Elimination of Hepatitis B: Is It a Mission Possible

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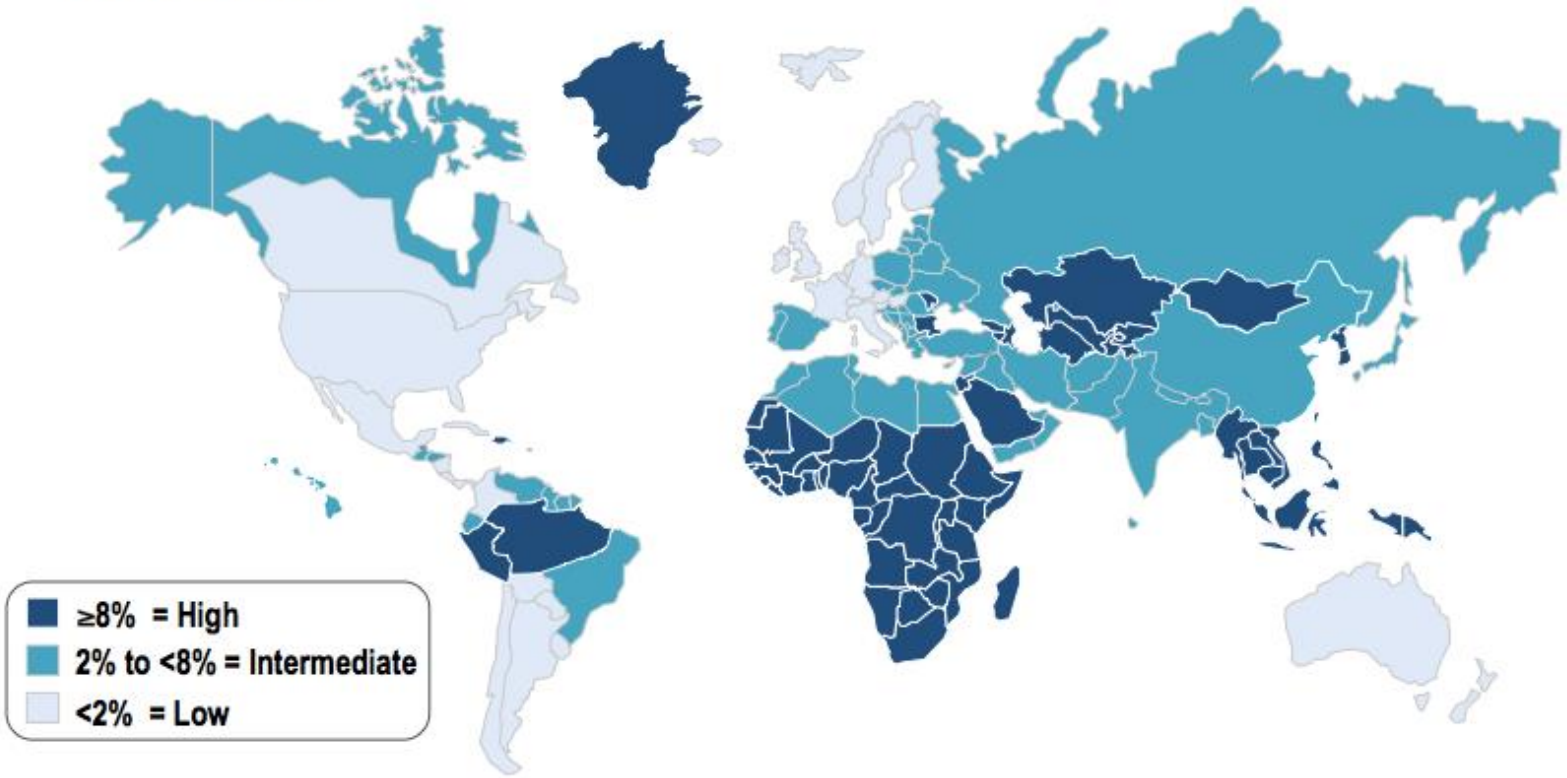
Outline

- Introduction
- Effective primary prevention
- Management of CH-B patients
  - Treatment response of nucleos(t)ide analogue (NUC)
  - New treatment to clear HBsAg (functional cure)
- Conclusions

Chronic hepatitis B (CHB) is a significant health problem

- An estimated 240 million people worldwide are living with CHB[1]

