Mother-to-child transmission of hepatitis B in sub-Saharan Africa

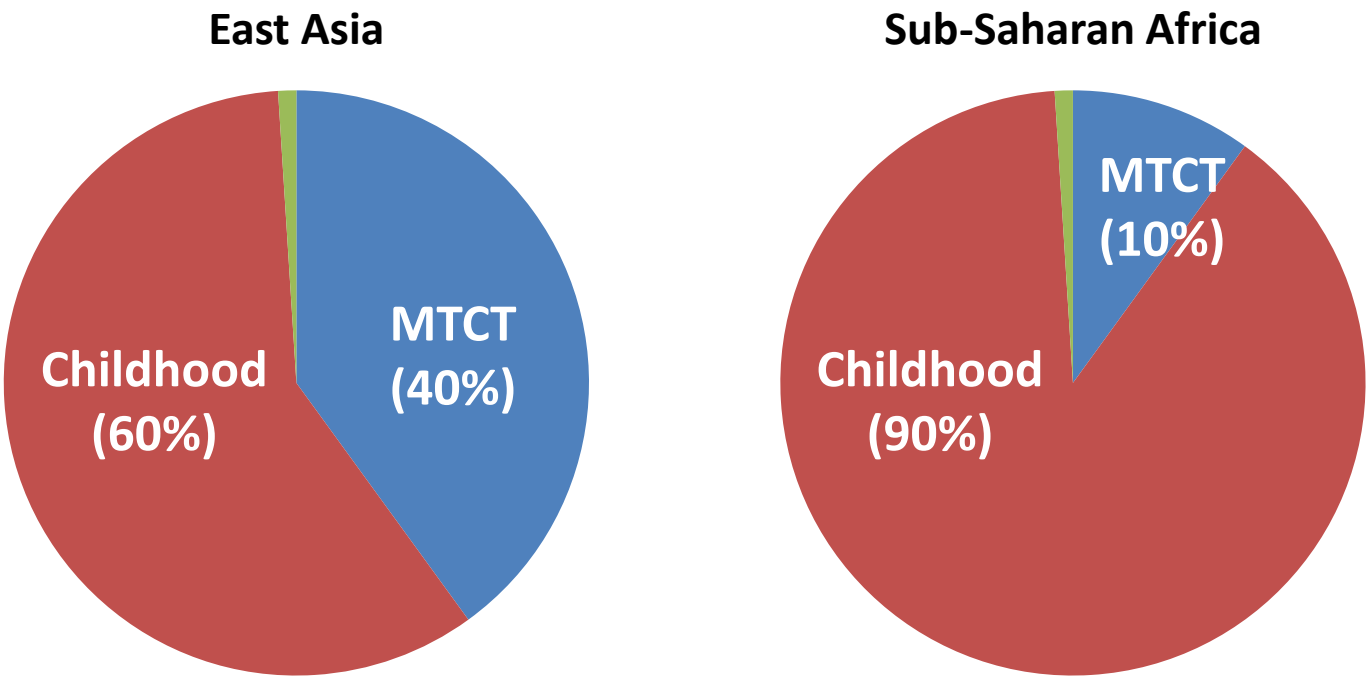
1 June 2017

Yusuke SHIMAKAWA

Institut Pasteur, Paris

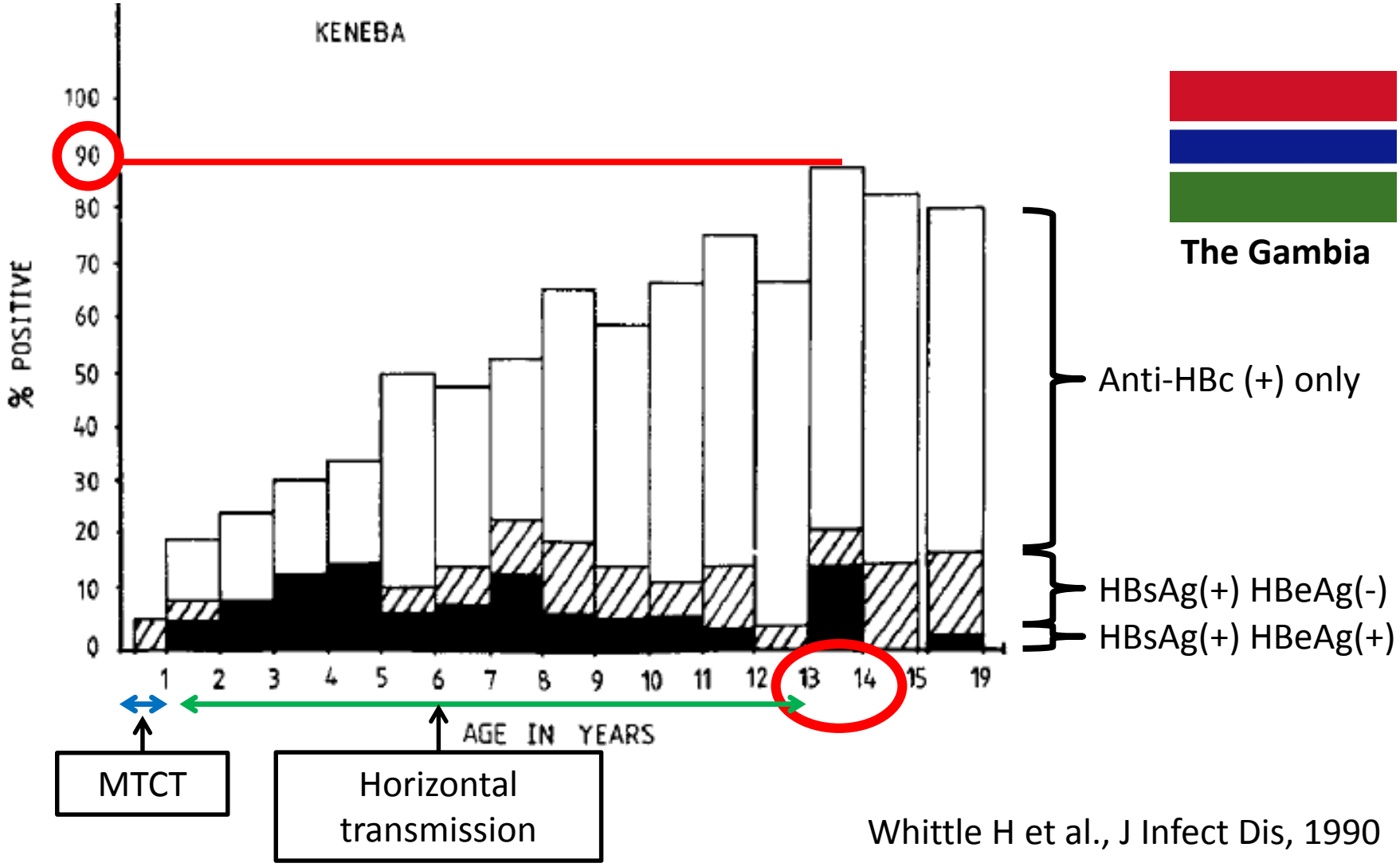
- Epidemiology of HBV in sub-Saharan Africa
- Why is the PMTCT of HBV important?
- Current situations and challenges in implementing PMTCT in sub-Saharan Africa

