Hepatitis for Life

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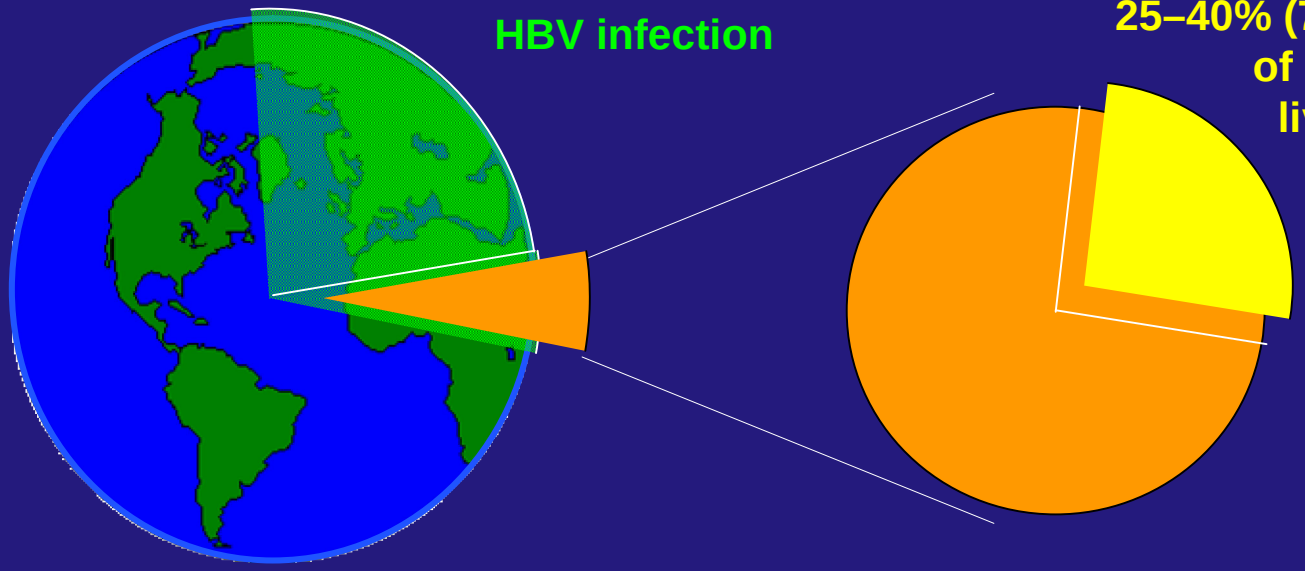
Waikato Hospital

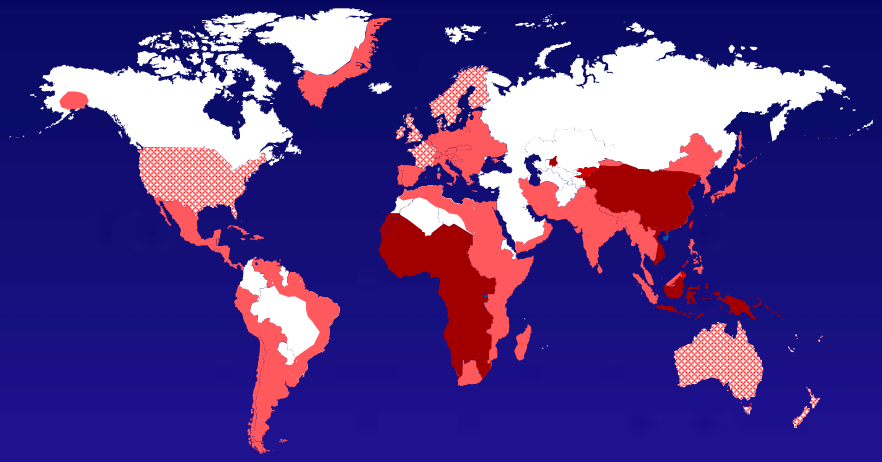
Is HBV a problem?

Global impact of hepatitis B



1. WHO Fact Sheets, available at www.who.int Accessed September 24 2004
2. Conjeevaram et al. *J Hepatology* 2003;38:S90–S103
3.Lee. *N Engl J Med* 1997;337:1733–1745
4. Lok. *N Engl J Med* 2002;346:1682–1683

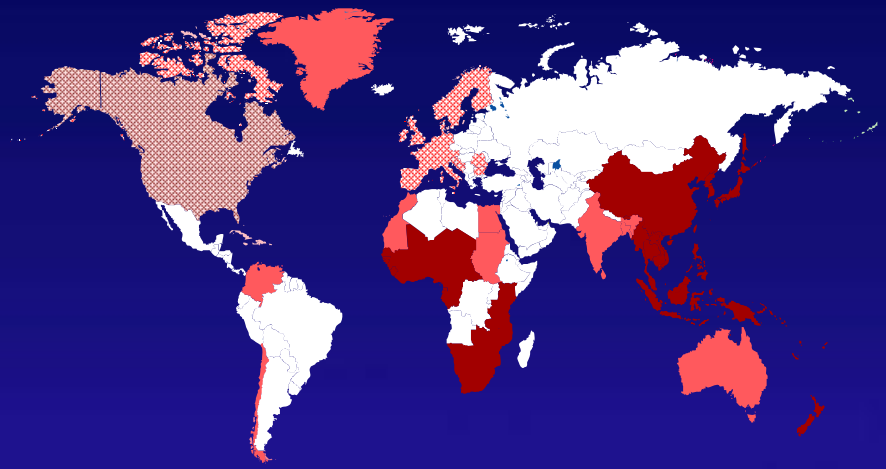
Prevalence of HBV and Incidence of Hepatocellular Carcinoma (HCC)