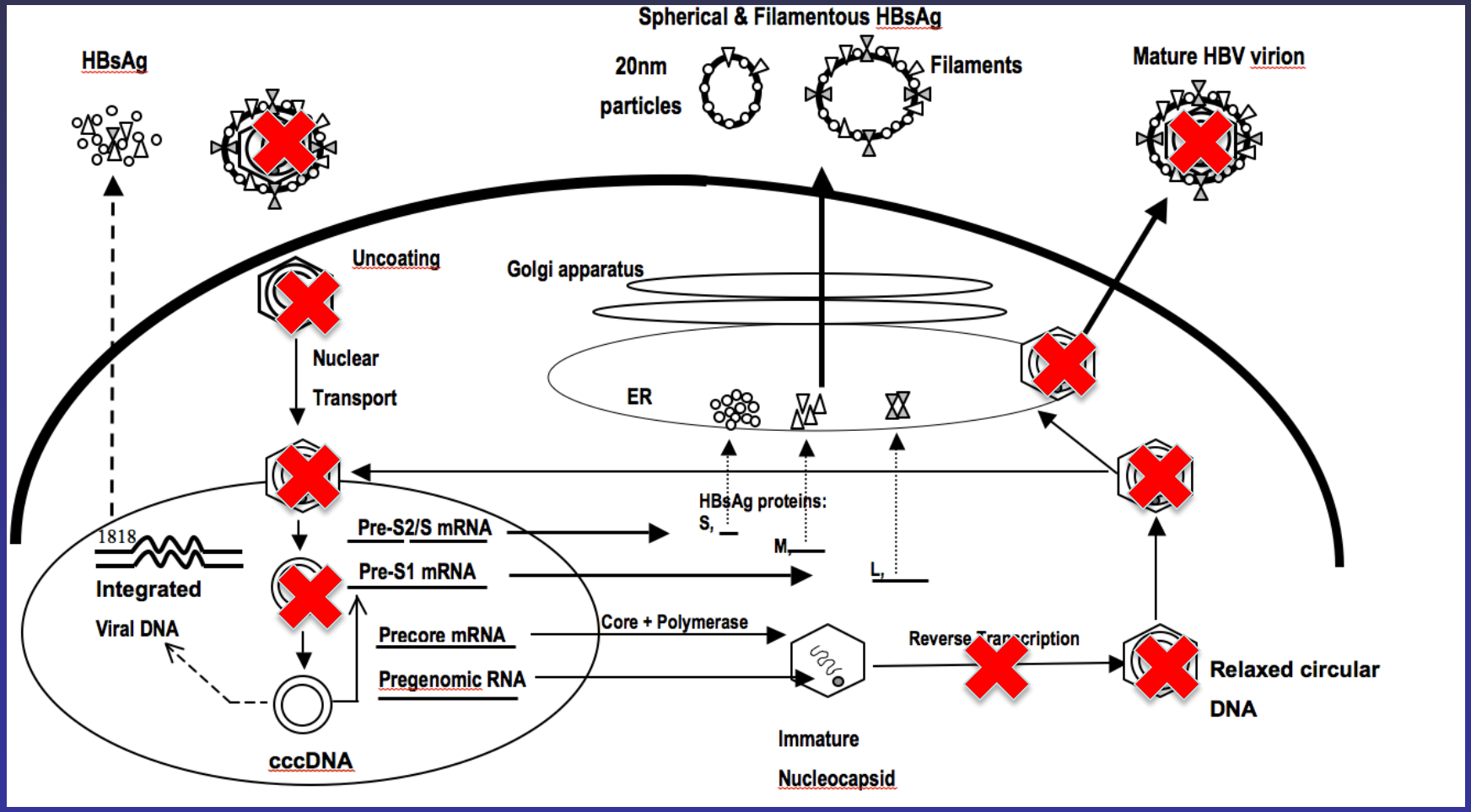


CHB=chronic hepatitis B; HBsAg=hepatitis B surface antigen. Map adapted from CDC

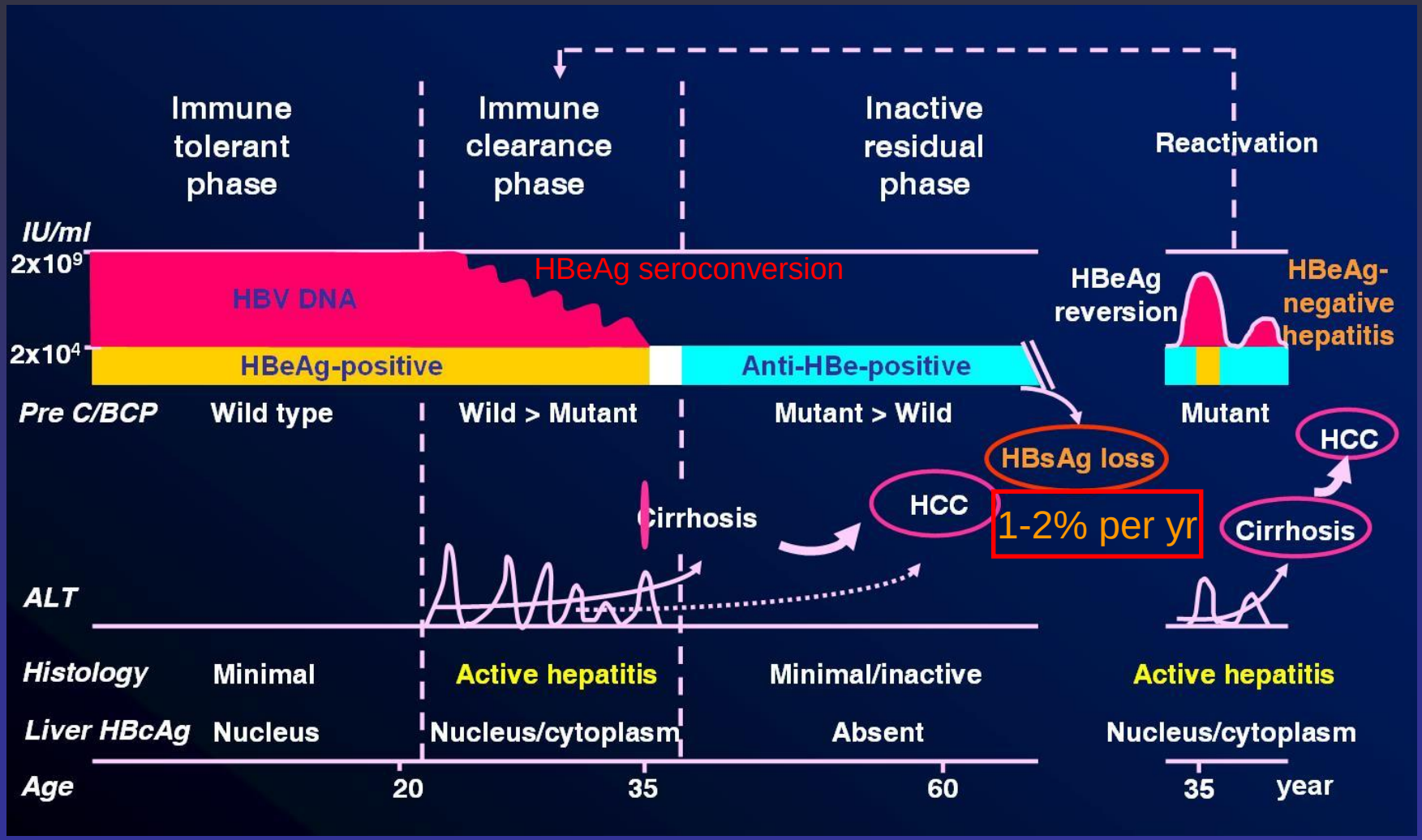
1. WHO. Hepatitis B fact sheet. www.who.int/mediacentre/factsheets/fs204/en/. Updated July 2016. Accessed March 17, 2017; 2. Chen et al. Slow decline of hepatitis B burden in general population. J Hep. 2015.

HBV Replication Cycle

- HBV DNA level
- HBsAg level



Natural History of HBV Carriers



Liaw & Chu. Lancet 2009.

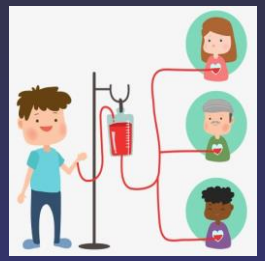
How to Control Chronic Viral Infection

- To prevent new viral infection
- To clear the virus in the patients with chronic infection
  - If not, is it possible to minimize the damage ?