Modes of Transmission



Edmunds WJ et al., Epidemiol Infect, 1996

Sero-prevalence in children



Whittle H et al., J Infect Dis, 1990

Determinants of frequency of MTCT

	East Asia	Sub-Saharan Africa
% pregnant women with positive HBsAg	10%	10%

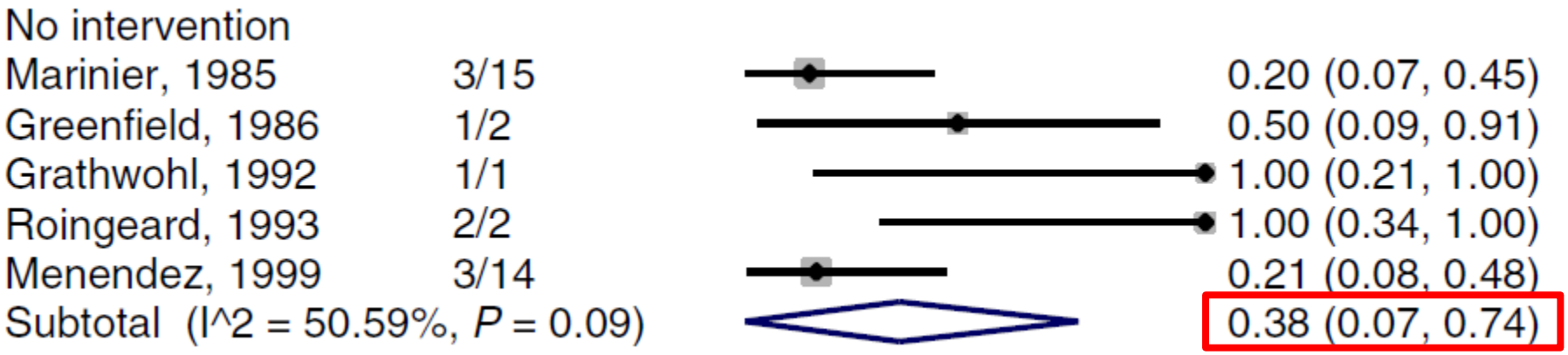
WHO, 1990
Edmunds WJ et al., Epidemiol Infect, 1996
Howell J et al., J Viral Hepat, 2014

Determinants of frequency of MTCT

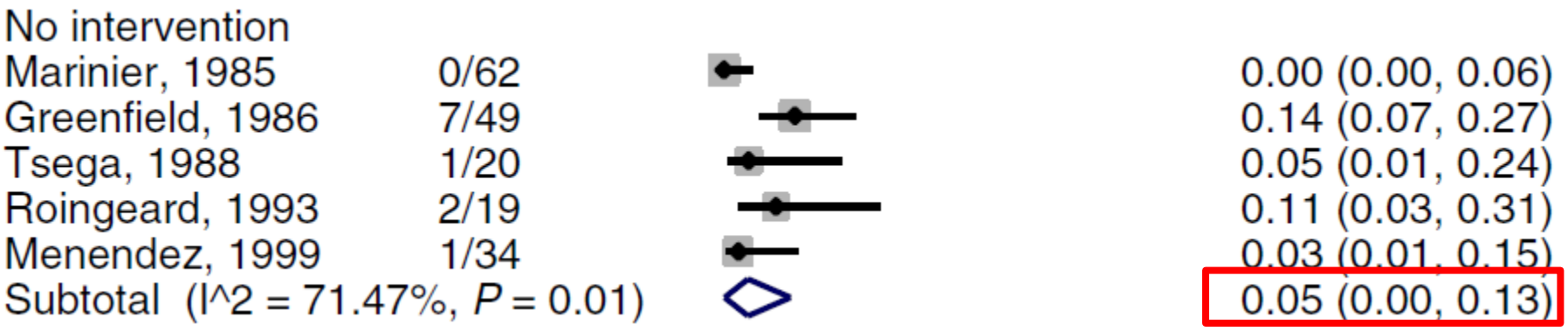
	East Asia	Sub-Saharan Africa
% pregnant women with positive HBsAg	10%	10%
% pregnant women with positive HBeAg	40% ⟷	10%
Risk of MTCT from HBsAg+/HBeAg+ women	70-90%	
Risk of MTCT from HBsAg+/HBeAg- women	5-30%	

WHO, 1990
Edmunds WJ et al., Epidemiol Infect, 1996
Howell J et al., J Viral Hepat, 2014