World prevalence of HBV carriers

HBsAg carriers – prevalence

- **<2%**
- **2–7%**
- **>8%**
- **Poorly documented**



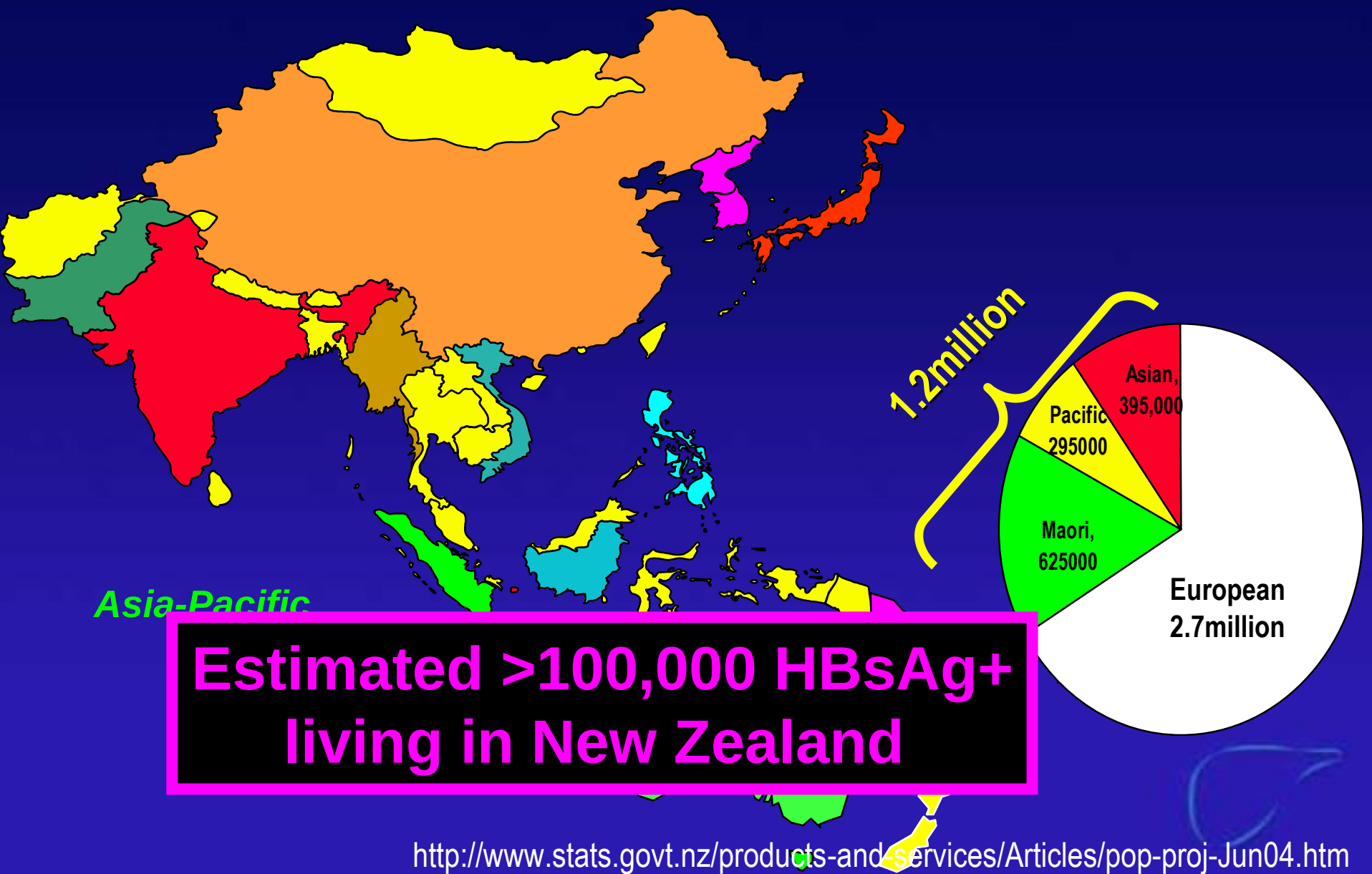
Annual incidence of primary HCC

Cases/100,000 population

- **1–3**
- **3–10**
- **10–150**
- **Poorly documented**

WHO 1999

NZ impact of HBV

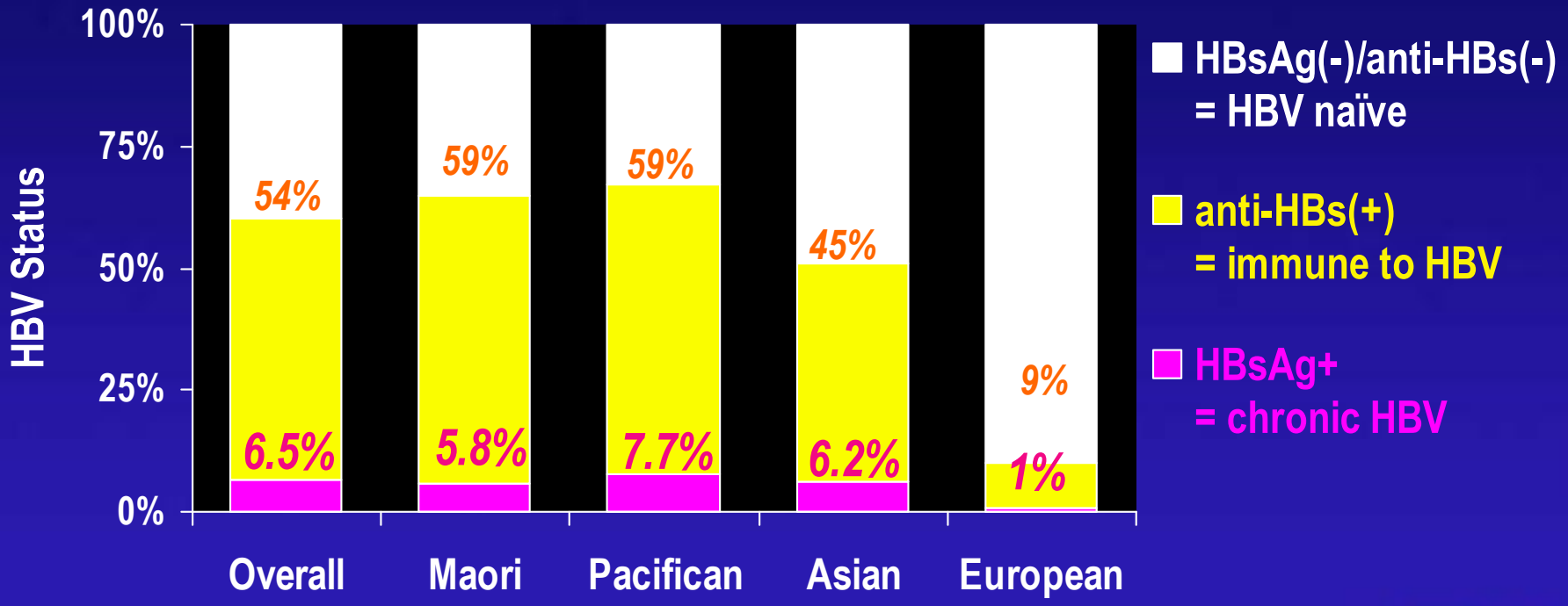


Estimated >100,000 HBsAg+ living in New Zealand

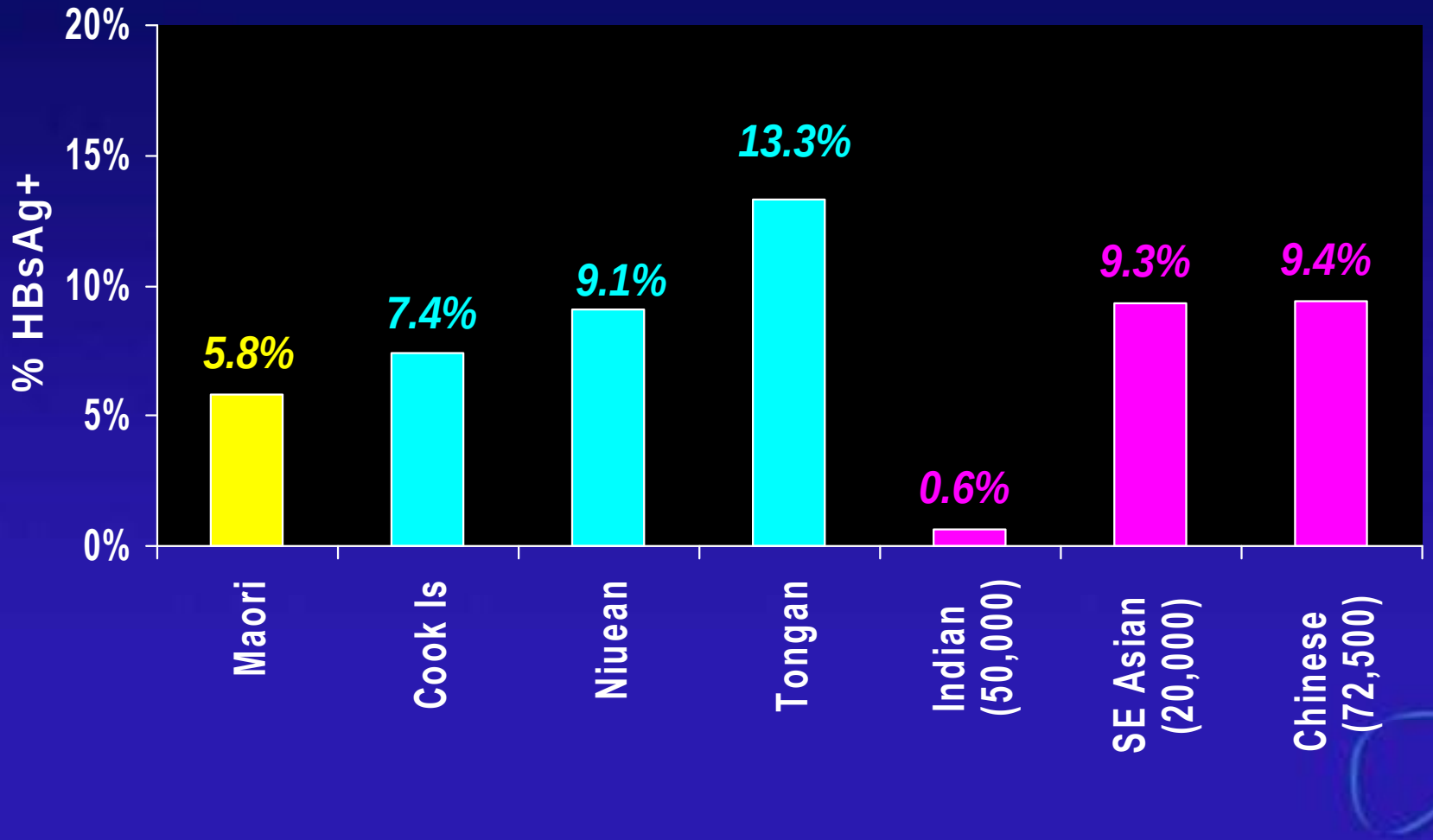
http://www.stats.govt.nz/products-and-services/Articles/pop-proj-Jun04.htm