To Prevent New Viral Infection

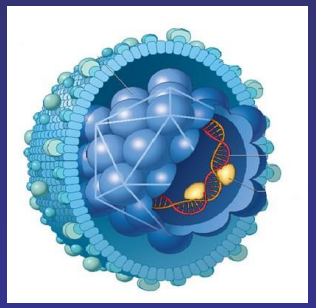
HBV Transmission

Transfusion

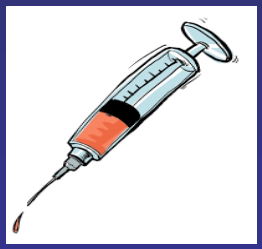


Mother to baby

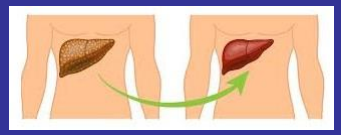
Individuals with multiple sexual partners



Contaminated needle



Organ and tissue transplantation



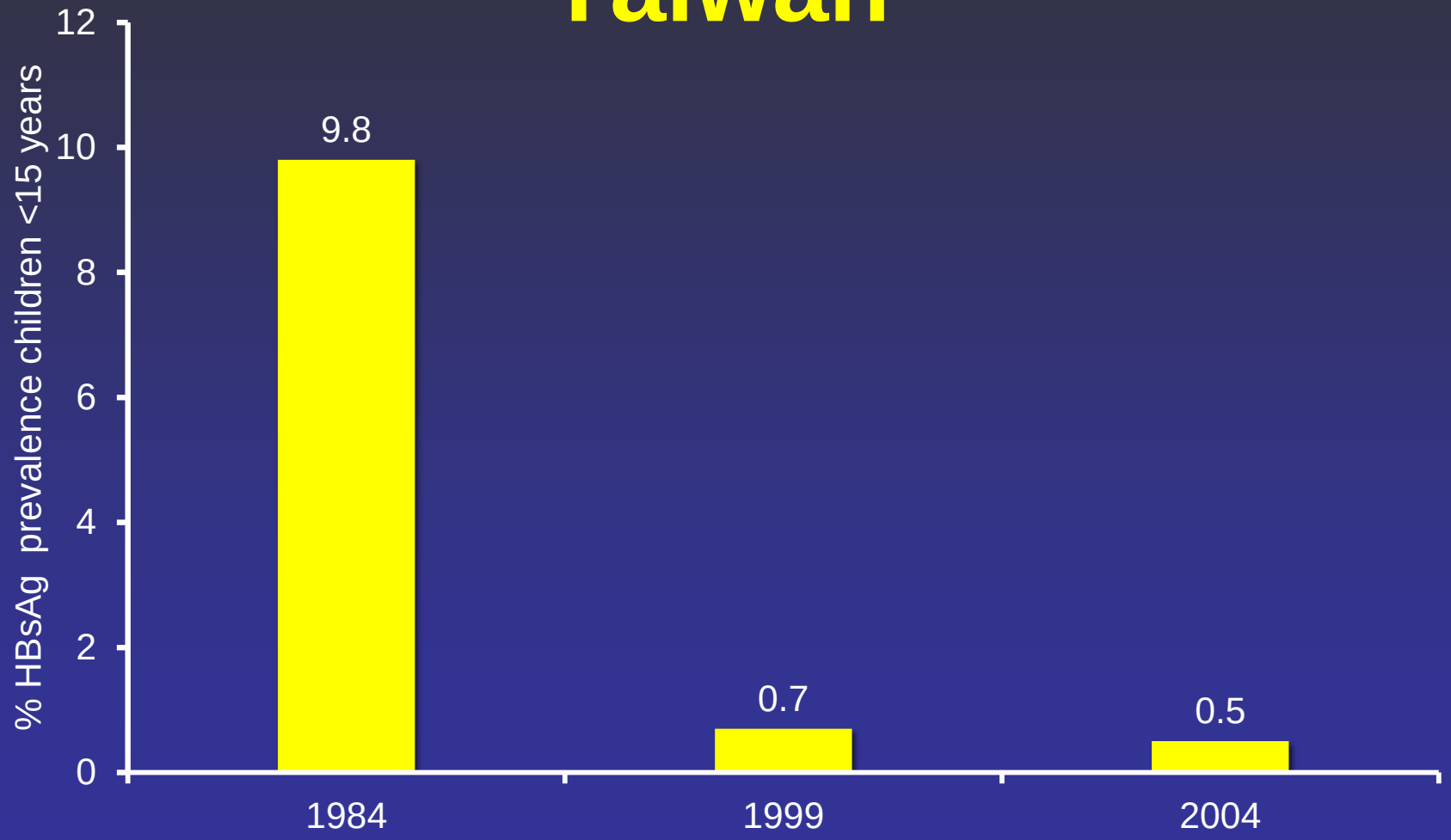
Child to child

HBV is Prevented By Currently Available Safe & Effective Vaccine

- Vaccination is the mainstay of hepatitis B prevention.[1]
- Since 1984, countrywide immunization for newborns in Taiwan
- The vaccine coverage rate is 97%