Risk of MTCT from HBsAg(+) HBeAg(+) mothers



Risk of MTCT from HBsAg(+) HBeAg(-) mothers



Keane E, Funk AL, Shimakawa Y. Aliment Pharamacol Ther, 2016

Determinants of frequency of MTCT

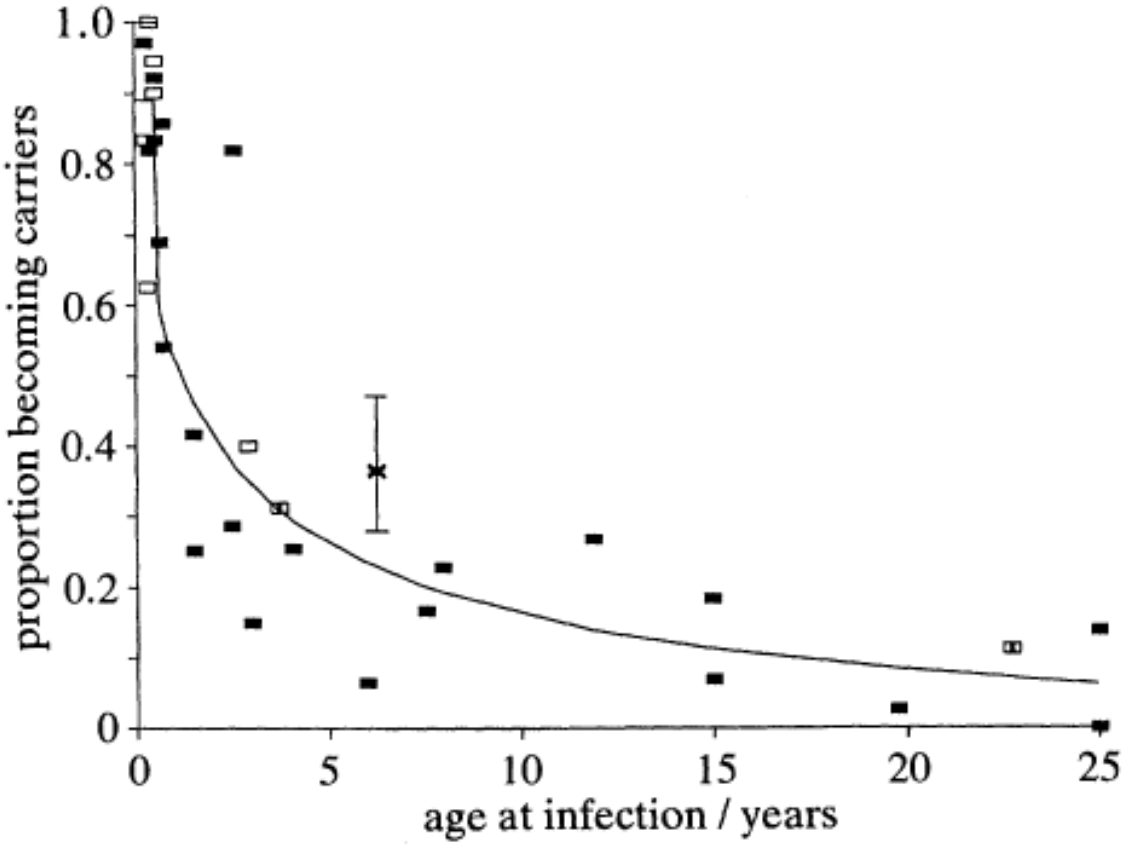
	East Asia	Sub-Saharan Africa
% pregnant women with positive HBsAg	10%	10%
% pregnant women with positive HBeAg	40%	10%
Risk of MTCT from HBsAg+/HBeAg+ women	70-90% ⟷	38%
Risk of MTCT from HBsAg+/HBeAg- women	5-30% ⟷	5%

Keane E, Funk AL, Shimakawa Y. Aliment Pharamacol Ther, 2016

Compared to Asia, the frequency of MTCT in sub-Saharan Africa was low.

However, its prevention is still important in Africa for two reasons.

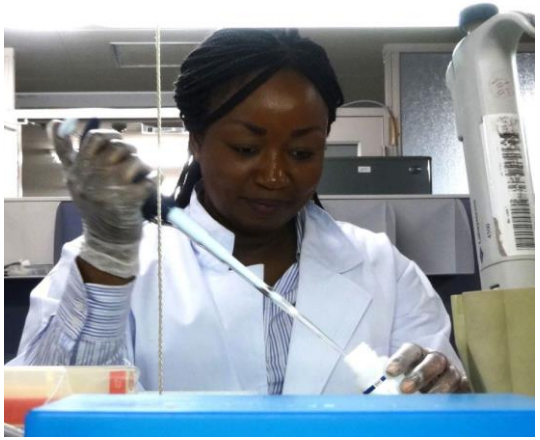
1. Risk factor for chronic infection



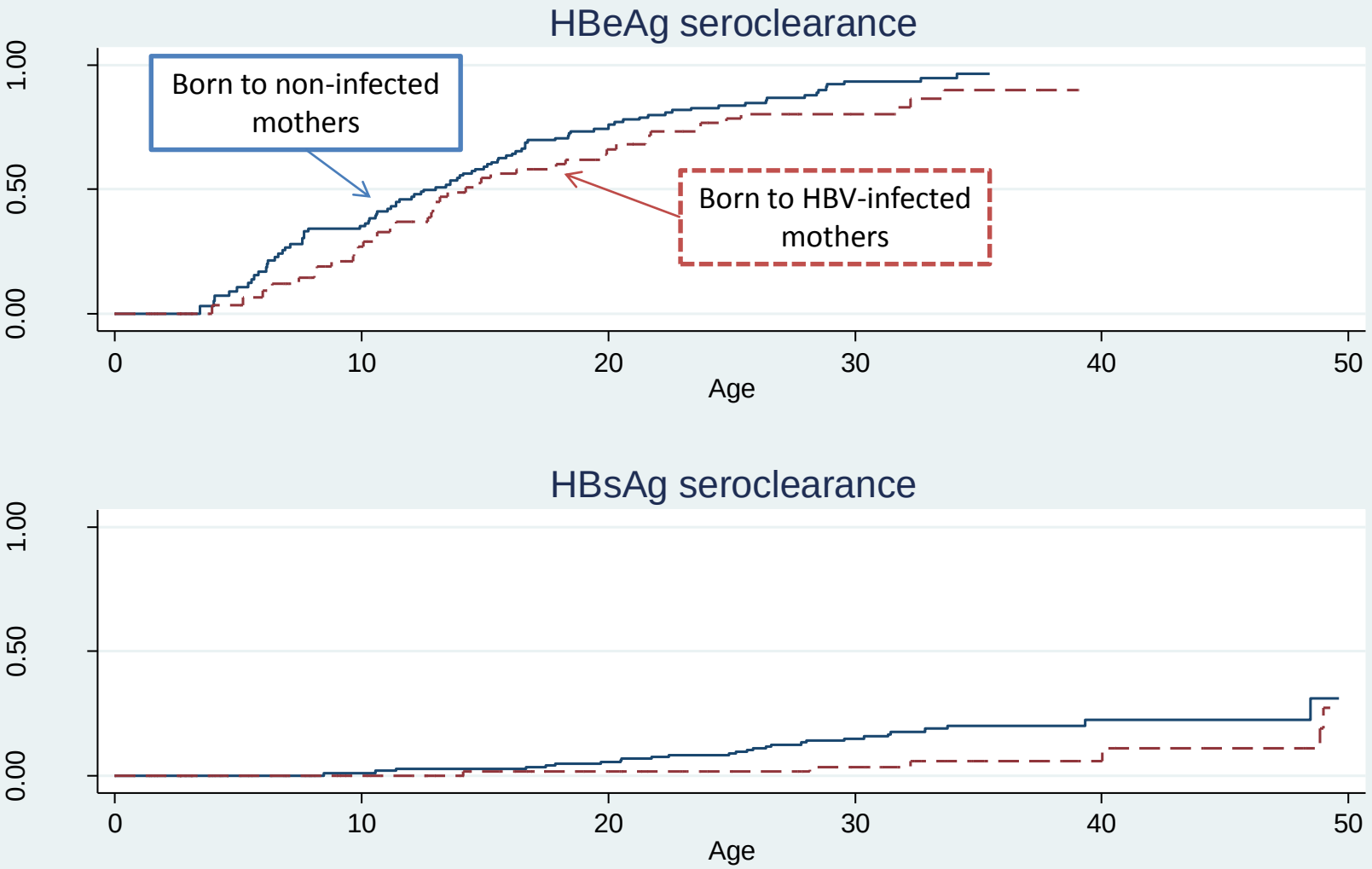
Edmunds WJ et al., Proc R Soc Lond B, 1993

