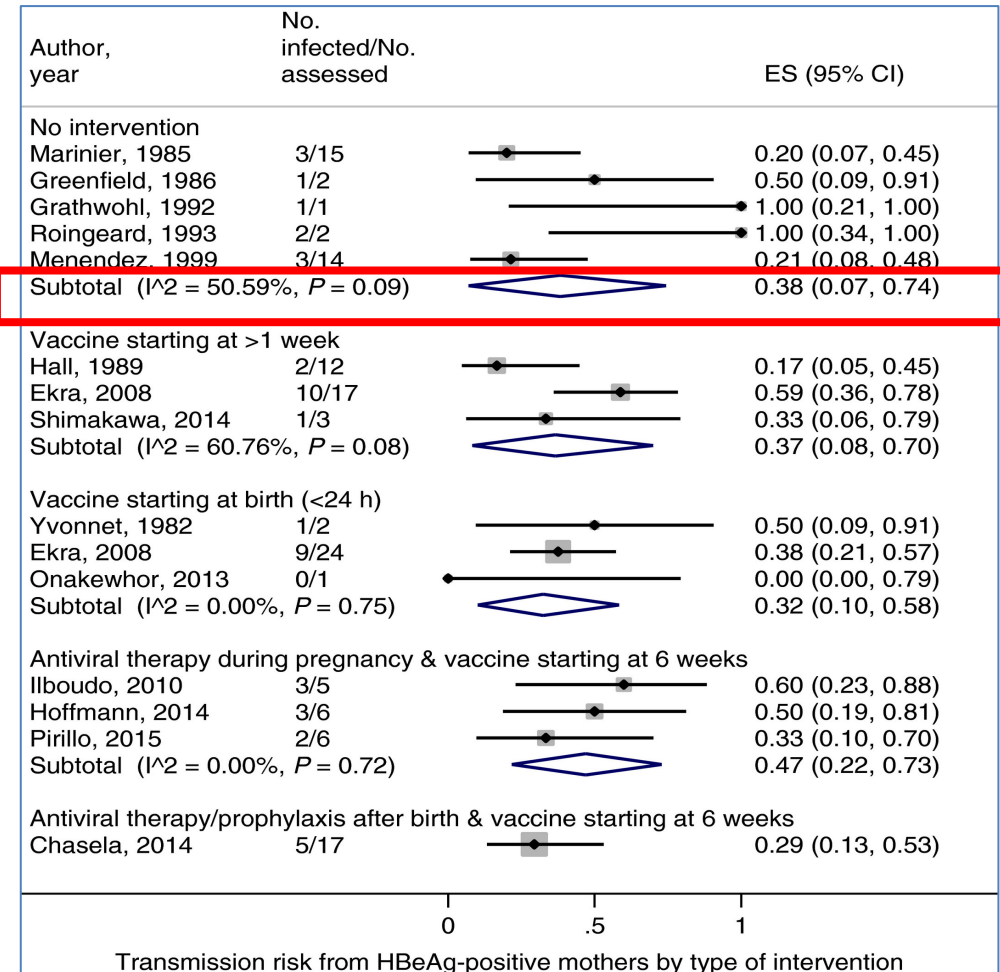
- HIV-positive infants: 21/161 infants HBV positive :13.0%; 95% CI 6.8-19.9
- HIV-negative infants: 12/161 HBV positive: 7.5%; 95% CI 2.5-13.7
- P value NS