National HBV Screening Programme

177,292 Screened *(July 1999 - July 2002)*
⇨ 11,300 HBsAg+ identified

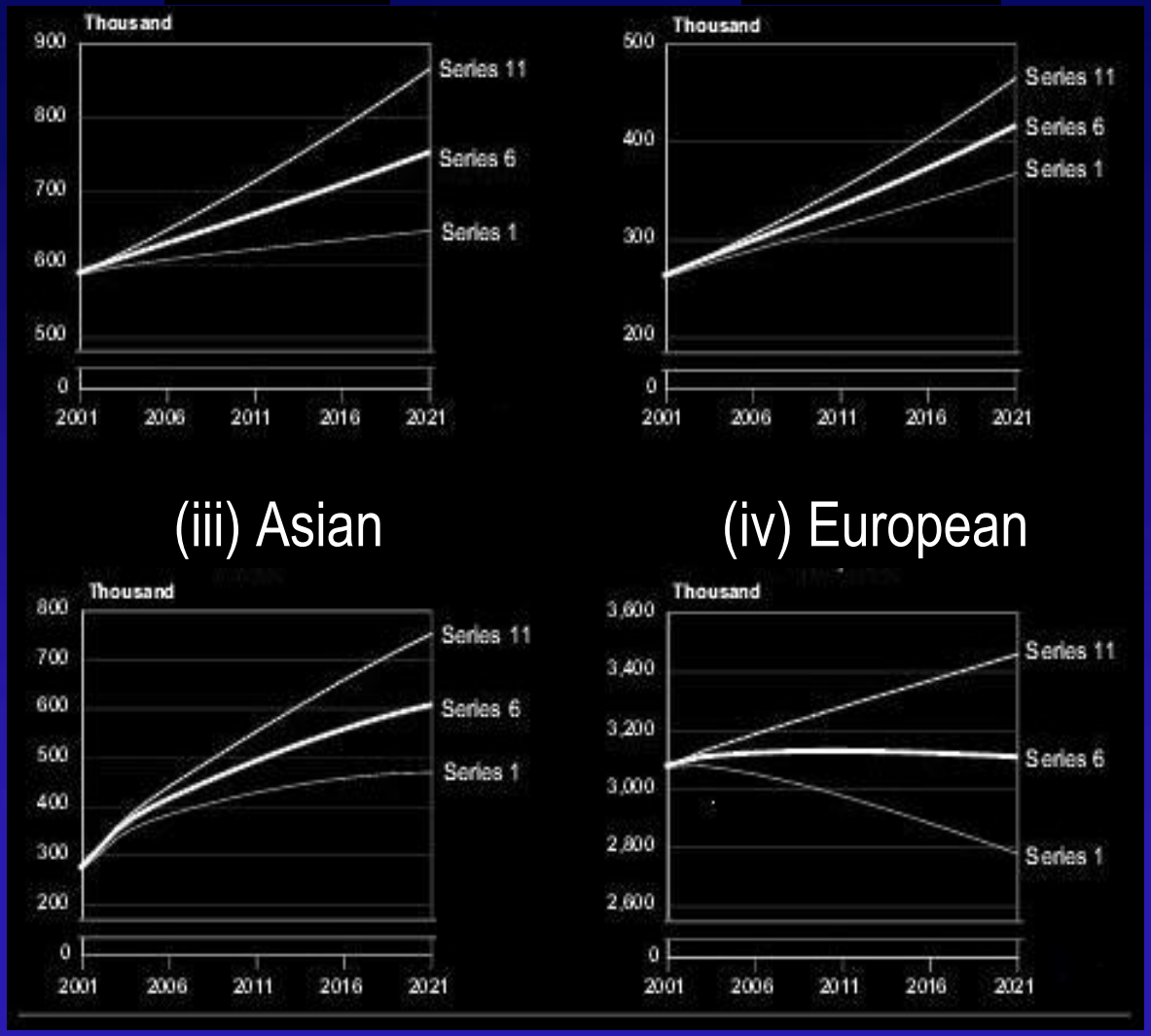


National HBV Screening Programme
Prevalence Rates according to Ethnicity



Projected Ethnic Populations 2001-’21

(i) Maori



(ii) Pacific

(iii) Asian

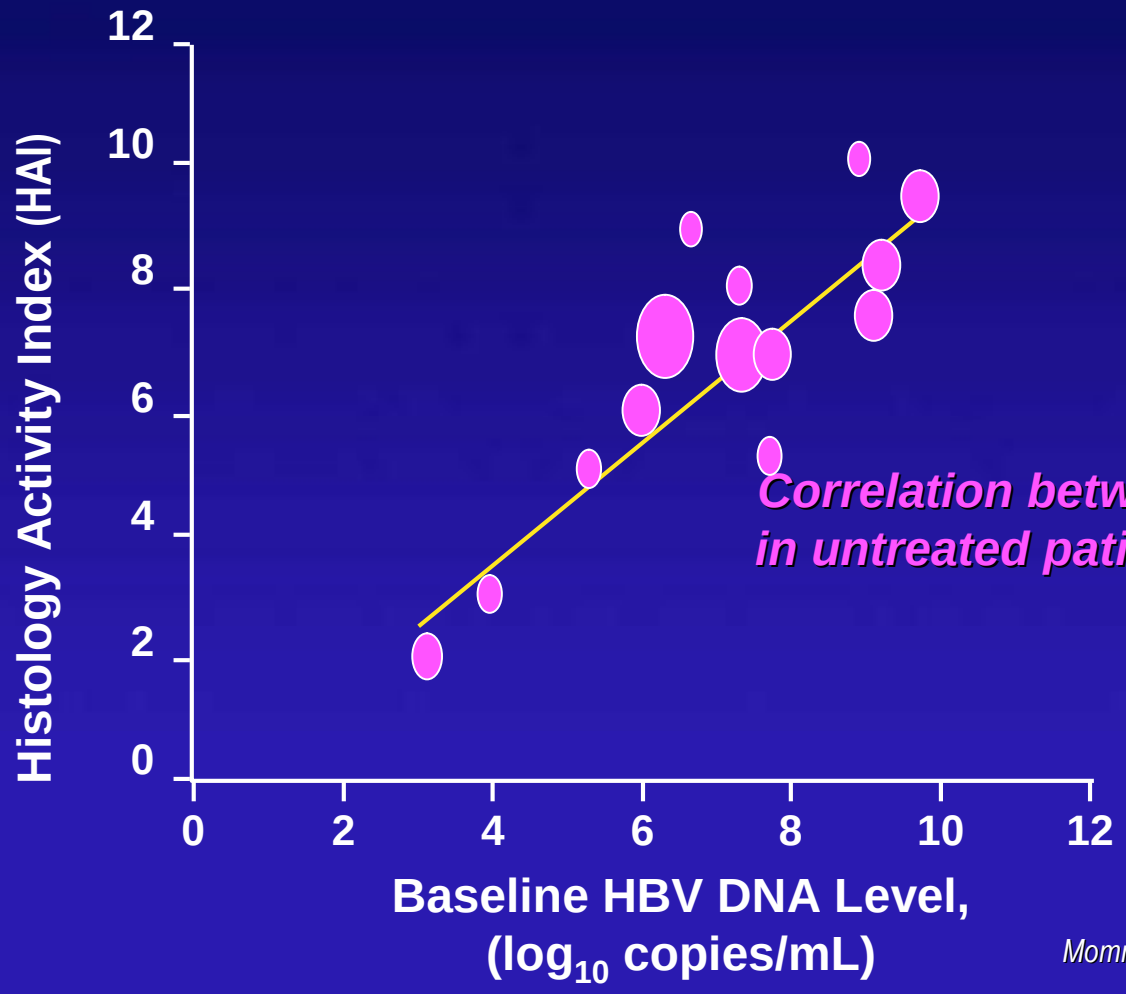
(iv) European

http://www.stats.govt.nz/products-and-services/Articles/pop-proj-Jun04.htm

They are all healthy carriers!

Viral Load determines Disease Activity

Review of 26 prospective studies (n=3428)



Correlation between HAI and HBV DNA in untreated patients (r=0.78; P=0.0001)

Mommeja-Marin H et al. Hepatology 2003

Viral Load predicts Disease Progression

Risk Evaluation of Viremia Elevation & Associated Liver Disease

- prospective, multicenter, observational cohort study (REVEAL)

1991-1992: recruitment

7 Taiwanese townships
Individuals aged 30–65 years eligible
(n = 89,293)

Baseline HBsAg+
(n=9800)

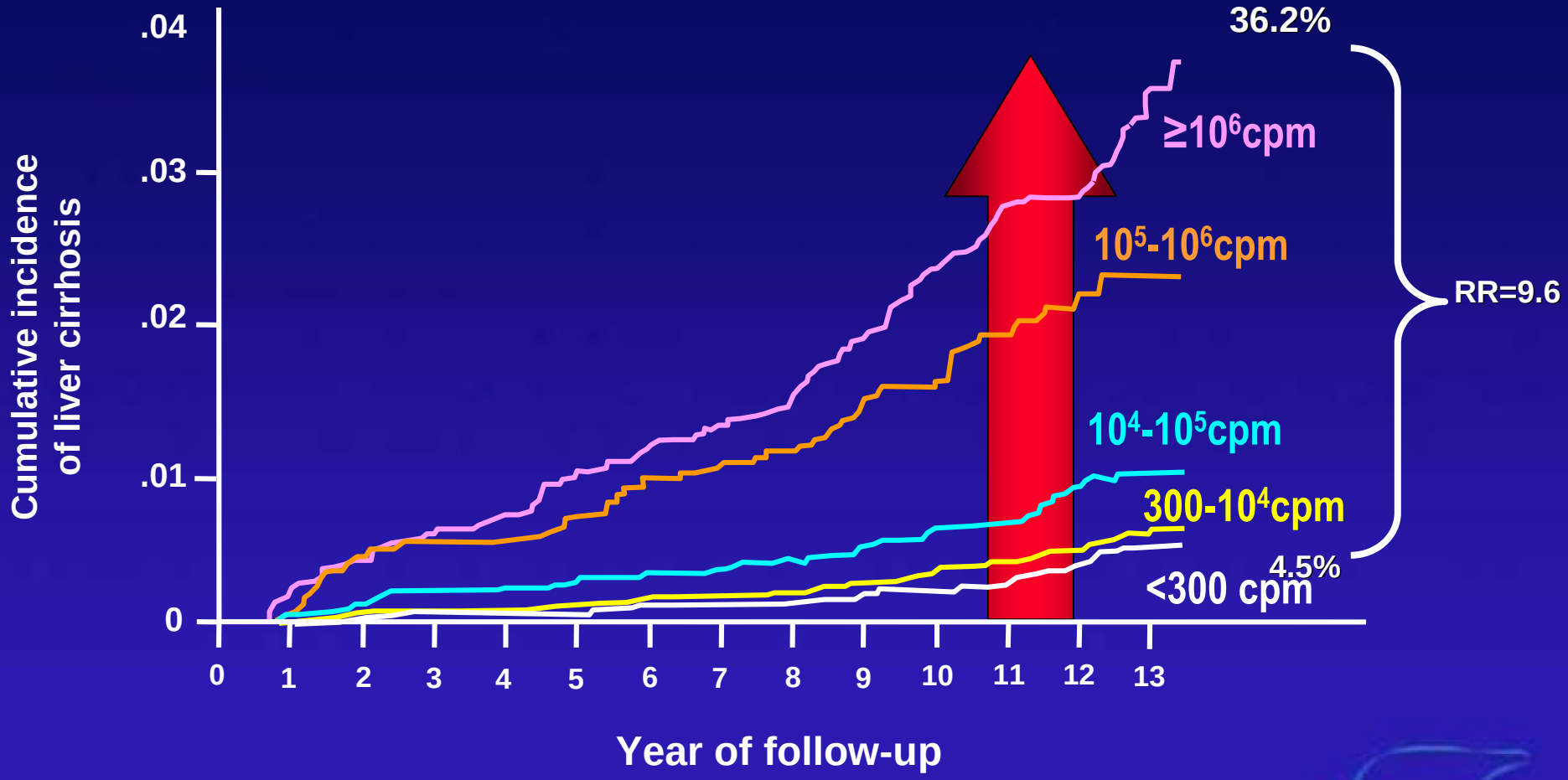
Baseline HBV DNA
(n = 3851)

Follow-up analysis
For Cirrhosis/HCC
(n = 3774)