2. Risk factor for Liver Disease

- Longitudinal population-based study in The Gambia
- People with chronic HBV infection
  - 88 born to HBV-infected mothers
  - 165 born to non-infected mothers
- After 28 years of follow-up



Cumulative incidence of seroclearance by maternal HBsAg



Shimakawa Y et al., Gut, 2016

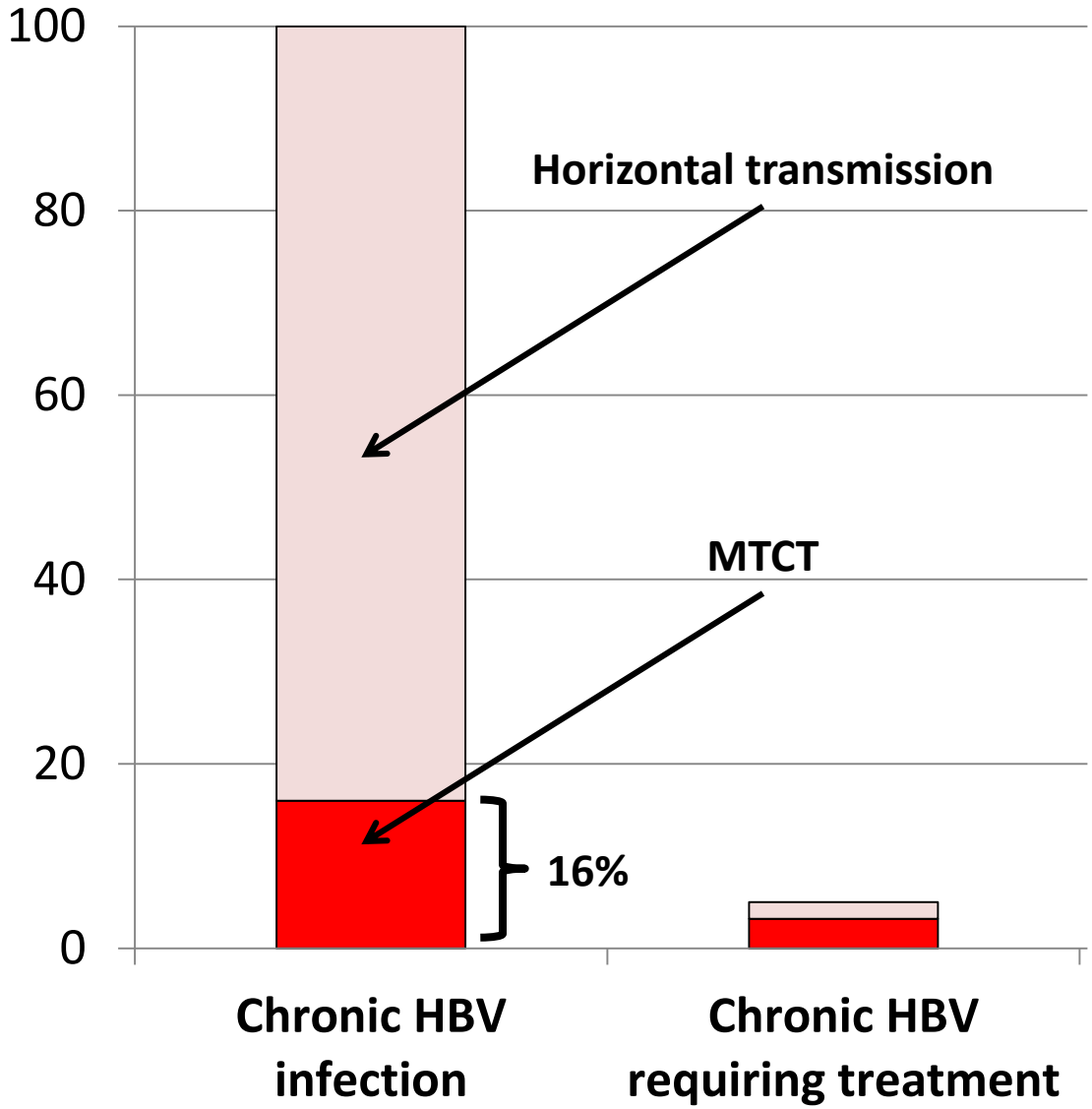
Incidence of liver cancer

Maternal HBV status	Person-years at risk	No. of events	Rate	95% CI
Negative	4 720	0	0 / 100 000	N/A
Positive	2240	2	89 / 100 000	22-356

Prevalence of significant liver fibrosis

Maternal HBV status	Proportion	Adjusted OR	95% CI	p
Negative	4%	1.0		
Positive	15%	5.0	1.6-15.4	<0.01

Shimakawa Y et al., Gut, 2016



Shimakawa Y et al., Gut, 2016

Shimakawa Y et al., Lancet Infect Dis, 2016

It is critical to prevent HBV MTCT in Africa to achieve the WHO's global elimination strategy to reduce:

- **Incidence of new chronic infection**
- **Mortality from chronic infection**

HBV MTCT IS A NEGLECTED PROBLEM IN AFRICA

Hepatitis B vaccine

- Integrated in the national program in all the African countries
- Coverage in Africa: 76% WHO, Wkly Epidemiol Rec, 2016
- As a combined vaccine: 6-10-14 wks
  - Pentavalent (DTaP-Hib-HepB)
  - Hexavalent (DTaP-Hib-IPV-HepB)
- Vaccine failure: 1%
  - Majority (60-90%) are due to MTCT before the vaccine was given

Ekra D et al., Vaccine, 2008
Mendy M et al., Plos One, 2013
Shimakawa Y et al., Gut, 2016