## Concern

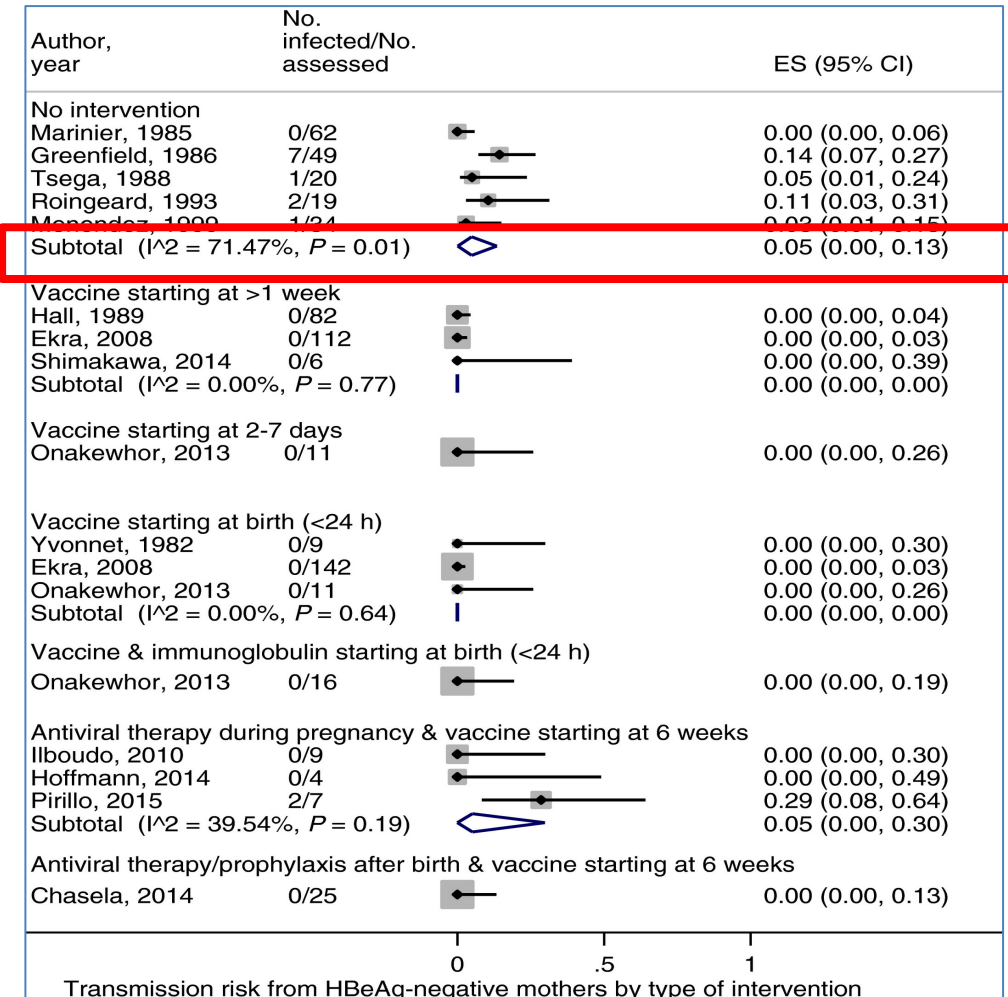
- High prevalence of HBV infection in children despite HBV vaccination
- Independent of HIV status

# Systematic review and meta-analysis: the risk of mother-to-child transmission of hepatitis B virus infection in sub-Saharan Africa