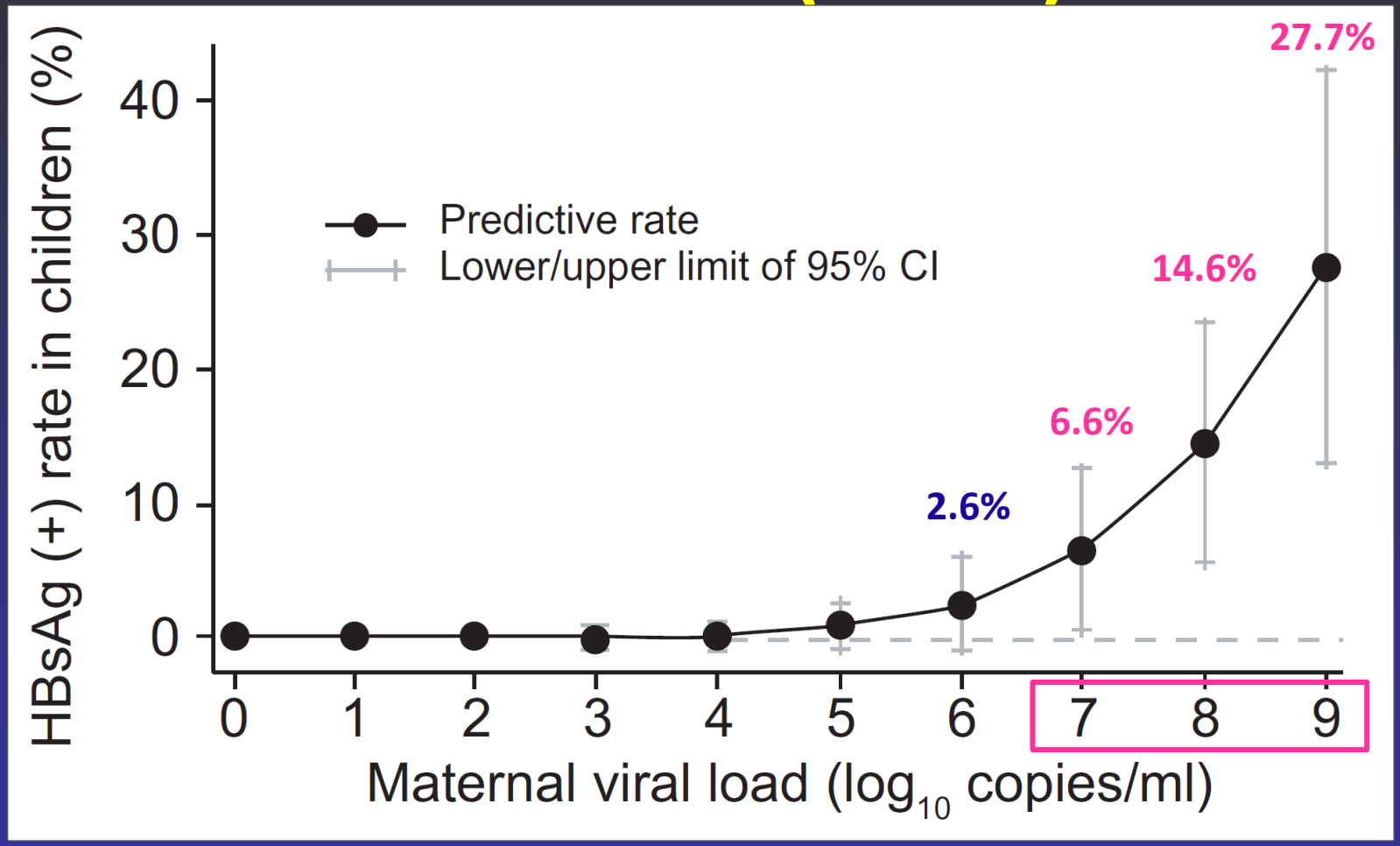
[1]http://www.who.int/mediacentre/factsheets/fs204/en/.

HBsAg Prevalence In Children <15 Years Of Age In Taiwan



Adapted from: Ni YH, et al. Gastroenterology 2007;132:1287–1293: Sarin S, et al. Hepatol Int 2016; 10:1–98.

Maternal Viral Load & Mother to Children Transmission (MTCT) rates



Wen et al. J Hepatol 2013;59:24

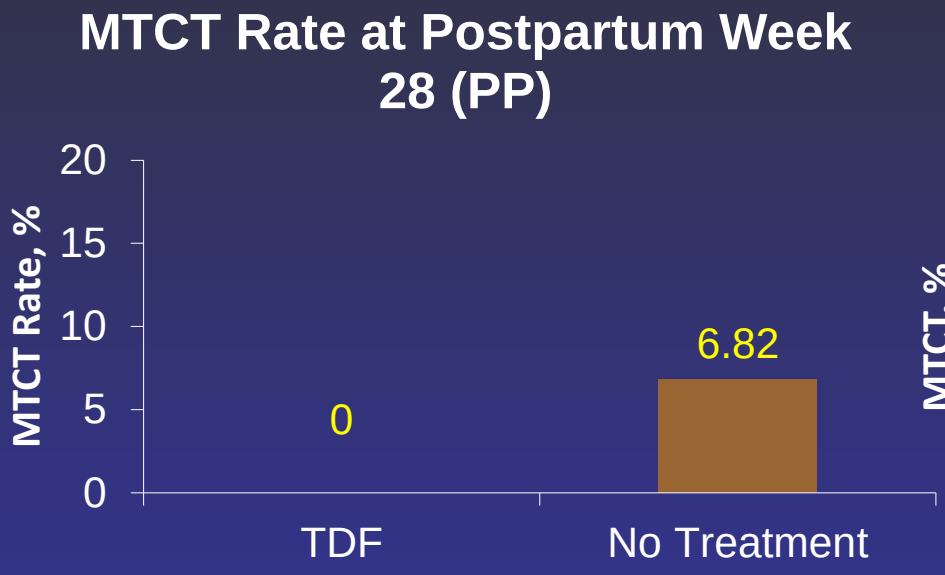
TDF Reduces MTCT of HBV in Highly Viremic Mothers (Taiwan)

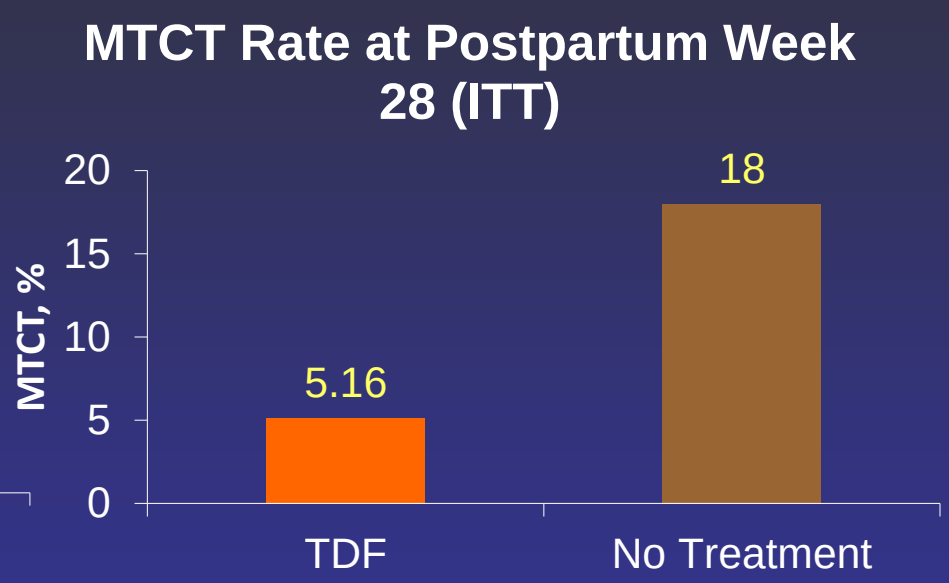
- Prospective, multi-center, non-randomized trial
- 118 HBeAg-positive pregnant women
- All the newborns received HBV vacc + HBIG
- TDF (n=62) from weeks 30-32 of gestation until 1 month post-partum or received no HBV therapy (n=56, control)