Only 10 countries in sub-Saharan Africa adopted birth dose vaccine

UNICEF/WHO, 2016

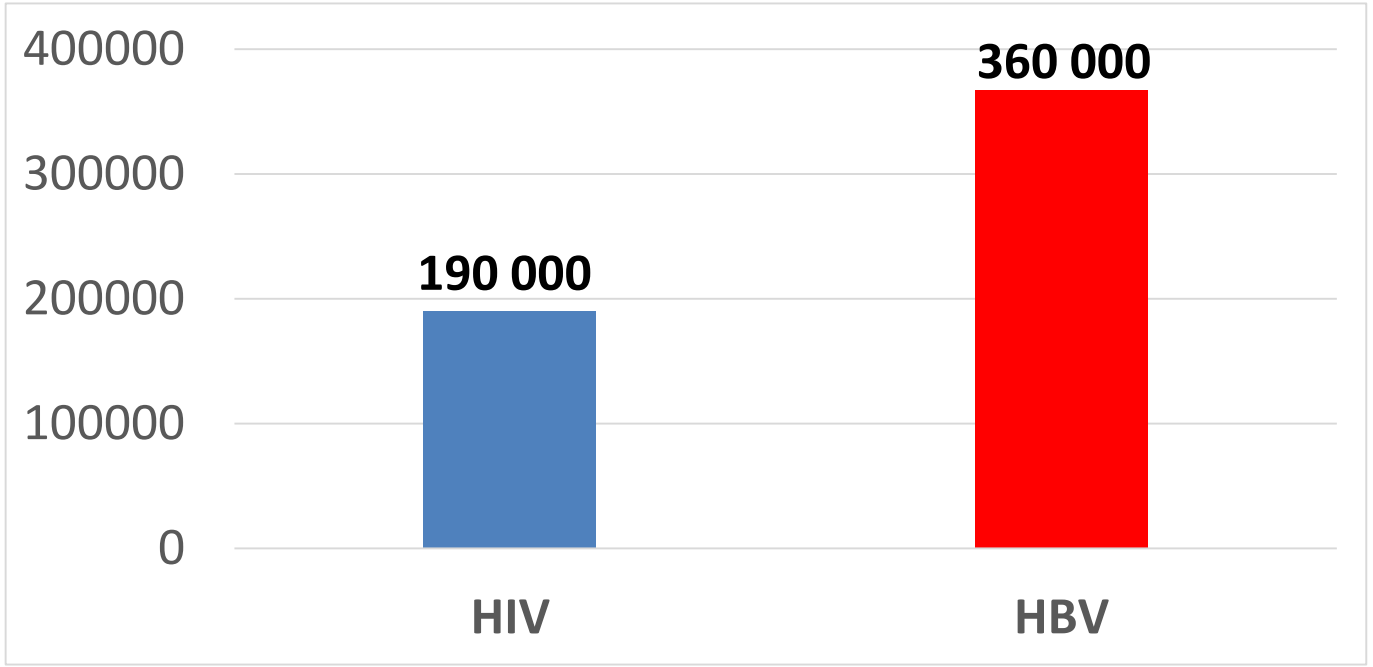
Why?

- GAVI does not support monovalent hep B vaccine
- Importance of HBV PMTCT has been poorly recognized
- Logistical challenges where the majority of women deliver their children at home

Kramvis A & Clements CJ, Vaccine, 2010
Shimakawa Y et al., BMC Public Health, 2014
Shimakawa Y et al., Gut, 2016

MTCT in sub-Saharan Africa
HBV > HIV

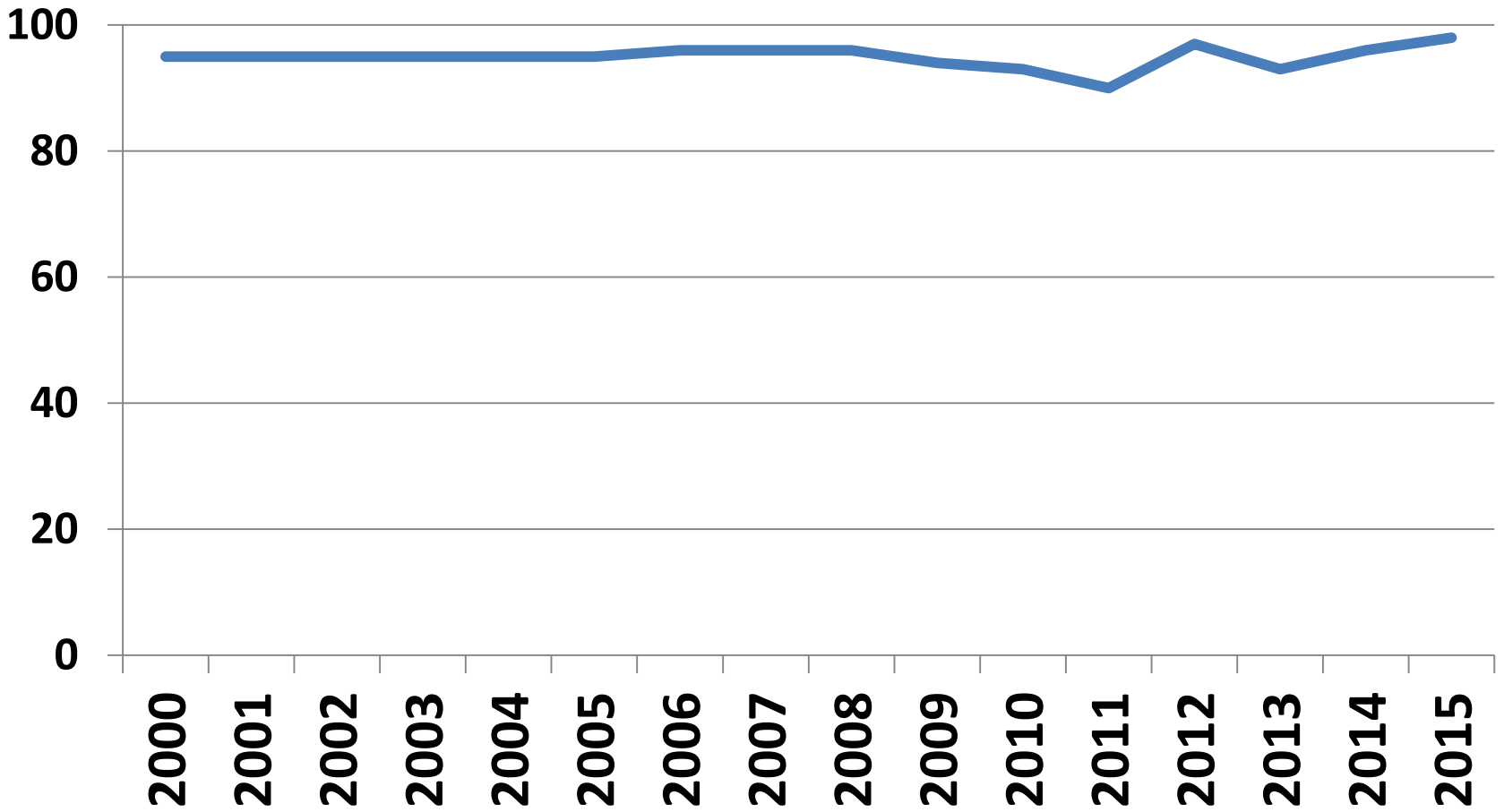
- Estimated number of infants infected in sub-Saharan Africa each year