## HBeAg POSITIVE Mothers



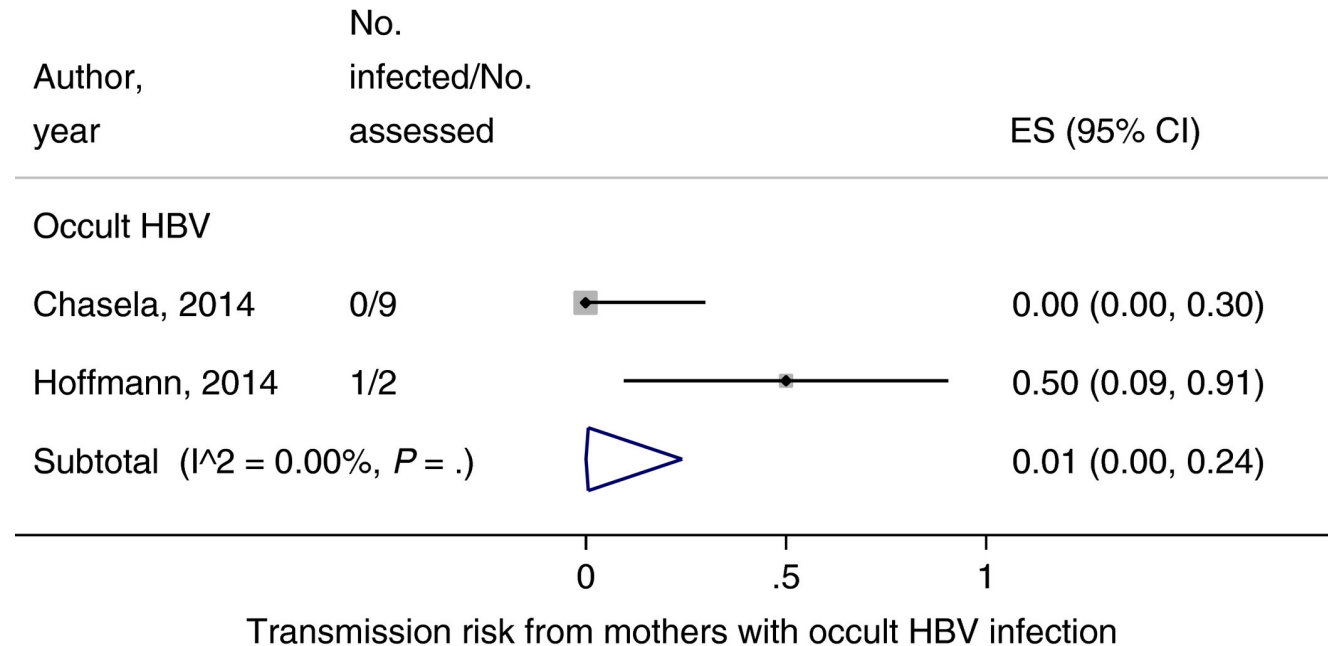
## HBeAg NEGATIVE Mothers



1% newborns annually infected with HBV at birth

# Systematic review and meta-analysis: the risk of mother-to-child transmission of hepatitis B virus infection in sub-Saharan Africa