June 2004:
43,993 PYs follow-up

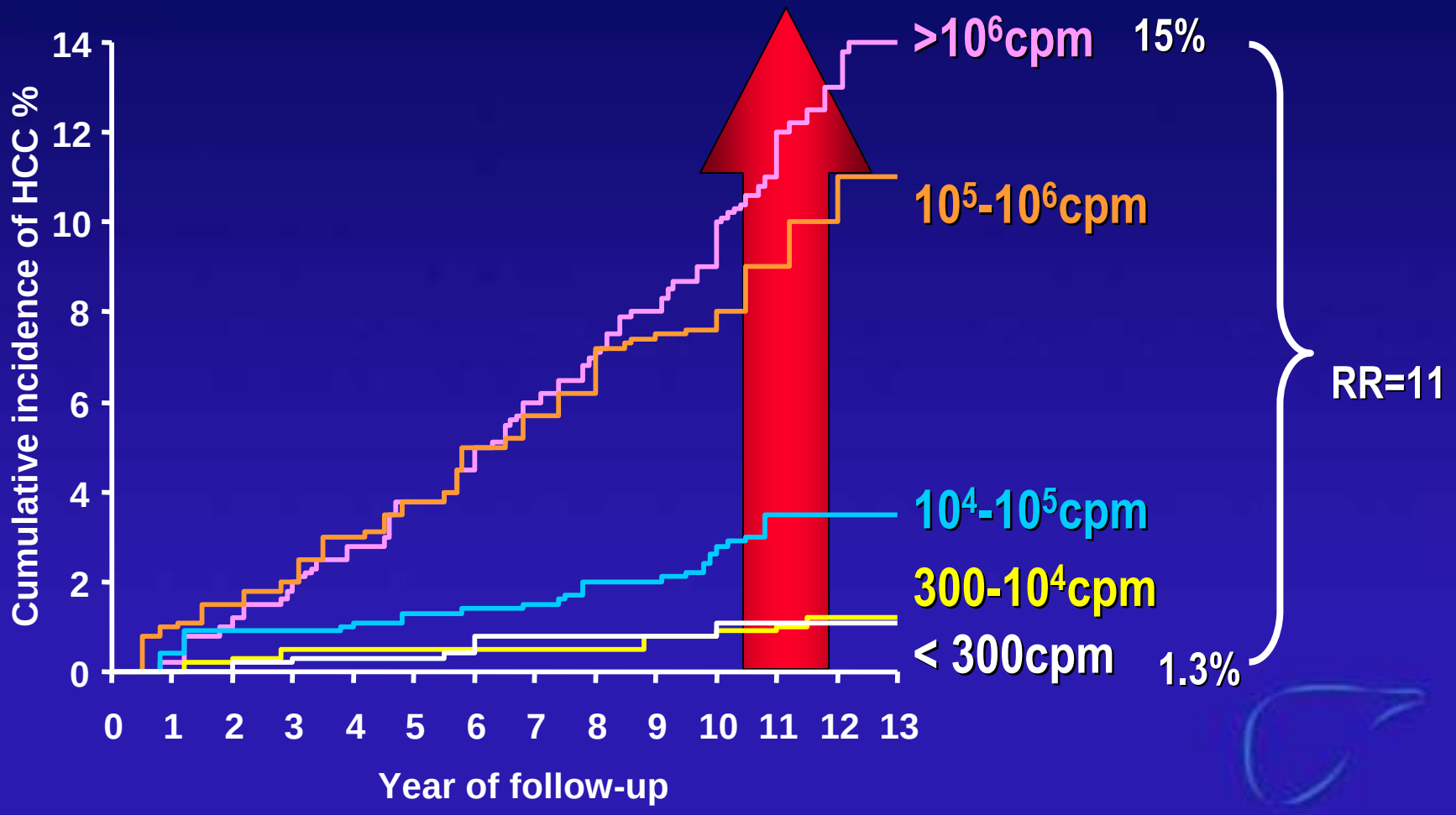
Chen CJ , *JAMA* 2006

Higher viral loads are associated with increased rate of cirrhosis

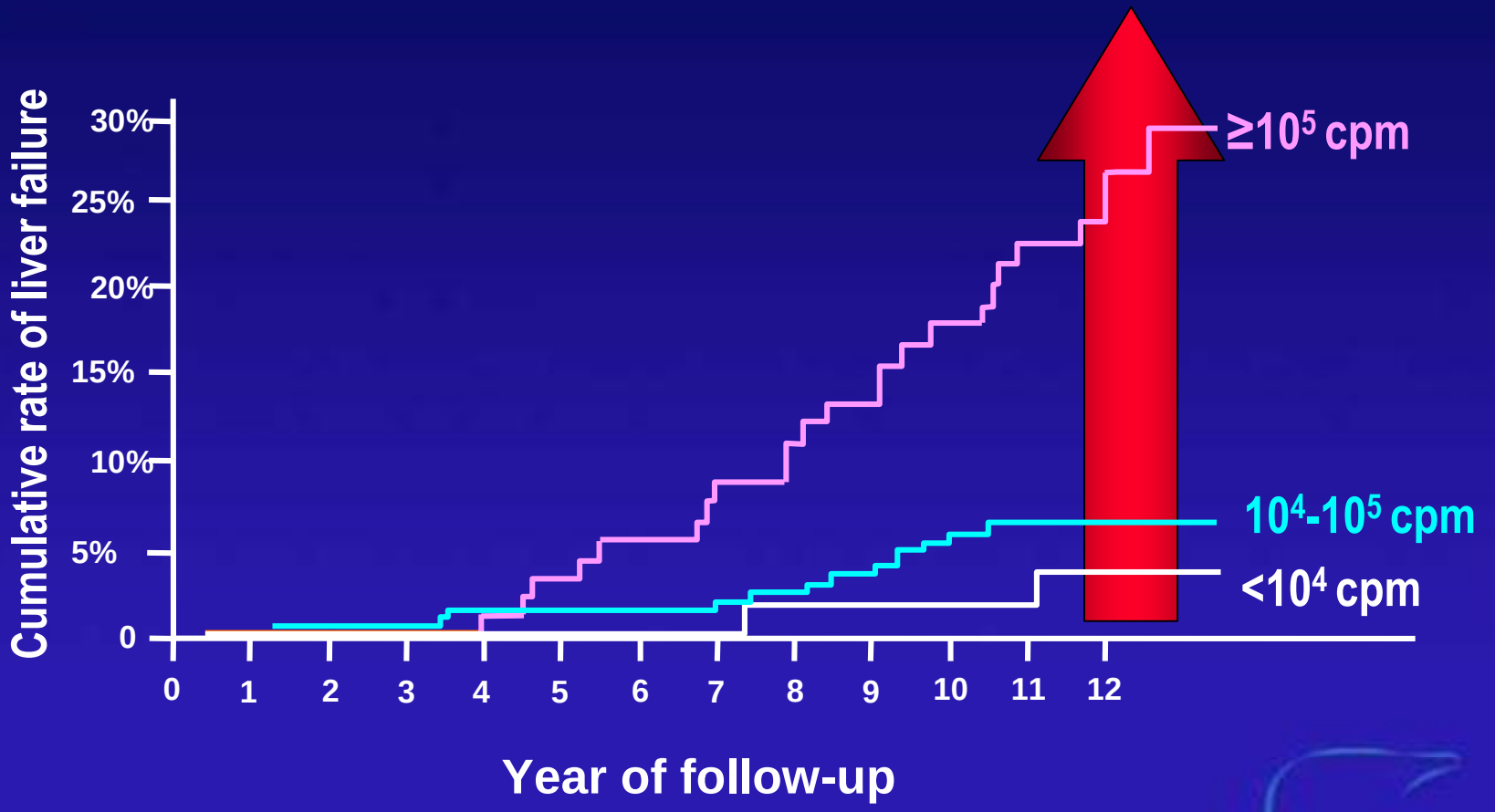


Iloeje UH *et al*. *Gastroenterology* 2006; 130: 678–86.

Higher viral loads are associated with increased rate of Hepatoma

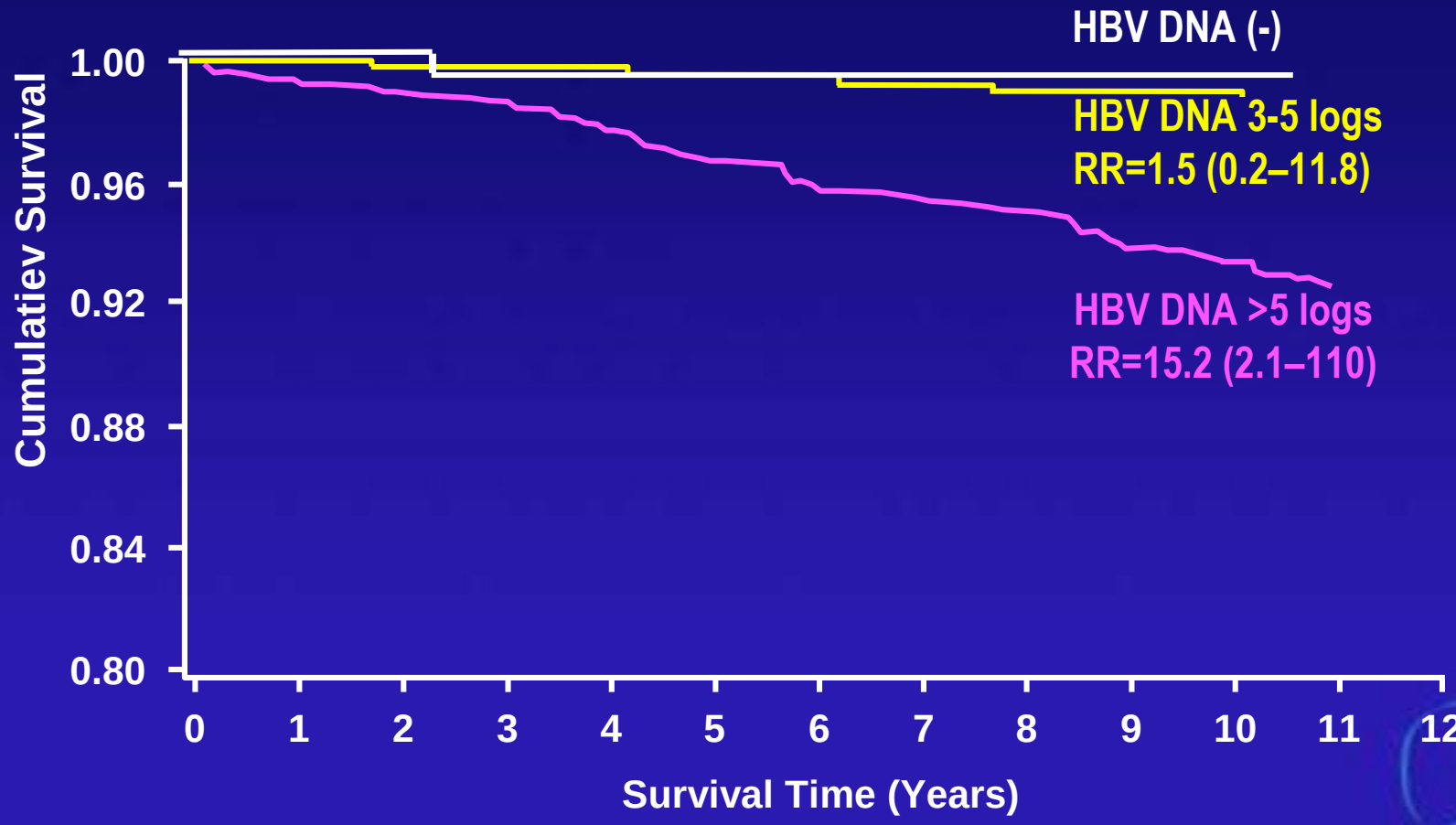


Higher viral loads are associated with increased rate of decompensation



Yang *et al. J Hepatol* 2005: 42(suppl 2); 195.