Keane E, Funk AL, Shimakawa Y, Aliment Pharmacol Ther, 2016

BARRIERS TO TIMELY ADMINISTRATION OF BIRTH DOSE

Birth dose vaccine coverage
The Gambia (WHO/UNICEF)

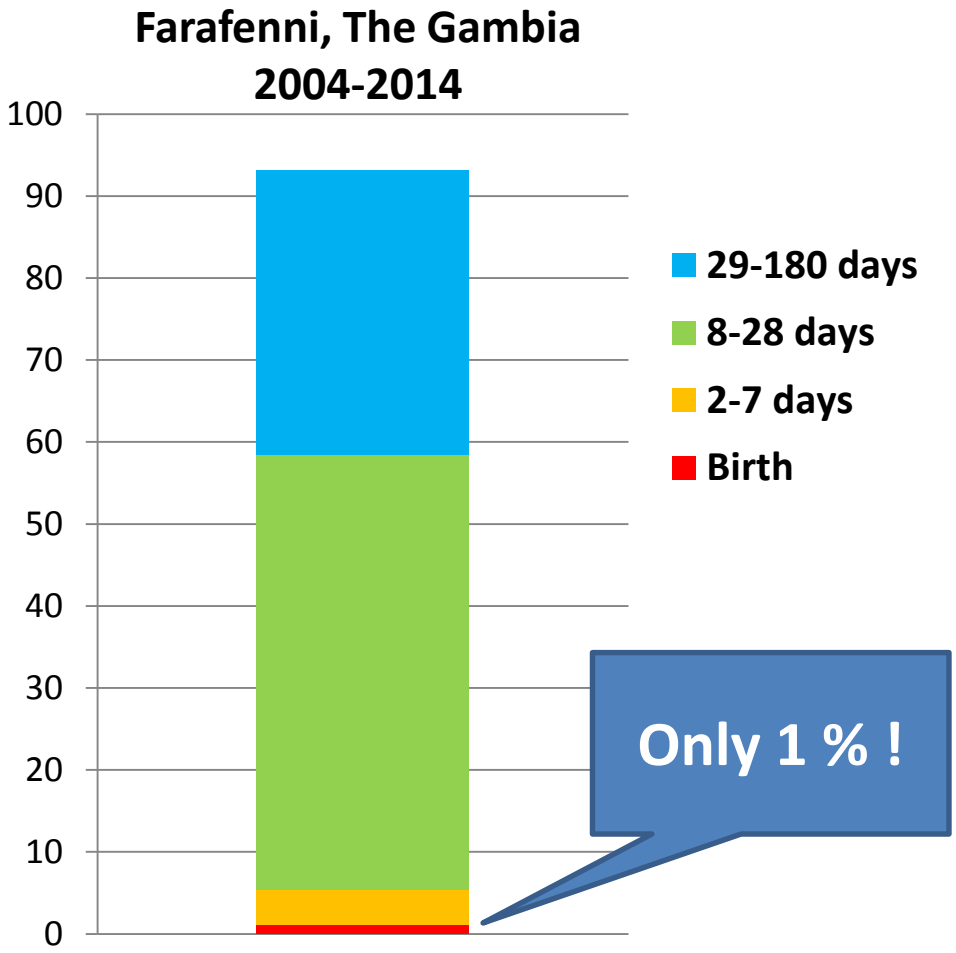


Barriers to timely administration of birth dose vaccines in The Gambia, West Africa

Vaccine 34 (2016) 3335–3341

Reiko Miyahara[a,b,c], Momodou Jasseh[a], Pierre Gomez[a], Yusuke Shimakawa[d],

- Only 1% are vaccinated at birth
  - Home birth 1.3%
  - Facility birth 0.6%



Low coverage even in facility-birth

- Hospital
  - No hep B vaccine (as there is no EPI team)
- Health Centers
  - There are vaccines, but no communication between maternity staff & EPI staff (two vertical programs)
- Reluctance of EPI staff to open multi-dose vial (10 doses/vial)
  - Although opened vial can be used for 28 days under the cold chain

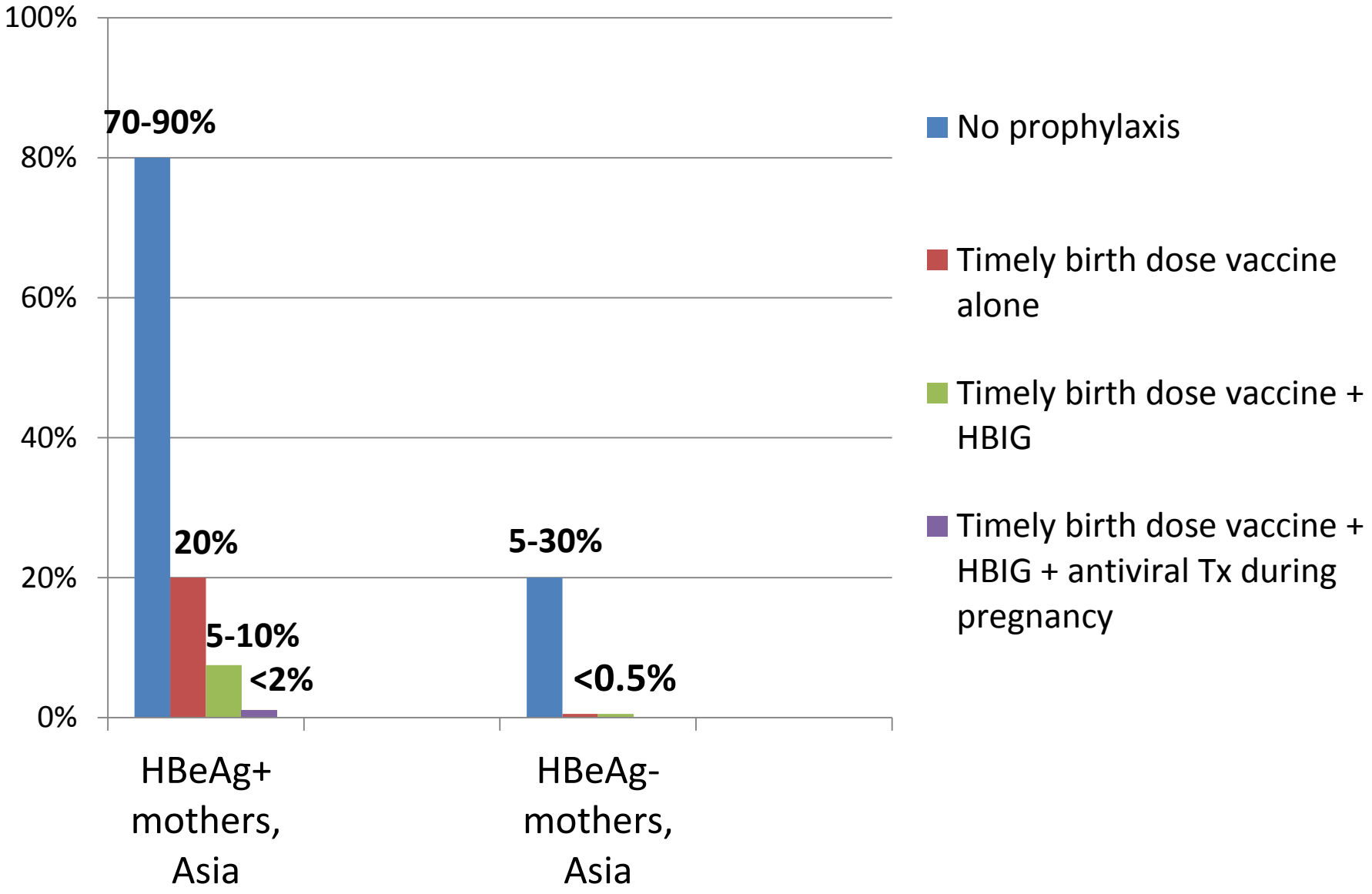
Miyahara R, et al., Vaccine, 2016
WHO, 2014