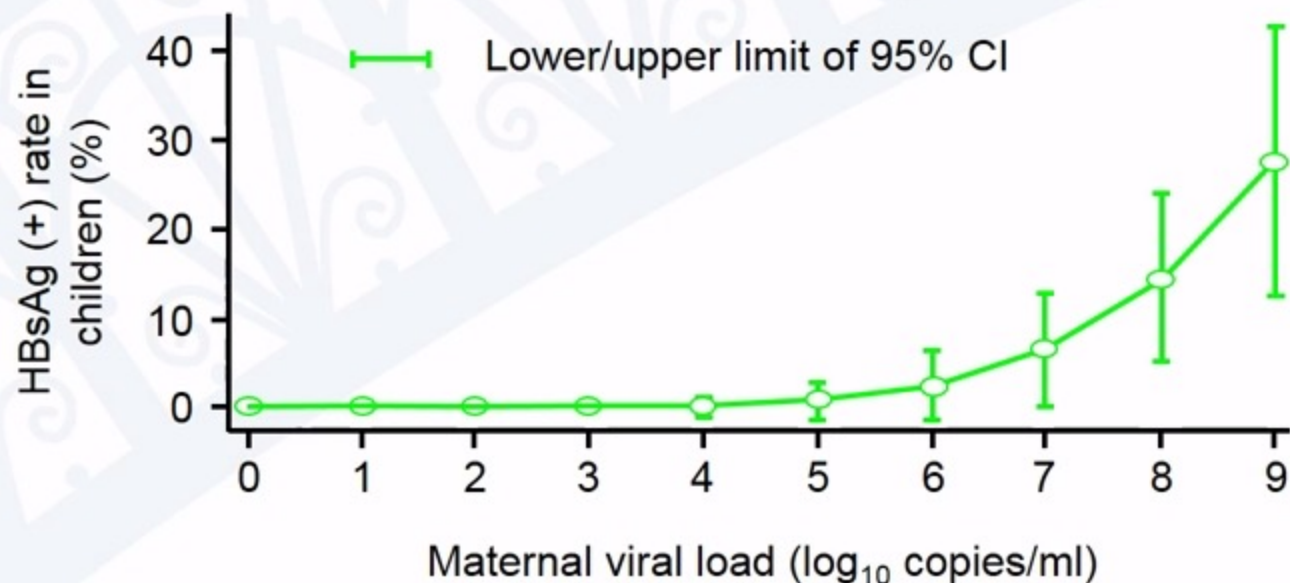
## Occult HBV Mothers





# HBV vaccine cannot protect all babies from high viral load carrier mothers

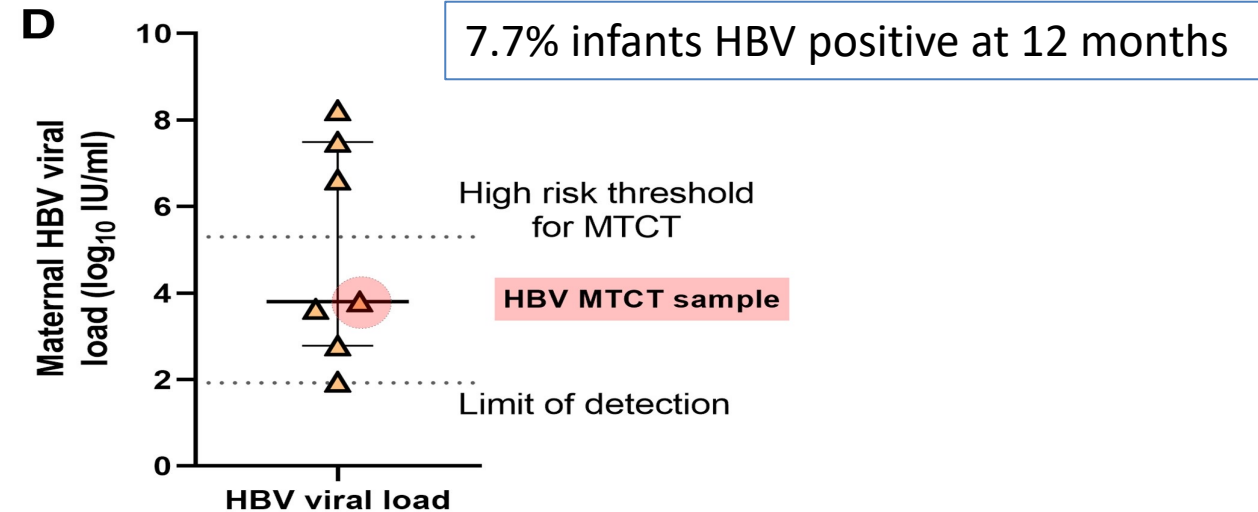
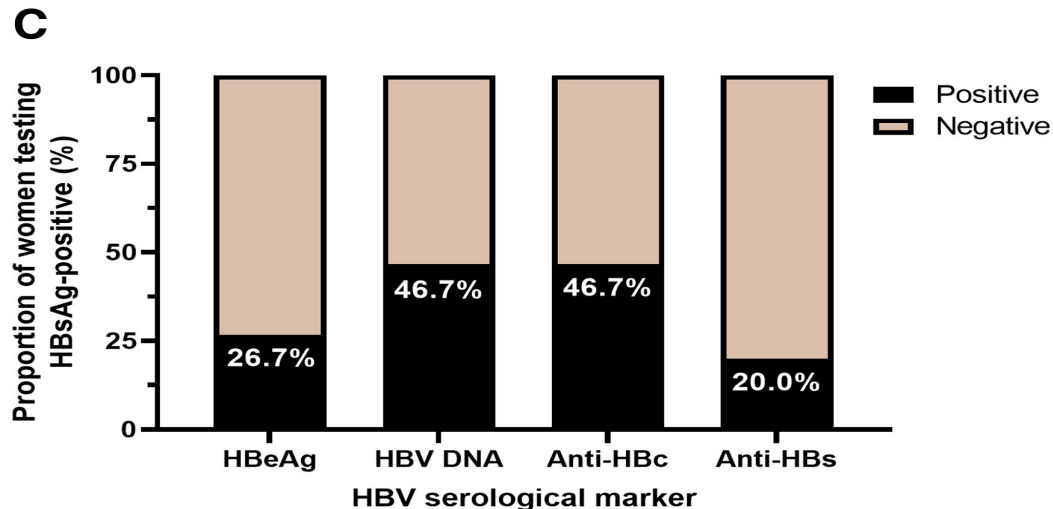