	TDF n=62	Control n=56	*p*-value
Infant Outcomes, n/N (%)			
HBV DNA positive at birth	4/65 (6.15)	17/56 (31.48)	0.0003
HBsAg-positive at Month 6	1/65 (1.54%)	6/56 (10.71)	0.0481

Chen HL et al. Hepatology 2015, 62:375-86

TDF Reduces MTCT of HBV in Highly Viremic Mothers (China)





- A RCT enrolling 200 HBeAg-positive pregnant women
- MTCT rate defined as the proportion of **infants with serum HBV DNA >20 IU/mL or HBsAg positivity** at 28 weeks of age.
- Similar safety profile between groups
- No difference in birth defect rates

ITT, intent to treat; MTCT, mother to infant transmission; PP, per protocol

Pan et al. NEJM, 2016; 374:2324-34

TDF May Not Reduce MTCT of HBV in Highly Viremic Mothers (Thailand)

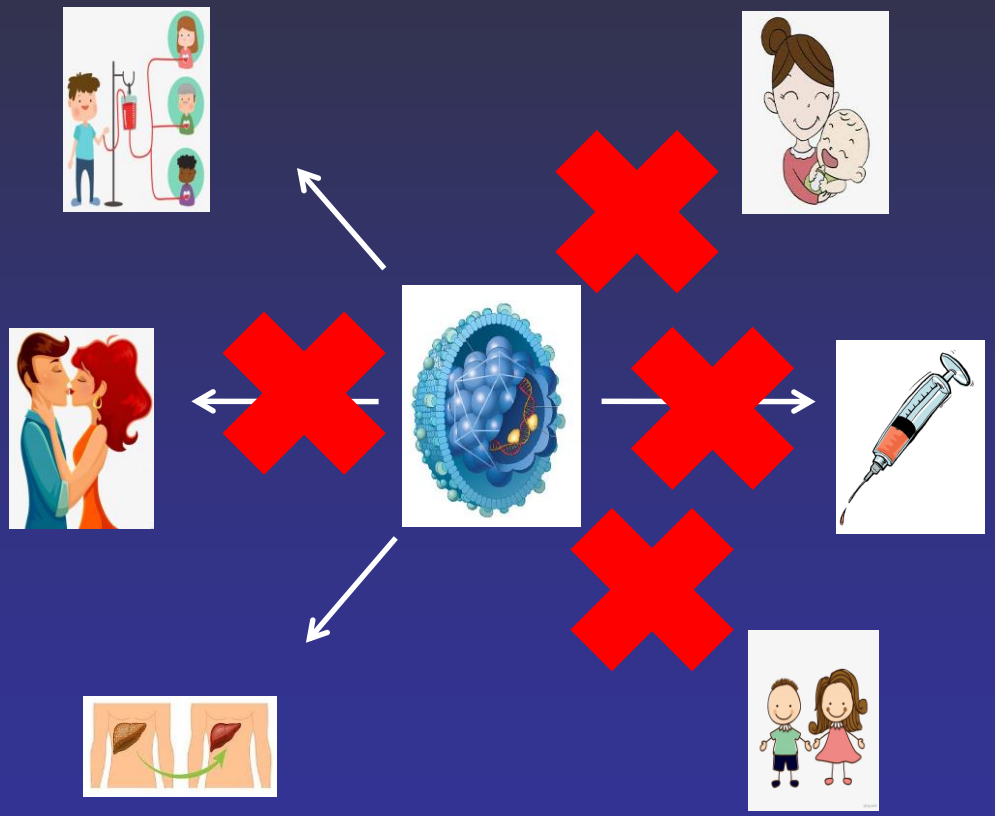
- Prospective, multi-center, randomized trial
- 331 HBeAg-positive pregnant women with CHB
- TDF from 28 weeks of gestation to 2 months post partum vs. Control
- Median time from birth to HBV vacc: 1.2hrs
- Median time from birth to HBIG: 1.3Hrs

	TDF n=147	Control n=147	*p*-value
Infant Outcomes, n/N (%)			
HBsAg-positive at Month 6	0/147 (0%)	3/147 (2%)	0.12

Jourdain et al, NEJM 2018 8;378:911-923

Primary Prevention is Effective

- Timely vaccination
- HBIG
- NUC at the 3rd trimester in highly viremic mother
- Development of Anti-HBs is protective