NéoVac

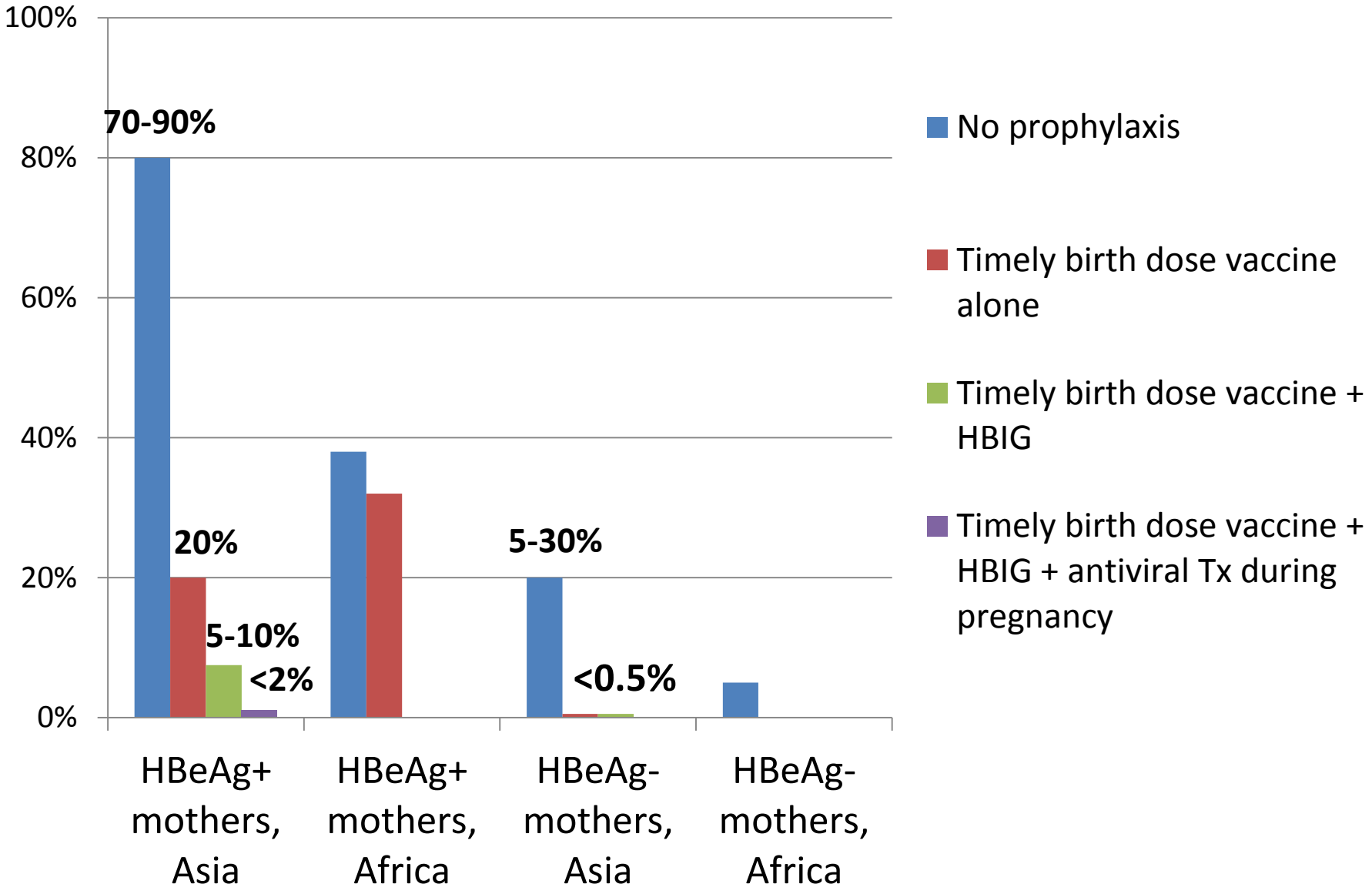
Neonatal Vaccination Against Hepatitis B in Africa

- To develop and evaluate a **community-based intervention** to improve the coverage of:
  - A timely birth dose of Hep B vaccine
  - Neonatal care practices that can improve child survival
- Senegal / Burkina Faso / Madagascar