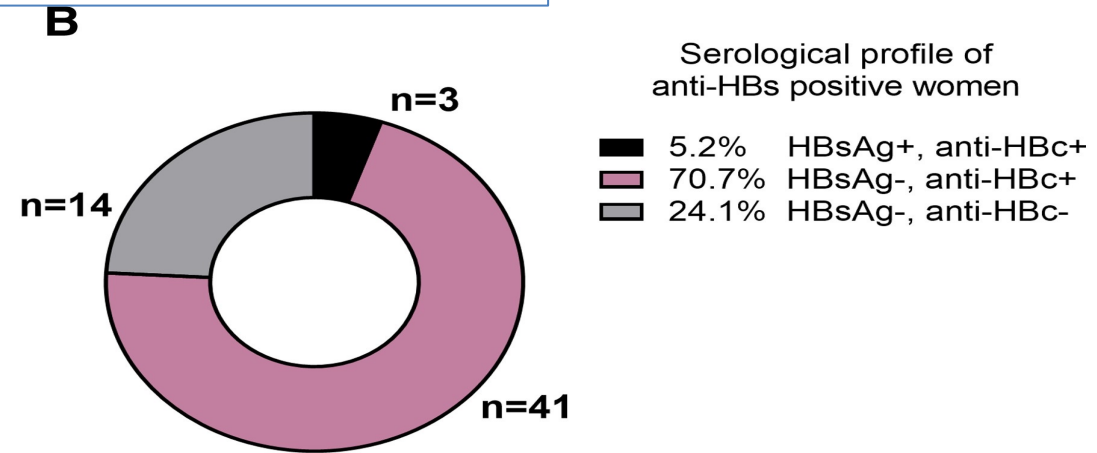
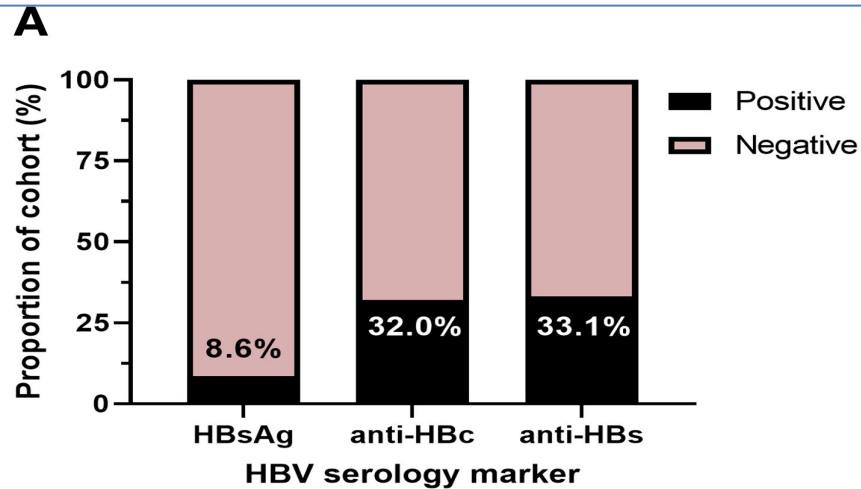
HBV DNA (log cp/ml)	Adjusted odds ratio	P value
5	0.9%	0.334
6	2.6%	0.165
7	6.6%	0.033
8	14.6%	0.001
9	27.7%	<0.001