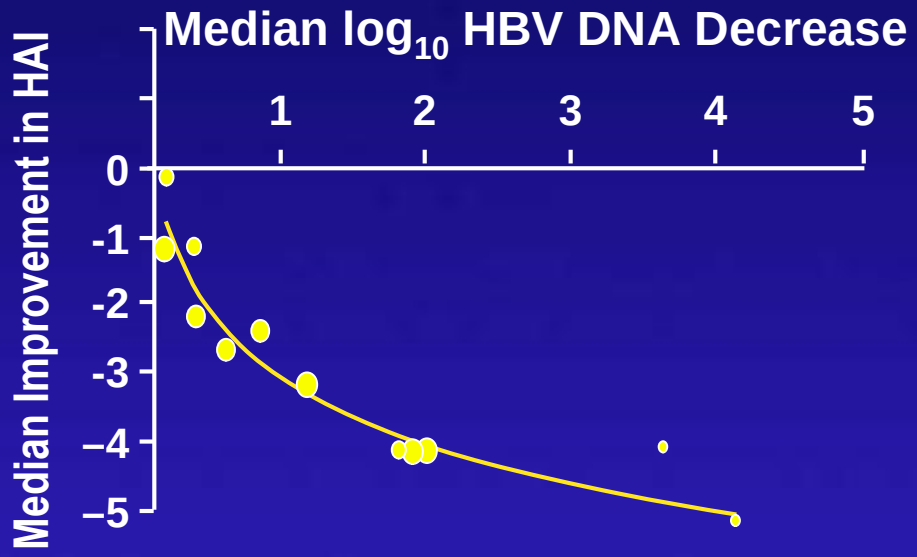
Higher Viral Loads are associated with increased Liver-related Mortality



Chen G et al., Am J Gastro, 2006

Viral Suppression reduces Disease Activity

Review of 26 prospective studies

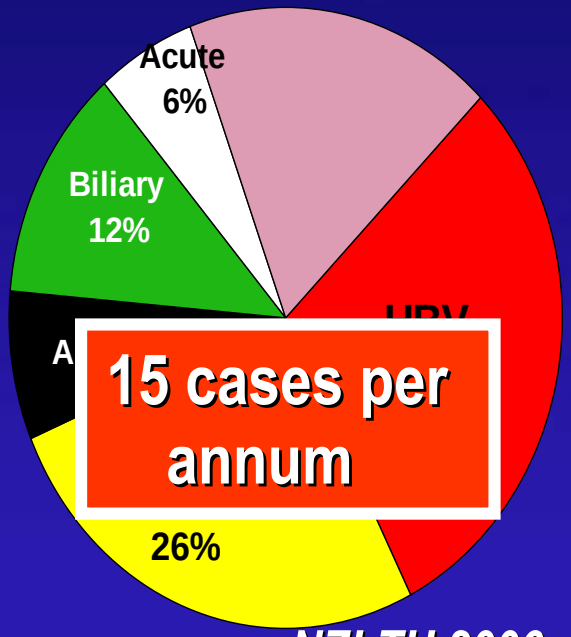


Correlation between change in HBV DNA and HAI with treatment (r=0.96; $P<3x10^{-6}$)

Mommeja-Marin H, *Hepatology* 2003

Impact of HBV Infection

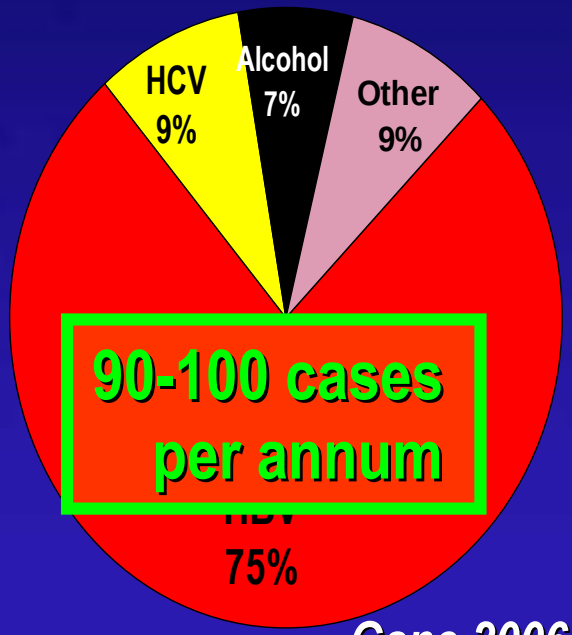
Liver Transplant 1998-2006 *(n=290)*



15 cases per annum

NZLTU,2006

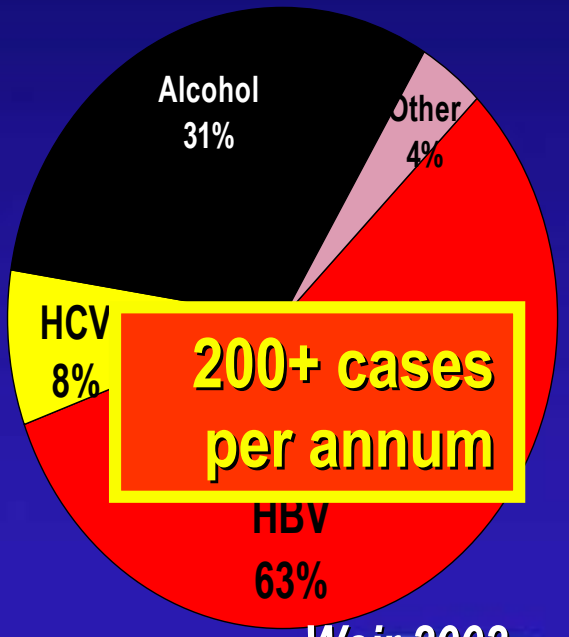
Hepatoma Clinic 2000-2006 *(n=544)*



90-100 cases per annum

Gane,2006

Liver-related Mortality 1999



200+ cases per annum

Weir,2002

Is HBV serology confusing

HBV serology

- sAg determines carrier status
- eAg determines replication
  - » (and infectivity)
- cAb confirms natural infection
- HBV DNA measures infectivity

Case studies

HBV

- 34 year old Maori woman
  - HBsAg pos
  - HBeAg neg
  - ALT 150
  - AFP 13.8
- Spider naevi
- Liver span normal

HBV

- Next best investigation
  - 1) Serum alcohol
  - 2) Liver biopsy
  - 3) HBV DNA
  - 4) U/S
  - 5) Triple phase CT scan

HBV

- Next best investigation
  - 1) Serum alcohol
  - 2) Liver biopsy
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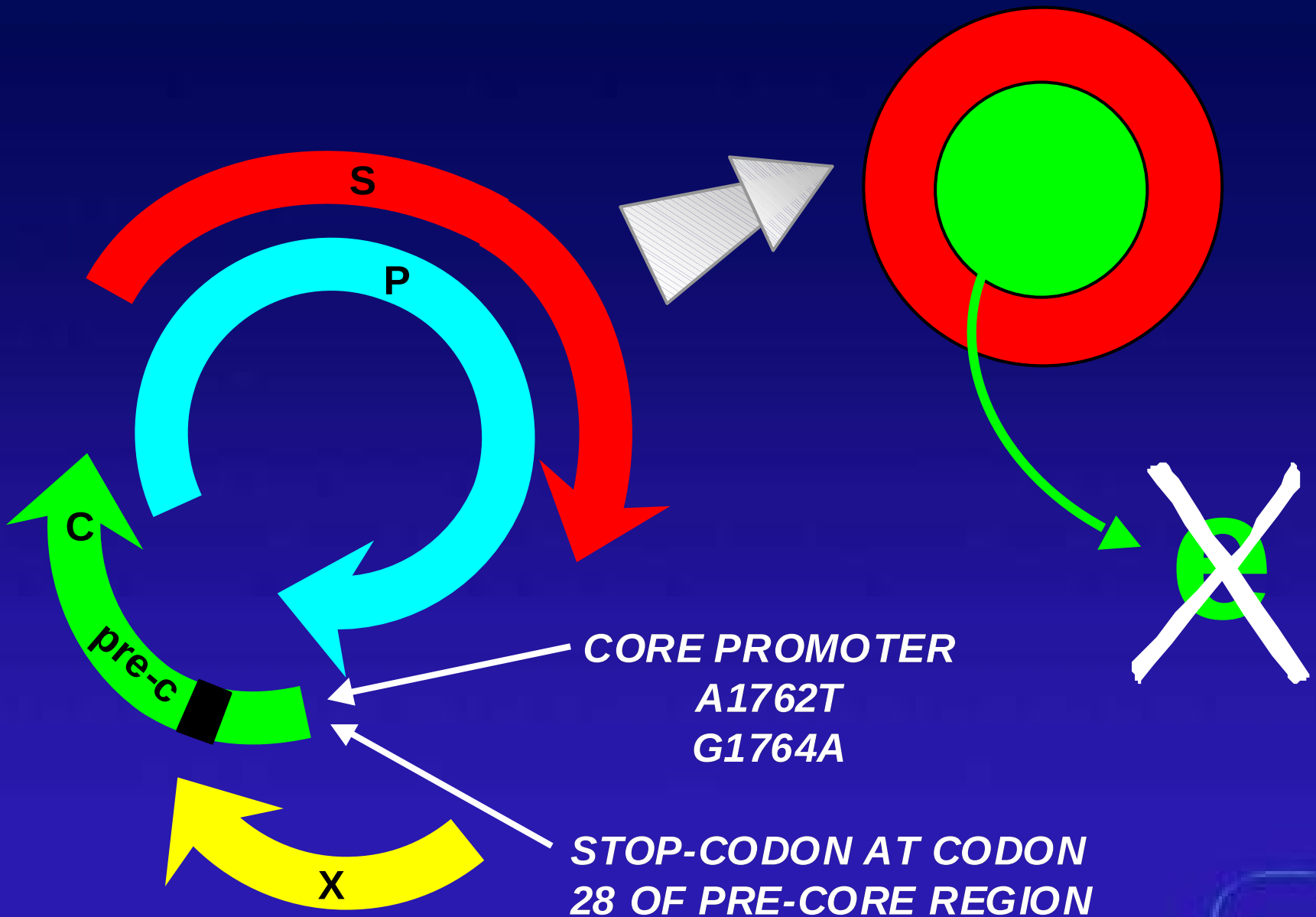
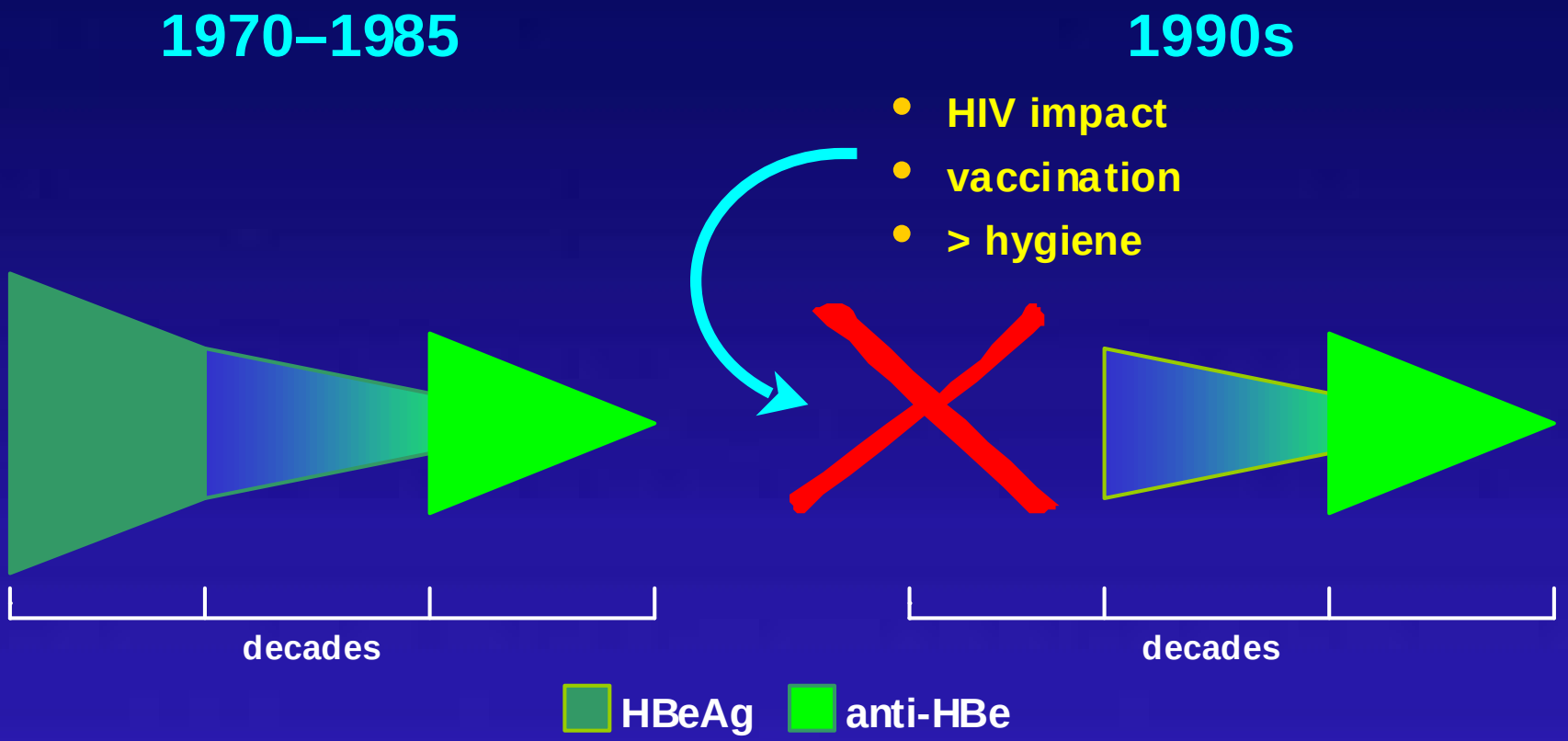