Management of CHB patients

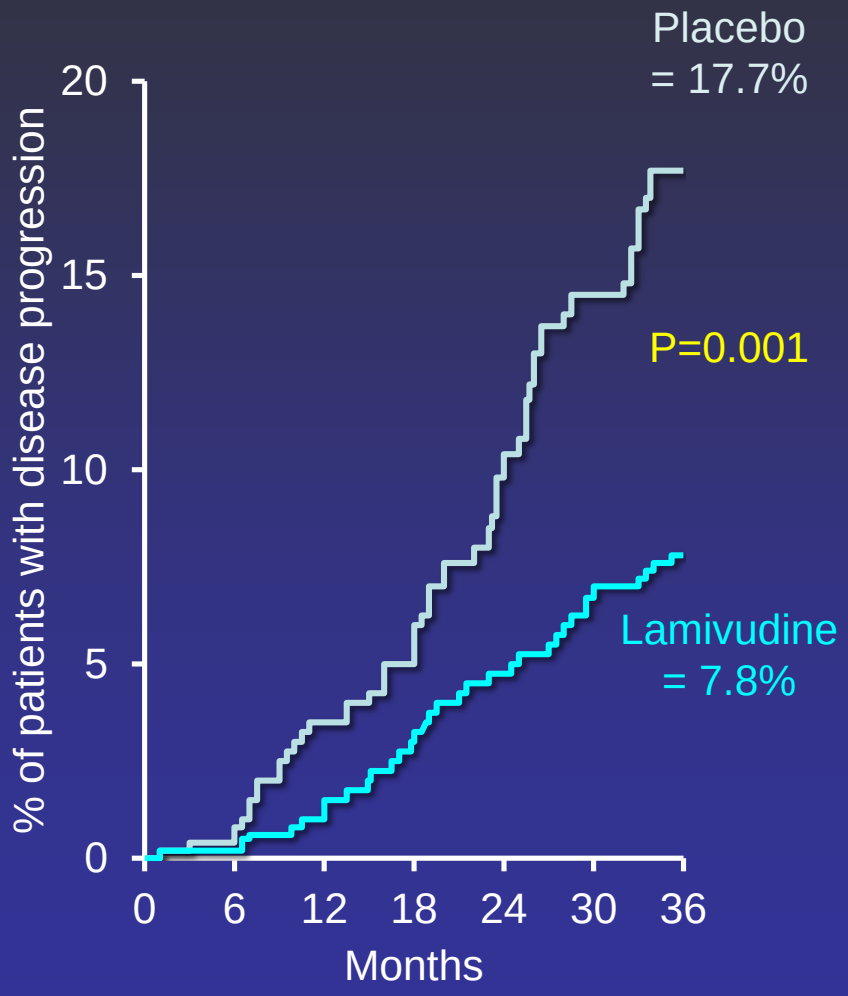
Treatment response of 8 year TDF

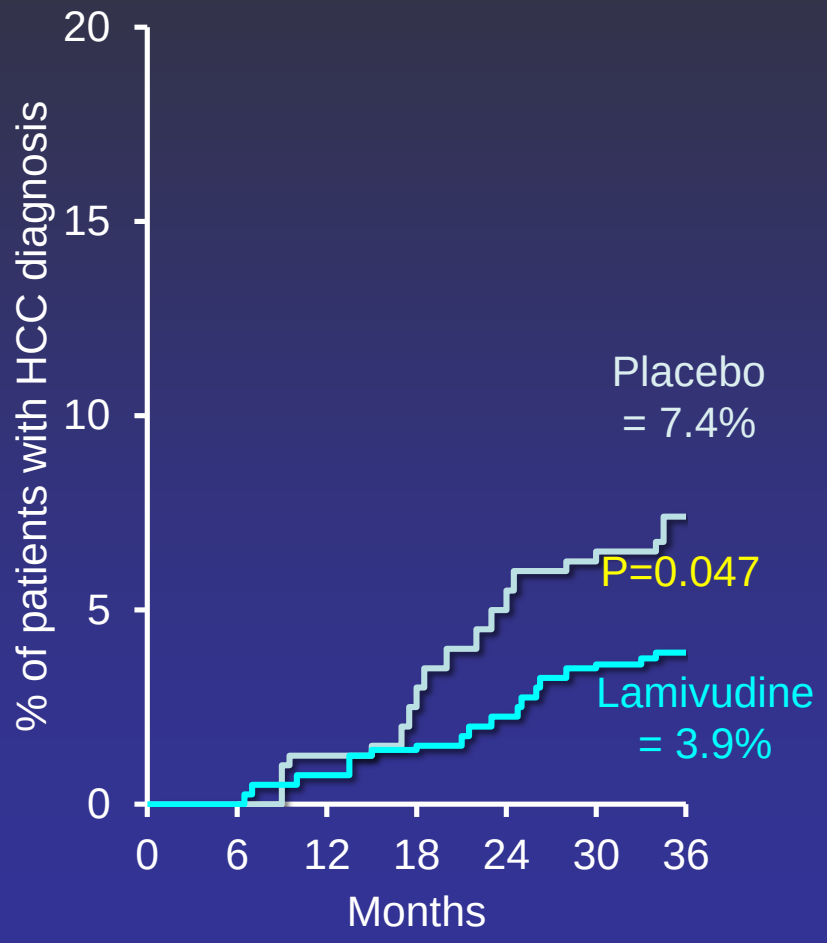
	HBeAg-	HBeAg+
HBV DNA <29 IU/mL (ITT)* %	74	58
HBV DNA <29 IU/mL (Observed), %	99.6	97
HBeAg loss / seroconversion†, %	NA	47/ 31
HBsAg loss[a]/seroconversion (KM%) ‡	1.1/0.7	12.9/10.3

[a]HBsAg loss in Study 102 (HBeAg-): 3 patients; Study 103 (HBeAg+): 28 patients
*Missing = failure; add one OAV not approved for HBV = failure[LTE-TDF])
† Missing = excluded; add one OAV not approved for HBV = included)
‡ KM% = Kaplan-Meier % (KM-ITT)
NA, not applicable

Marcellin, AASLD, 2014, Oral #229

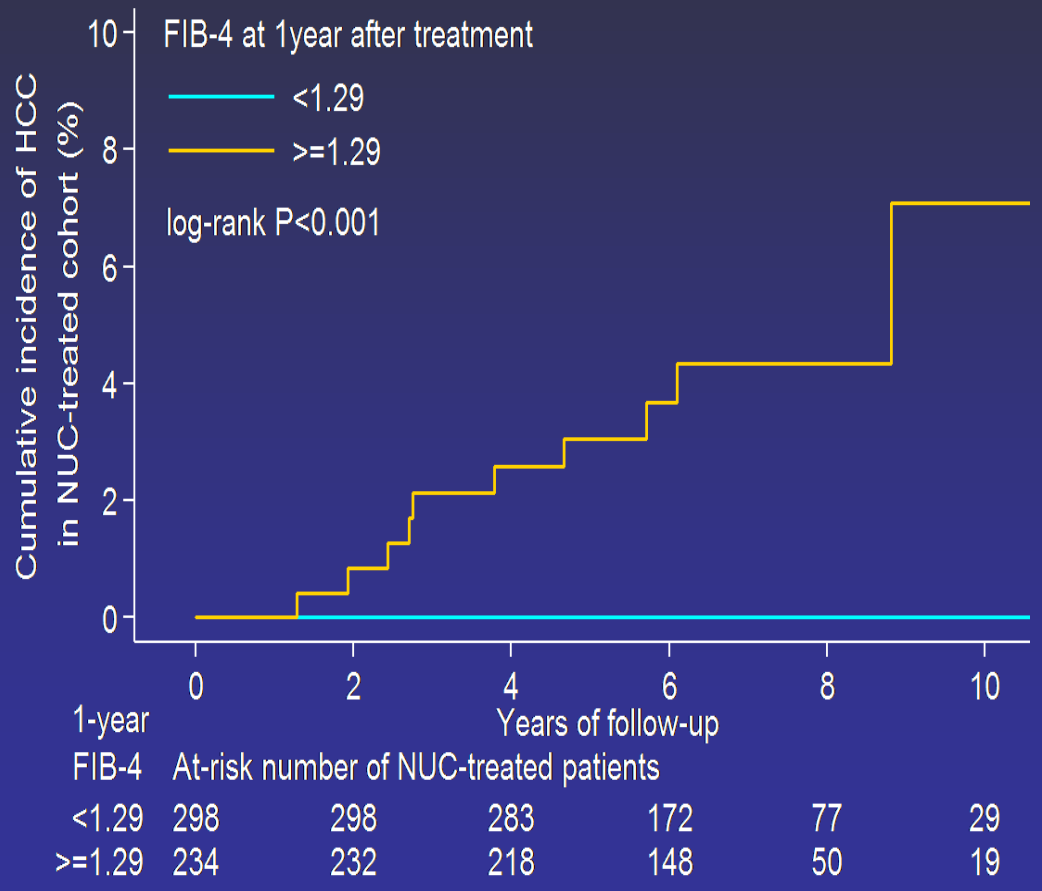
Indefinite NUC Tx Improves Outcomes In CHB Patients With Advanced Fibrosis





Adapted from: Liaw Y-F, et al. *NEJM* 2004;351:1521-31.