- 10 of 303 babies born to HBV carrier mothers had HBV infection despite HBV vaccination
- All mothers of infected babies had positive HBeAg
- All infected babies had 3 doses of vaccine with HBIG at birth

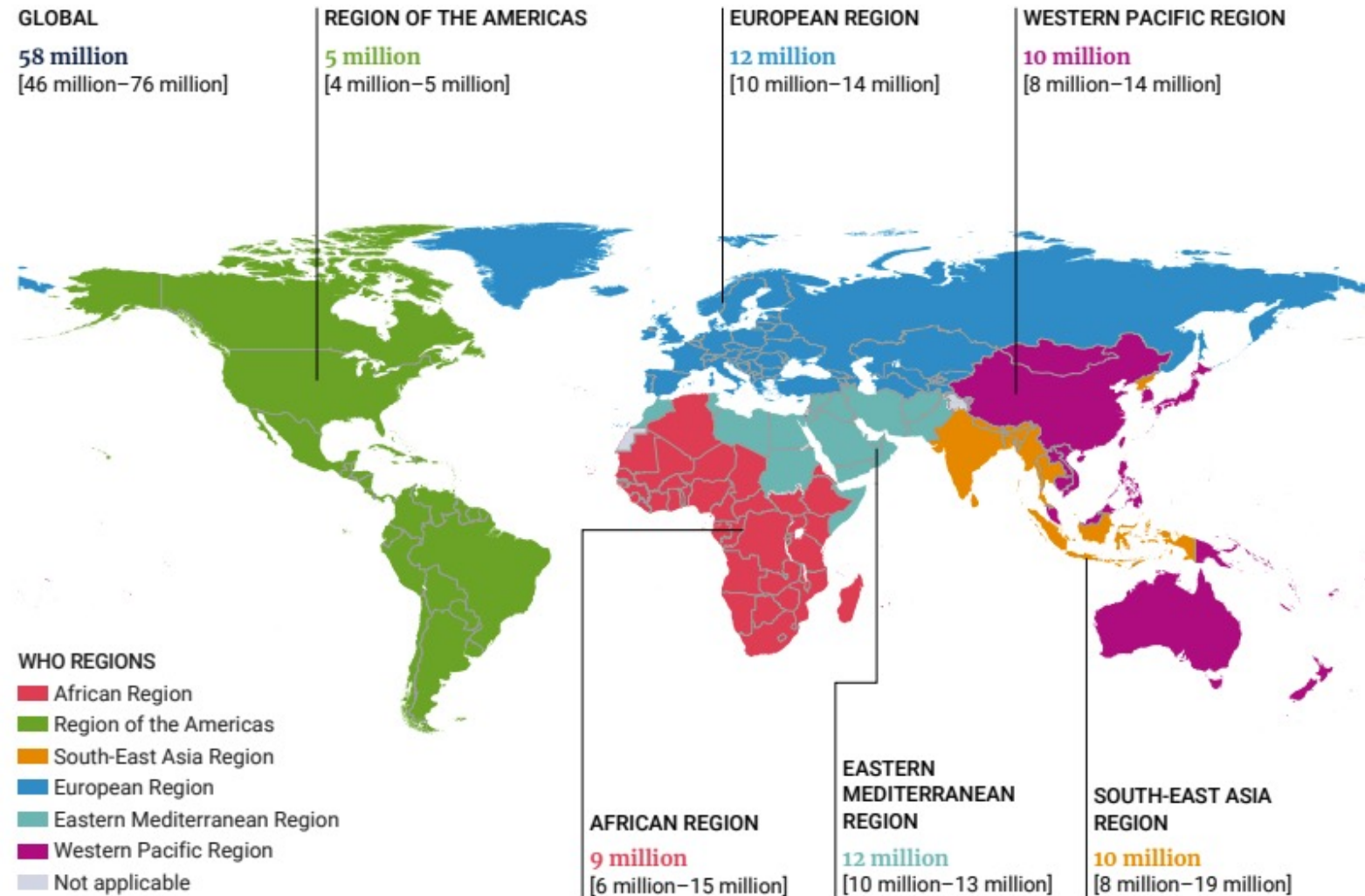
# HBV serologic profiles of mothers in a cohort of HIV MTCT pairs in KwaZulu-Natal