S
P
C
pre-c
X
CORE PROMOTER
A1762T
G1764A
STOP-CODON AT CODON
28 OF PRE-CORE REGION

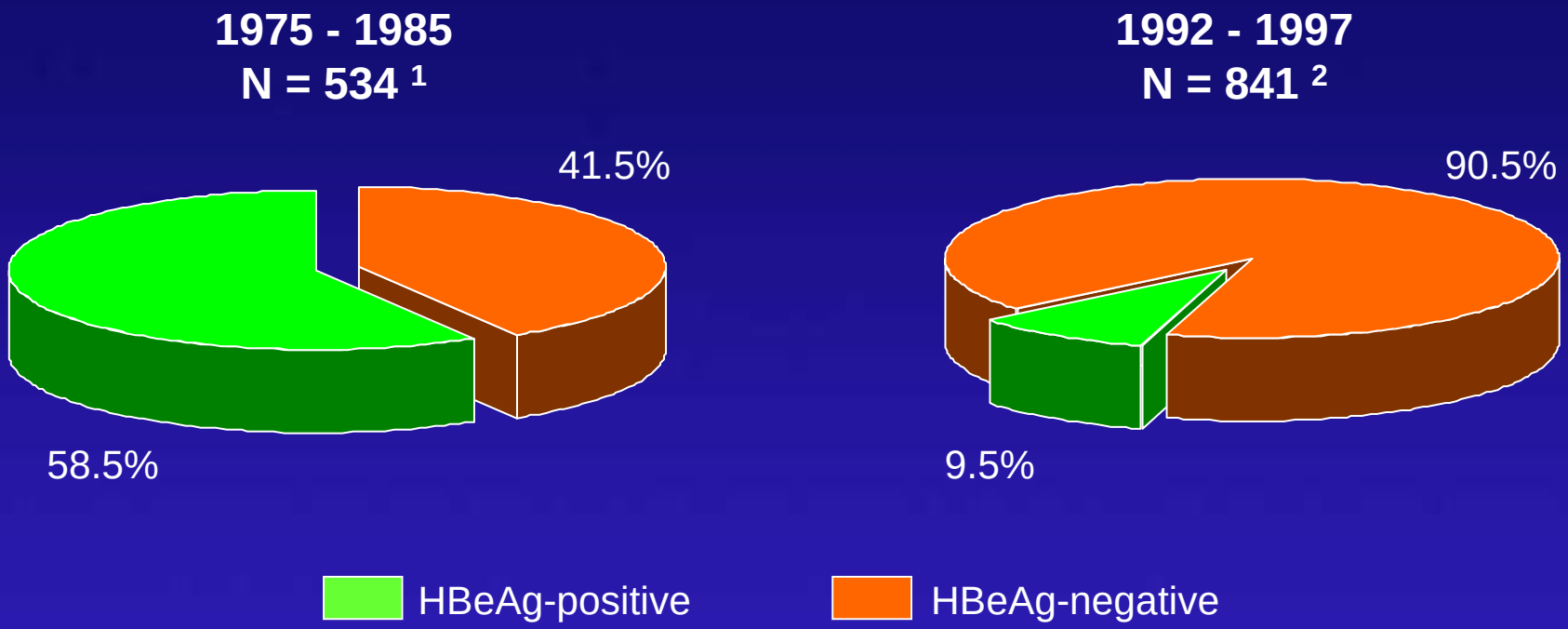
Selection of mutant HBV



Okamoto 1990; Raimondo 1990; Uchida 1994; Lai 1994

Increasing Prevalence of HBeAg-Negative Chronic HBV

HBsAg-positive Chronic hepatitis in Italy: HBeAg/anti-HBe status

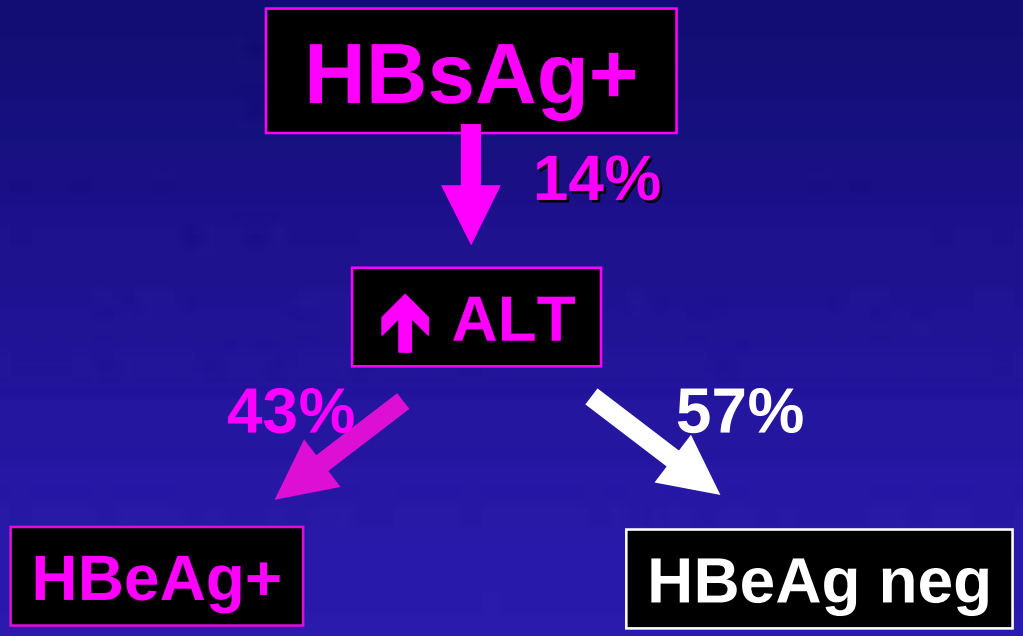


Rizzetto M, XI Triennial International Symposium on Viral Hepatitis and Liver Disease, 2003.