FIB-4 <1.29 (F2 marker) Defines Low HCC risk in HBV carriers on Indefinite NUC Tx



Tseng et al Am J Gastroenterol. 2017 112:1564-1574

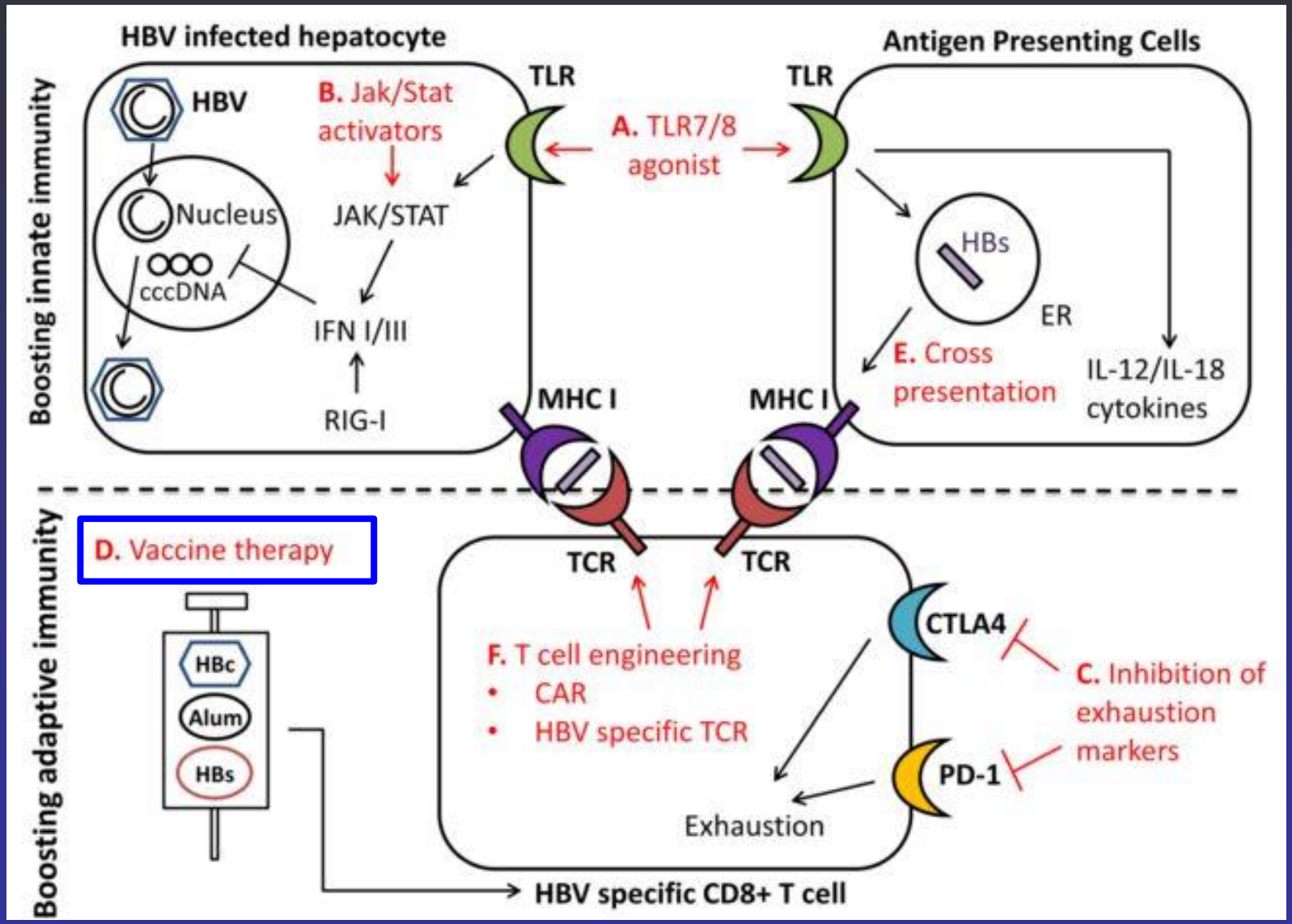
NUC treatment

- NOT effective in clearing HBsAg
- Effective in suppressing viral replication
  - It lowers risks of HCC and disease progression
  - HCC risk could be minimized if initiating NUC earlier

New Treatment to Clear HBsAg?