HBsAg positive were younger than HBsAg negative mean, 21.7 vs 25.5 years



- HBV VL of 6.6  $\log_{10}$  IU/mL and was aviremic for HIV

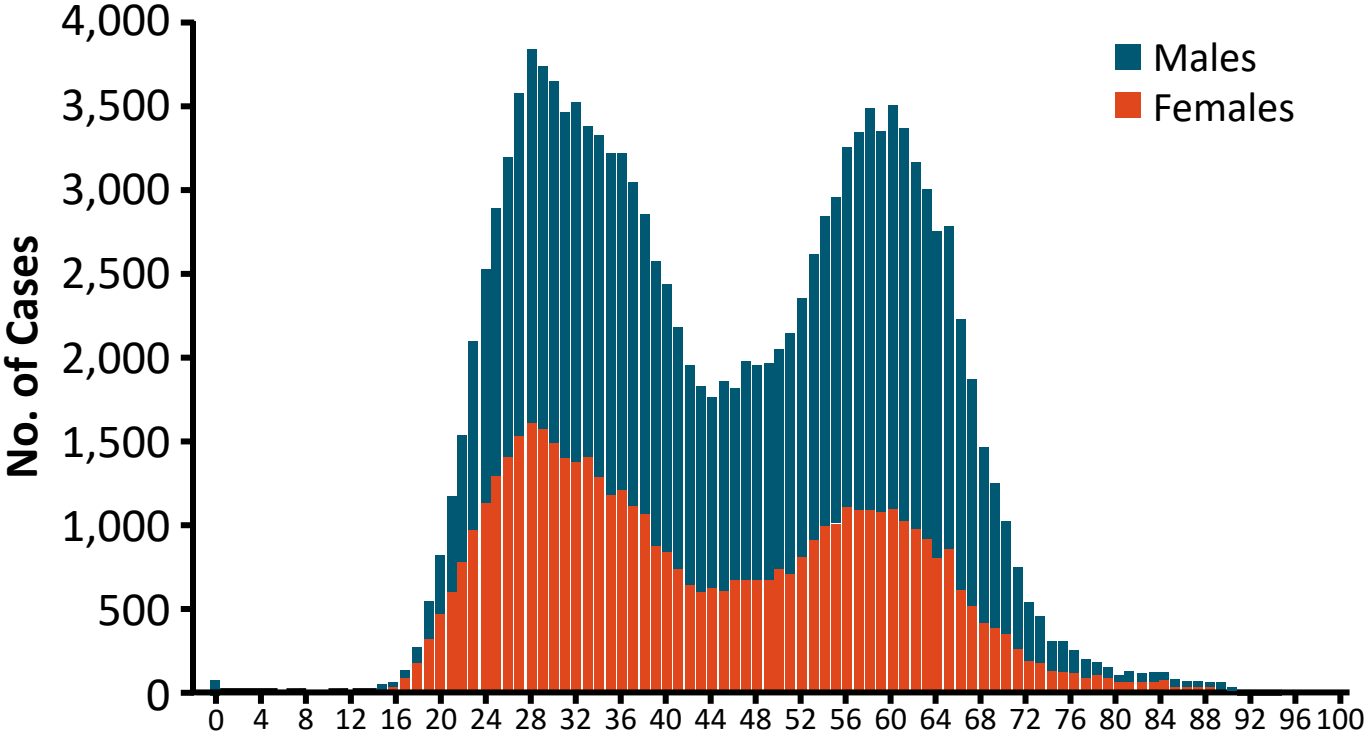
# Global Prevalence of Chronic HCV Infection, 2021