1. Giusti G, et al. *Ital. J. Gastroenterol.,* 1991; **23**:111-118; 2. Gaeta GB, et al. *J. Hepatol*., 2003

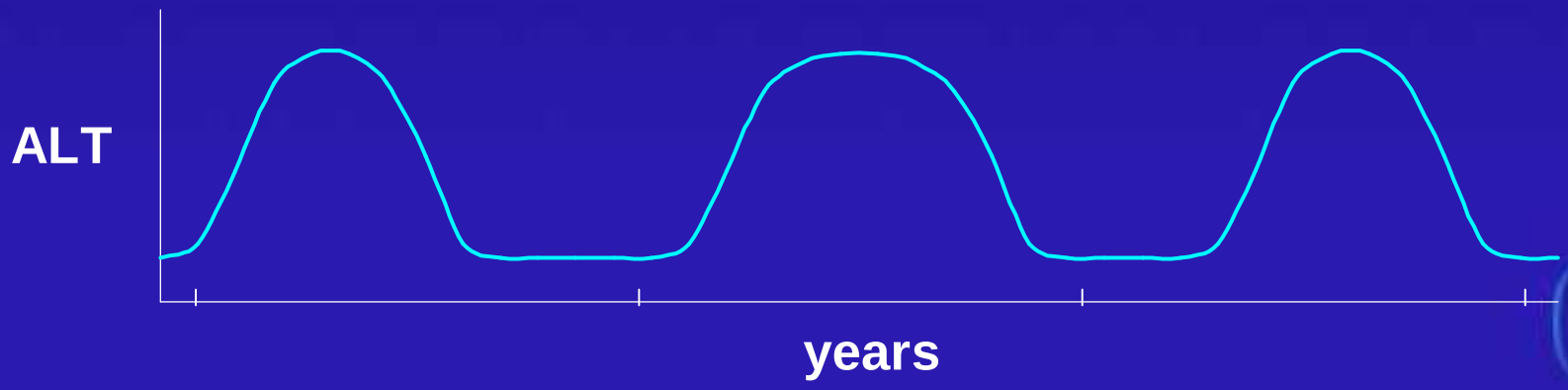
National HBV Screening Programme

Referred for Antiviral Therapy



Clinical and Virologic Course of HBeAg-ve Chronic HBV

Bilirubin (mg/100mL)	1.8	1.0	8.6	1.7	45
INR	1.0	1.0	1.5	1.3	3.7
Ascites	-	-	-	-	+
HBV-DNA	++	-	++	-	++
Anti-HBe	+	+	+	+	+



Screening for HCC

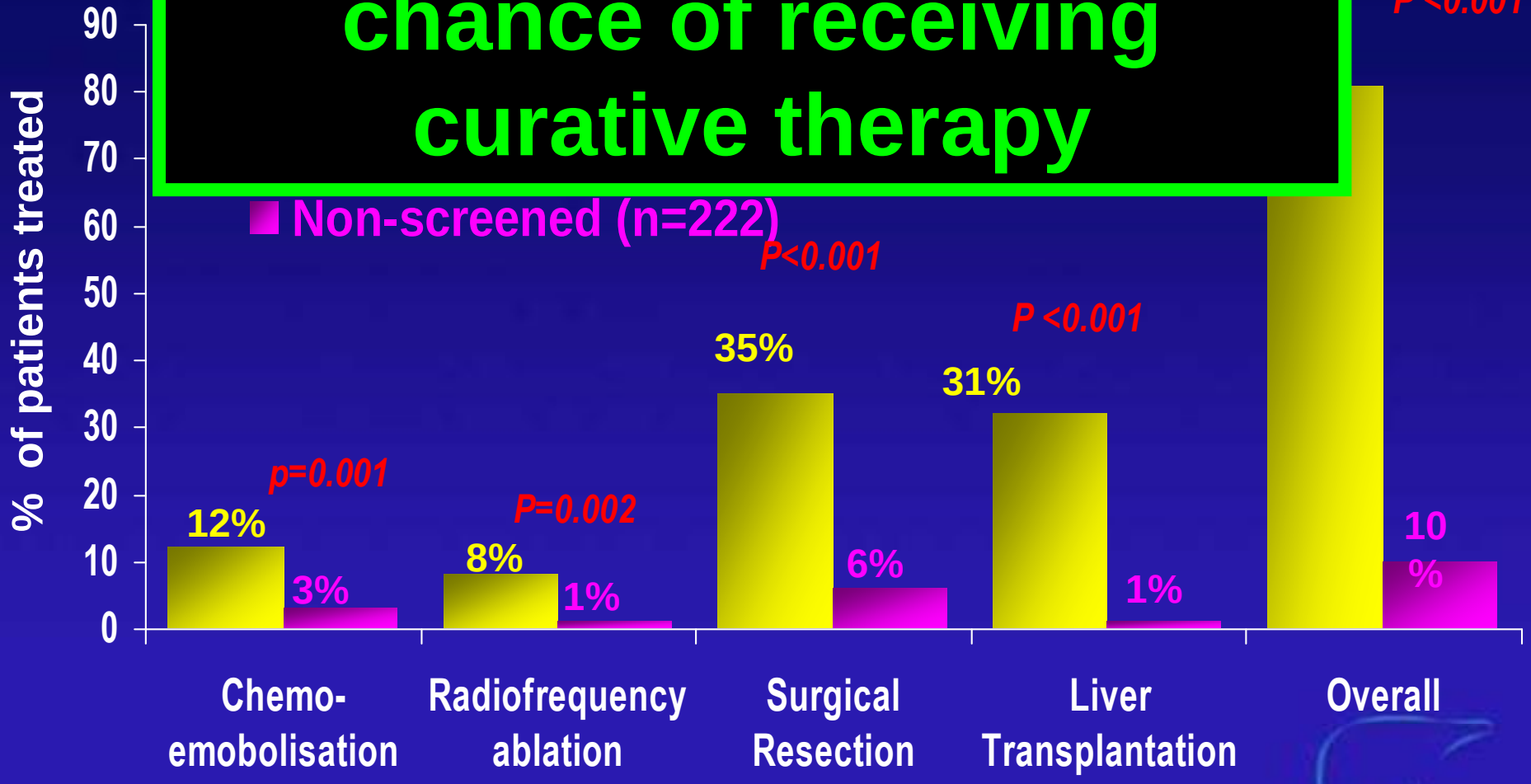
- 6 monthly AFP
- 12 monthly U/S

- Controversial on population basis
- Accepted as targeted screening

	Screen Detected (n=118)	Non-Screened (n=222)	p value
Male	82%	83%	*NS*
Age (median)	52 yrs	54 yrs	*NS*
Cirrhosis	76%	78%	*NS*
AFP Level <20	24%	24%	*NS*
Median AFP	*62 ng/ml*	*675 ng/ml*	***p<0.001***
Symptomatic	**1%**	**87%**	***p<0.001***