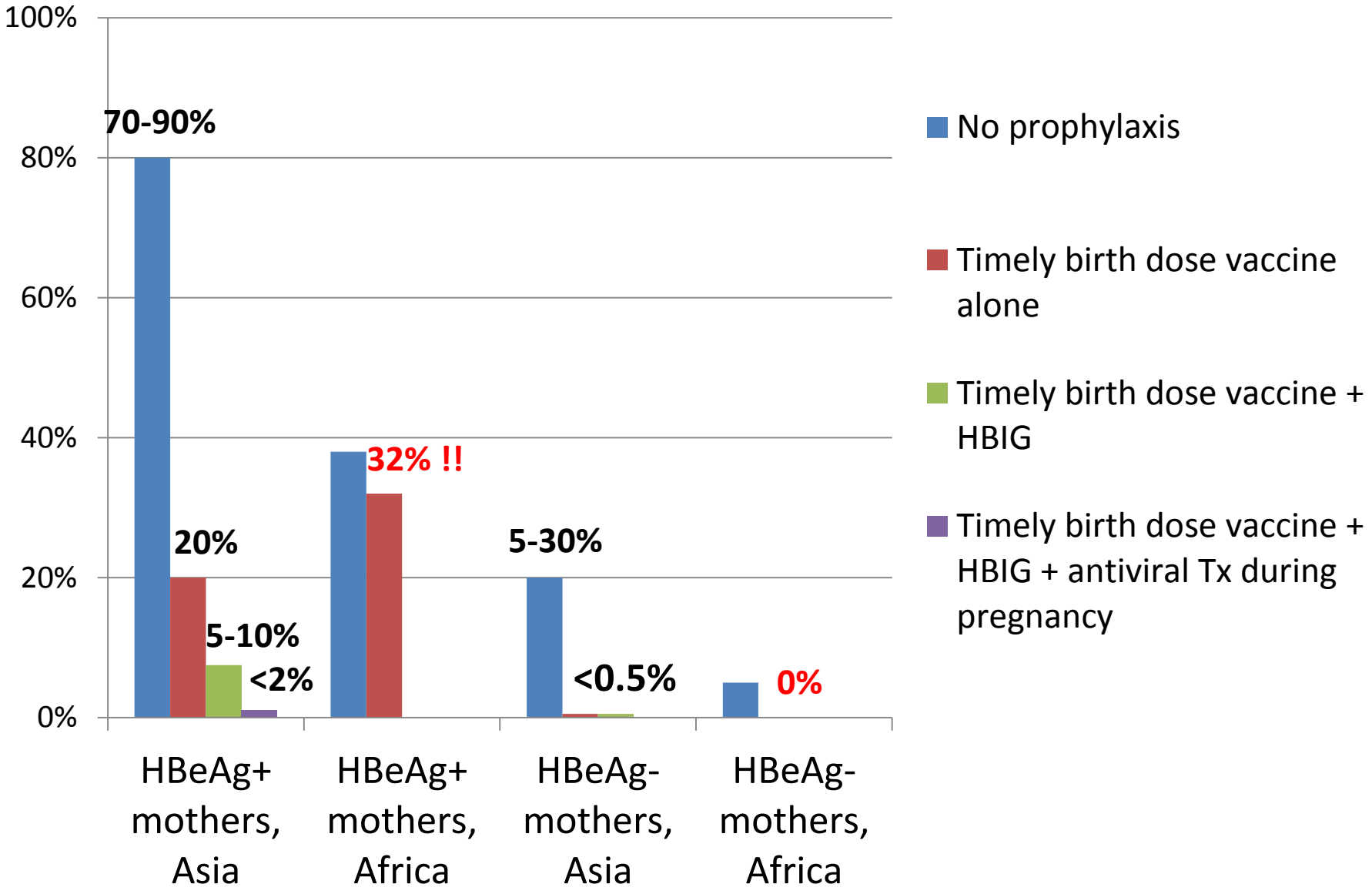
OTHER PREVENTIVE MEASURES



Lee C et al., Cochrane Database Syst Rev, 2006
Machaira M et al., J Antimicrob Chemother, 2015
Pan CQ et al., New Engl J Med, 2016
Keane E, Funk AL, Shimakawa Y. Aliment Pharamacol Ther, 2016



Lee C et al., Cochrane Database Syst Rev, 2006
Machaira M et al., J Antimicrob Chemother, 2015
Pan CQ et al., New Engl J Med, 2016
Keane E, Funk AL, Shimakawa Y. Aliment Pharamacol Ther, 2016



Lee C et al., Cochrane Database Syst Rev, 2006
Machaira M et al., J Antimicrob Chemother, 2015
Pan CQ et al., New Engl J Med, 2016
Keane E, Funk AL, Shimakawa Y. Aliment Pharamacol Ther, 2016

Need for additional preventive measures

- Hepatitis B immunoglobulin (HBIG)
  - Not practical in Africa
  - Cost / limited supply / safety
- Antiviral treatment during pregnancy
  - Atractive for Africa
    - % women delivering baby at health facilities: 50%
    - % women attending at least one ANC: 78%
  - Generalizability of Asian studies to African context
    - BD + HBIG + Antiviral Tx

UNICEF, 2016

Conclusions

- MTCT is less frequent in Africa than in Asia
- But, MTCT is responsible for 2/3 of HBV-related liver disease in Africa
- Birth dose vaccine is not well implemented
- Additional intervention may be necessary for those born to HBeAg(+) mothers
- Need for African model?
  - Antiviral Tx + birth dose vaccine
  - Antiviral Tx alone (without birth dose vaccine)

Thank you

- MRC Unit, The Gambia
  - Dr. Ramou Njie
  - Dr. Harr Njie
  - Dr. Gibril Ndow
  - Prof. Umberto D'Alessandro
- Imperial College, London
  - Dr. Maud Lemoine
  - Dr. Shevanthi Nayagam
  - Prof. Mark Thursz
- LSHTM
  - Dr. Christian Bottomley
  - Prof. Hilton Whittle
  - Sir Andrew Hall
- IARC/GHIS
  - Dr. Maimuna Mendy
- Inserm
  - Dr. Isabelle Chemin
- Gambia Government
  - Dr. Makie Taal
  - Mr. Bakary Sanneh
- Institut Pasteur, Paris
  - Dr. Tamara Giles-Vernick
  - Dr. Elizabeth Keane
  - Ms. Anna Funk
  - Prof. Arnaud Fontanet
- Institut Pasteur de Dakar
  - Dr. Muriel Vray
- IRD, Dakar
  - Dr. Cheikh Sokhna
  - Dr. Aldiouma Diallo
  - Dr El-Hadji Ba
- LAMIVAC (AMP & Centre Muraz)
  - Dr. Edouard Betsem
  - Dr. Espérence Ouedraogo
  - Prof. Nicholas Meda
- Institut Pasteur de Madagascar
  - Dr. Soa Fy Andriamandimby
  - Dr. Rila Ratovoson
  - Dr. Dolorès Pourette
- European Union
- Total Foundation