# Bimodal population distribution of HCV

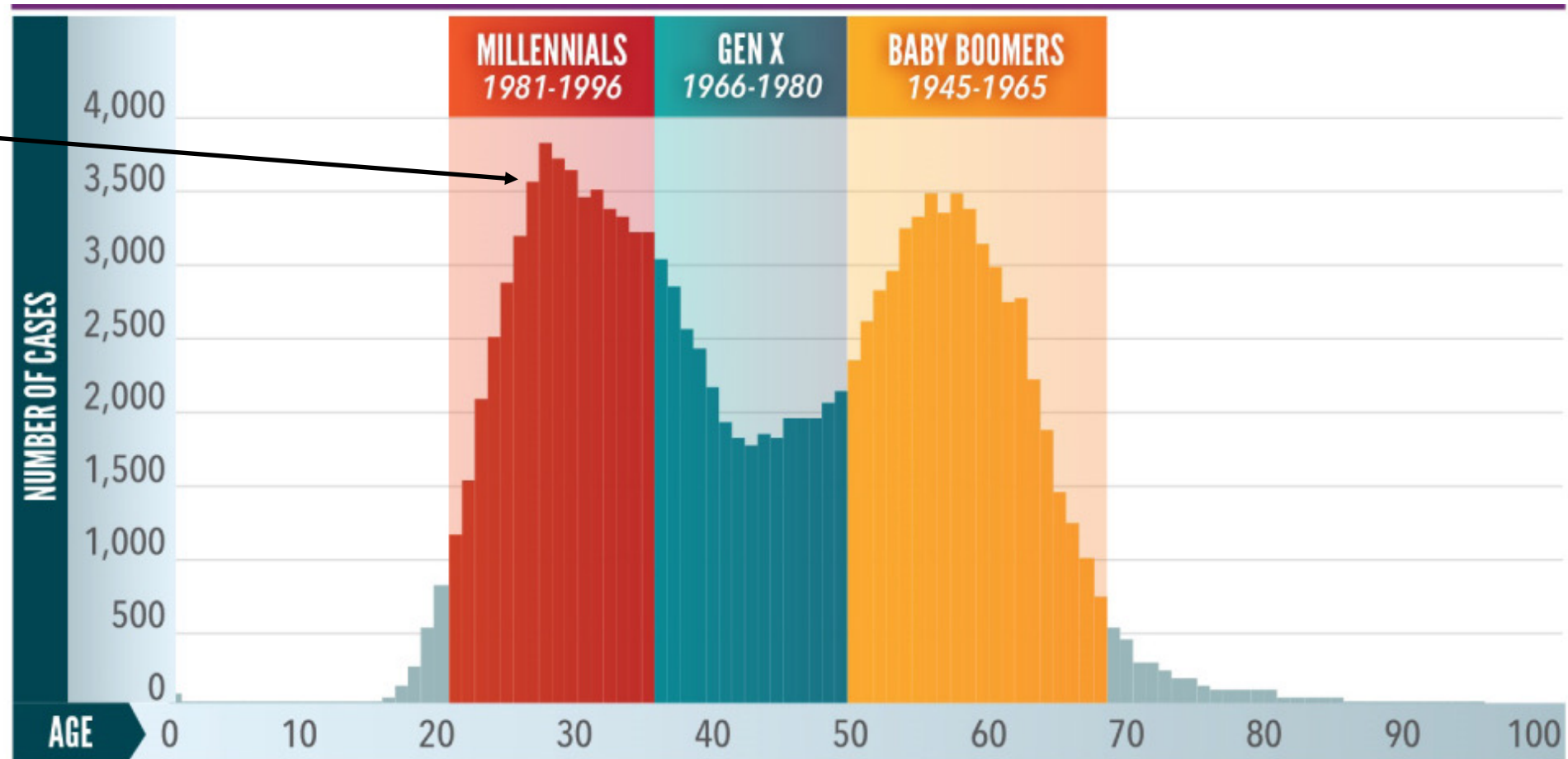
- Globally a Bi-Modal distribution of HCV
- Younger – new infections
- Older – longstanding infections

Bimodal Distribution of Chronic HCV Cases by Gender in 2018



# Bimodal HCV distribution: now includes reproductive-age women

Reproductive age women



SOURCE: National Notifiable Diseases Surveillance System, 2018

# Hepatitis C perinatal transmission

- ❖ 3.5 million children globally are HCV infected
- ❖ Most -> vertical transmission
- ❖ Vertical transmission risk: **1-6%** increasing to **10.8%** in HIV/HCV co-infection
- ❖ 3-5% infected infants progress to cirrhosis
- ❖ Passive transfer of maternal antibody remains detectable in exposed infants up to 18 months of age
- ❖ HCV RNA may not be detectable immediately in infected infants

# Hepatitis C and Pregnancy?

## **Pregnancy has no effect on chronic HCV infection**

- No net effect on ALT
- Pregnancy an immunosuppressive state so HCV viral load tends to rise during pregnancy and drop after delivery

## **Increased risk of Cholestasis of Pregnancy**

- Pooled OR 20.40 [95% CI, 9.39-44.33]

## **Increased risk of gestational diabetes**

# Does hepatitis C influence infant outcomes?

## ? increased risk of adverse perinatal outcomes

- Preterm delivery, low birth weight infants, congenital anomalies, neonatal deaths
- Preterm delivery, low birth weight
- Confounders are substance use
- **Egyptian study:** - IUGR in 10%
  - Apgar scores at 1 and 5 minutes significantly lower
  - Greater neonatal ICU admission ( $p < 0,001$ )



# Managing MTCT risk

## Factors enhancing HCV MTCT

- **HIV infection**
- Amniocentesis risk << chorionic villus sampling
- Foetal monitoring during labour (foetal scalp monitors), prolonged rupture of membranes, episiotomies and forceps delivery
- Caesarean section not recommended to reduce risk of transmission
- On balance, breastfeeding benefits dominate (cracked nipples avoid)

# Summary

- **MTCT of hepatitis B and C remain an integral risk to the global ongoing burden of viral hepatitis**
- **Hep B compelling indication for aggressive interventions**
- **Hep C increasing risk of MTCT**
- **Strategies and management to eliminate this route of transmission is the basis of any elimination intervention**