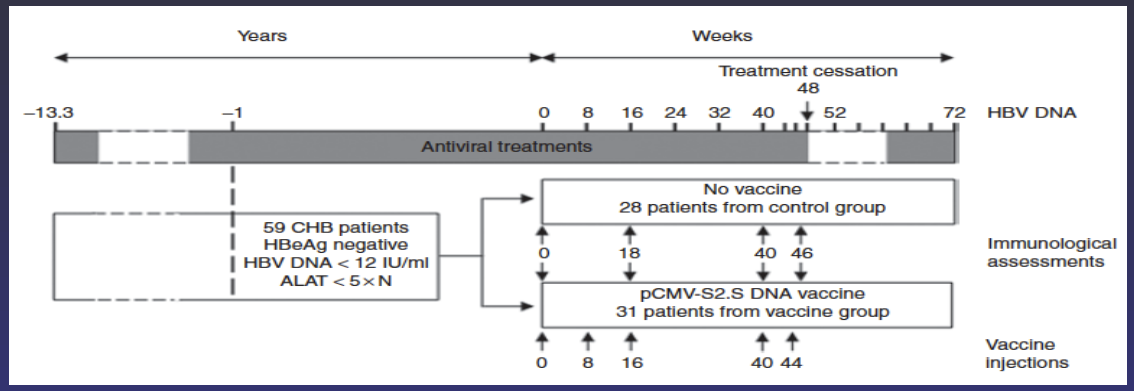
Taking immunotherapy as example

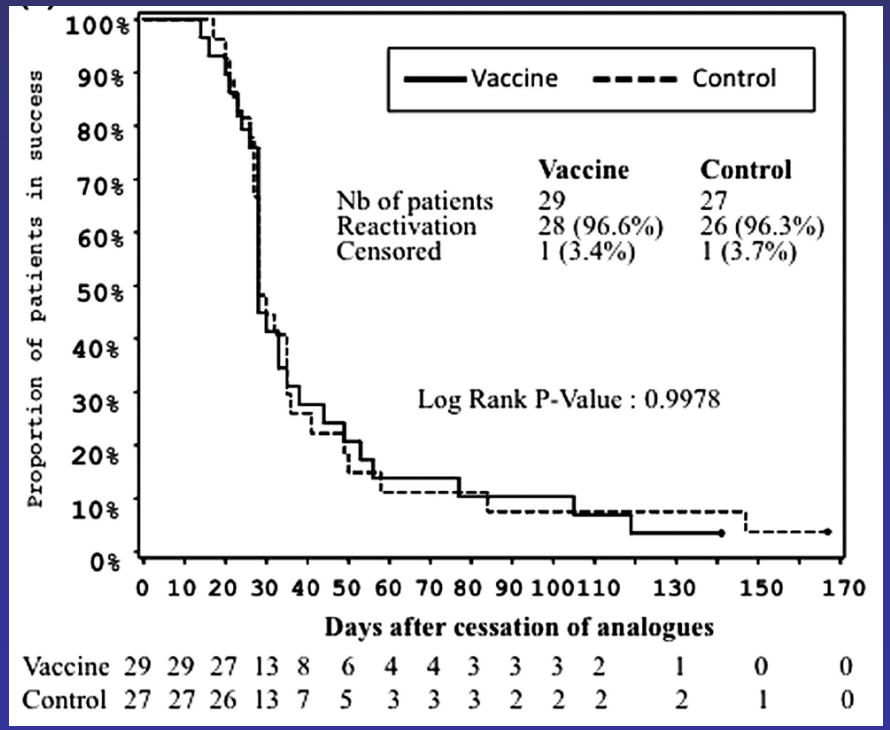
Potential Immunotherapeutic



Yang N & Bertoletti A, Hepatol Int, 2015

A Clinical Trial of HBV Therapeutic DNA Vaccine

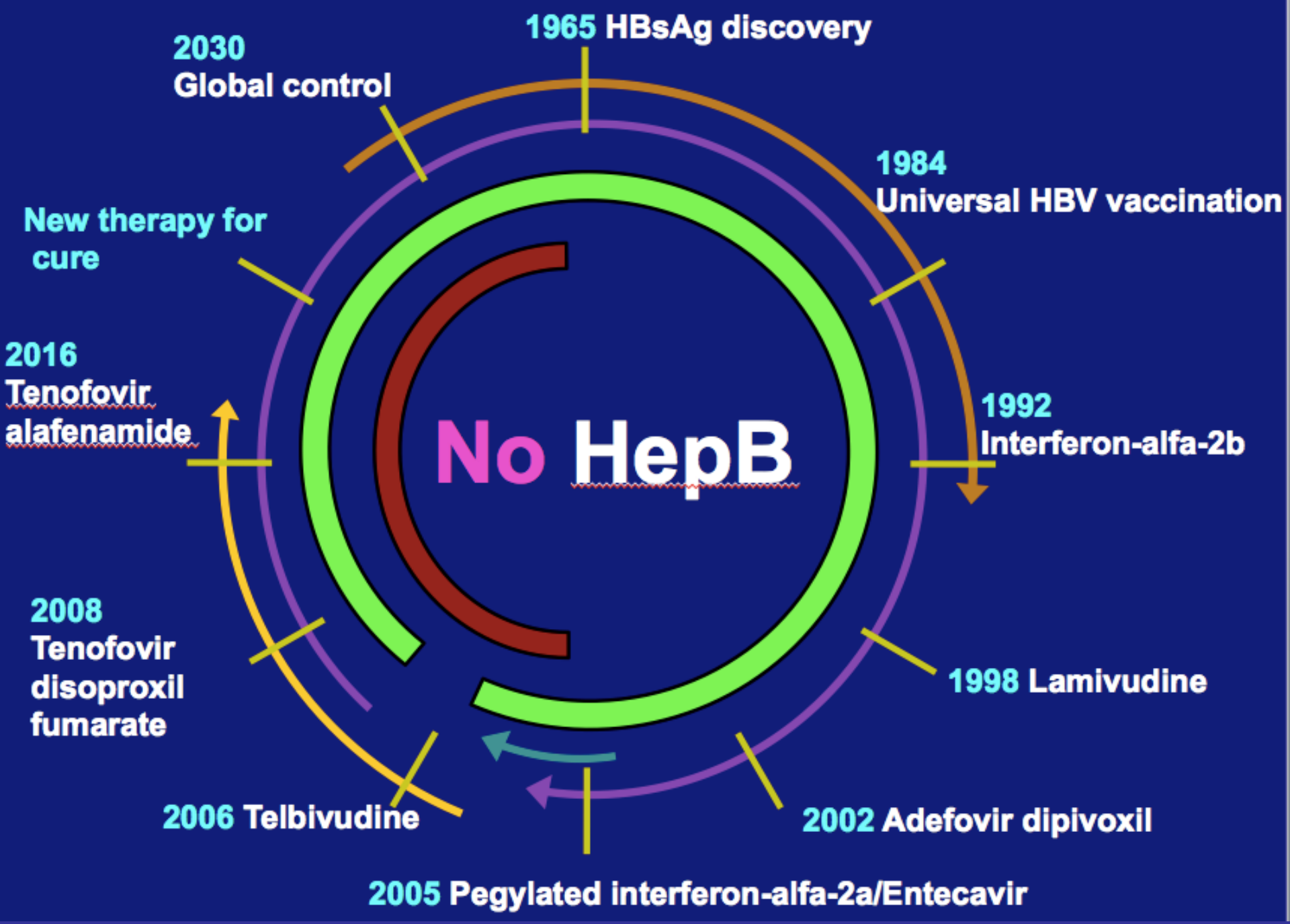




Fontaine H et al. Gut. 2015;64: 139-47

Conclusions

Primary prevention	Early NUC Tx	New Tx to clear HBsAg	When to eliminate HBV	Control of HCC and cirrhosis
✓			80 years later	No
✓	✓		80 years later	Lower the risks
✓	✓	✓	Within decades	Minimize the risks



Kao JH. JID 2017 (cover image)

Taiwan
Formosa, Beautiful Island

Thank You for Your Attention

TAIWAN