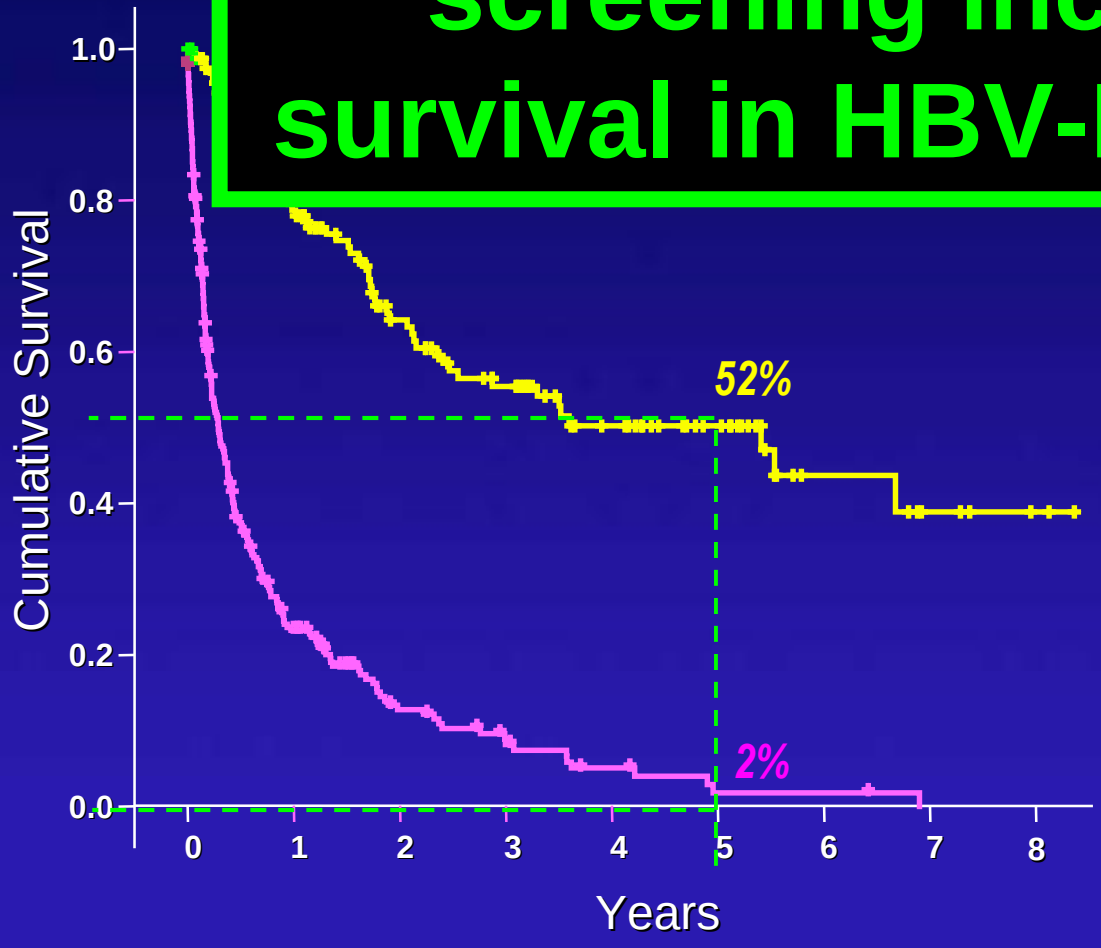
Screened vs. Non-screened

screening increases chance of receiving curative therapy



Screened vs Non-screened
Survival in Hepatocellular Carcinoma

screening increases survival in HBV-Hepatoma



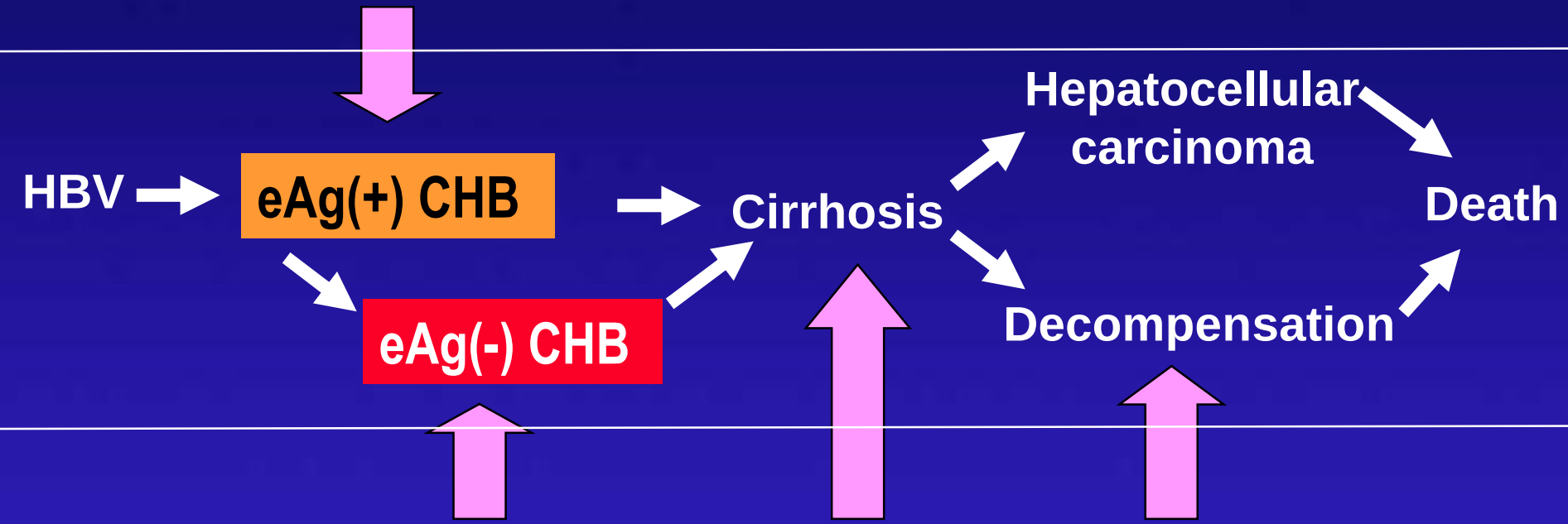
P<0.0001

Screened group (n=118)
Median survival = 1974 days (66 months)

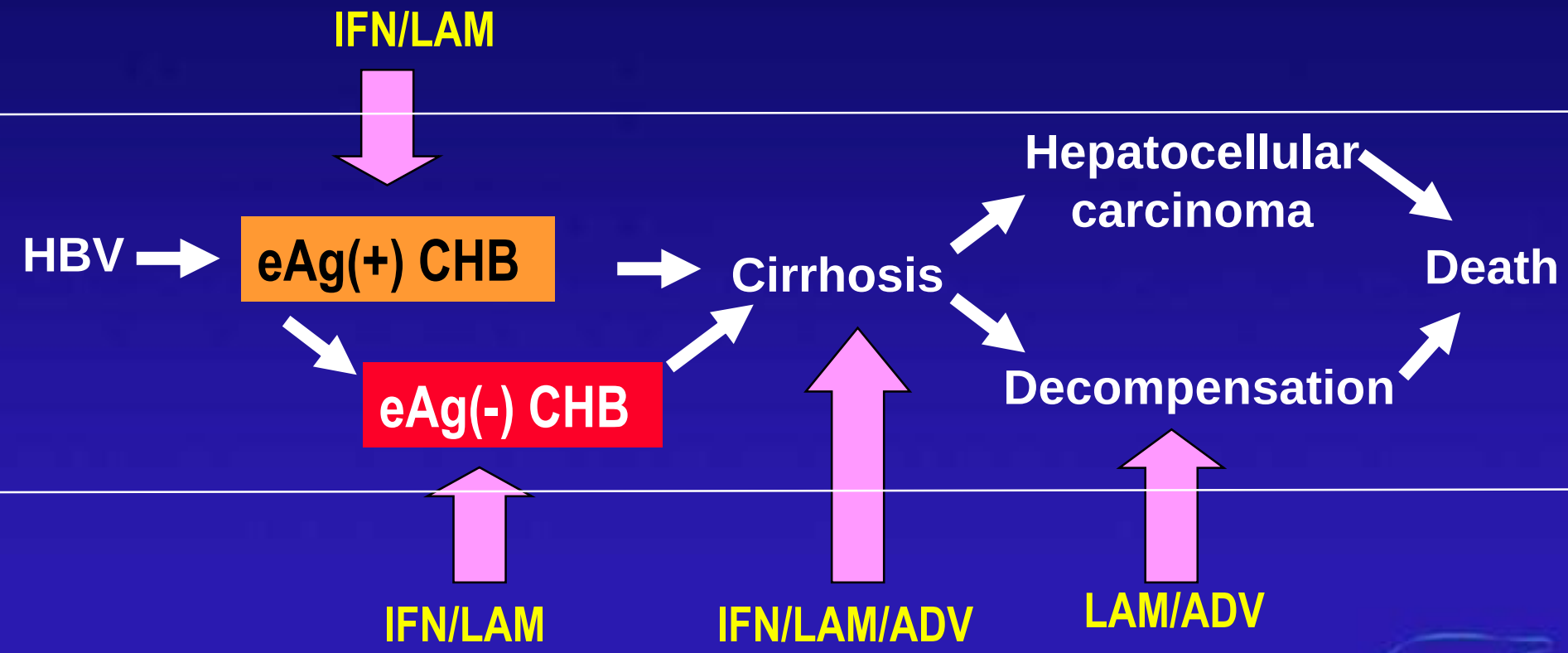
Non-screened group (n=222)
Median survival = 107 days (3 months)

Treatment options for CHB

Treatment options for CHB



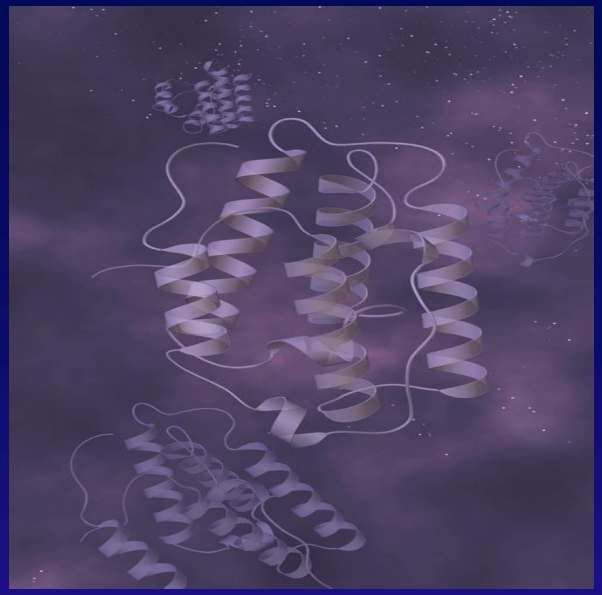
Treatment options for CHB



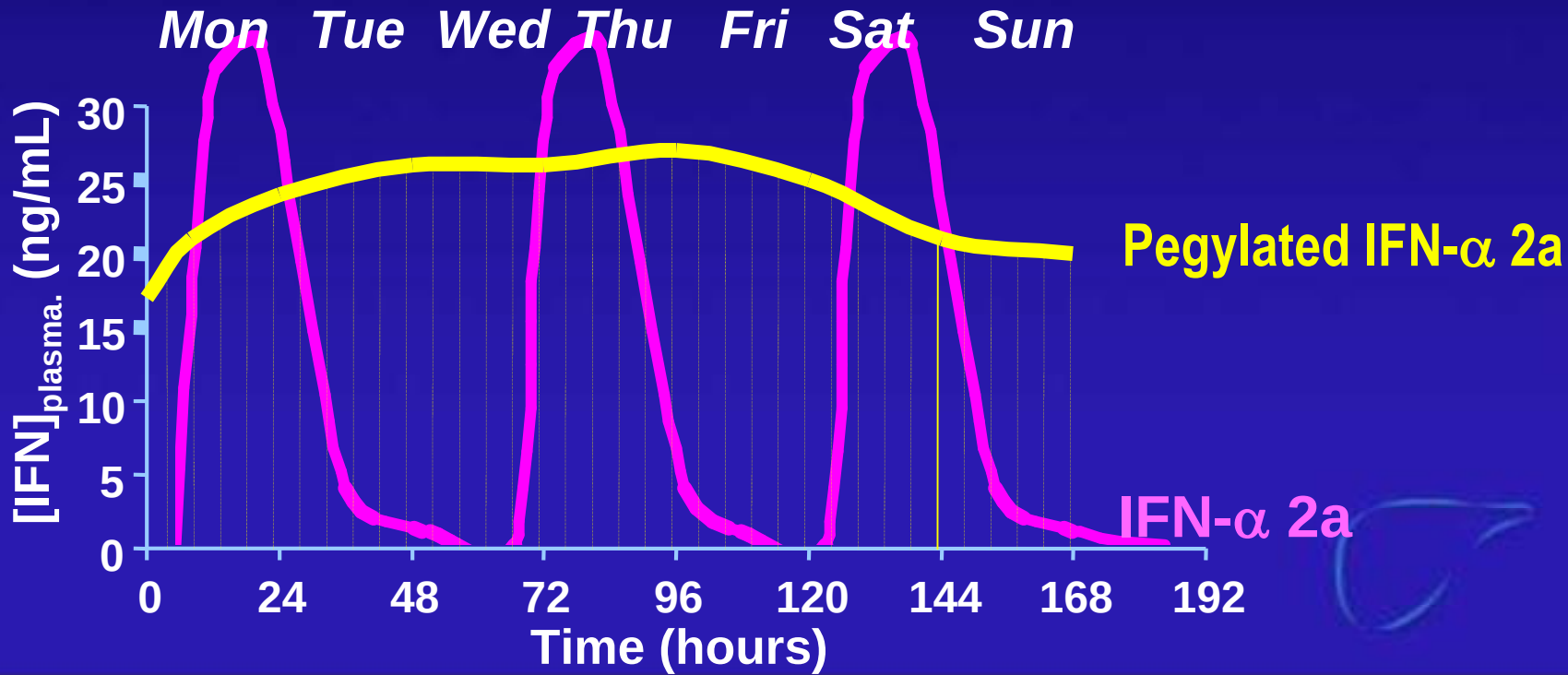

Rikschataxi Berlin
www.rikschataxi.de
messenger

- Interferons
- Nucleoside/Nucleotide Analogues

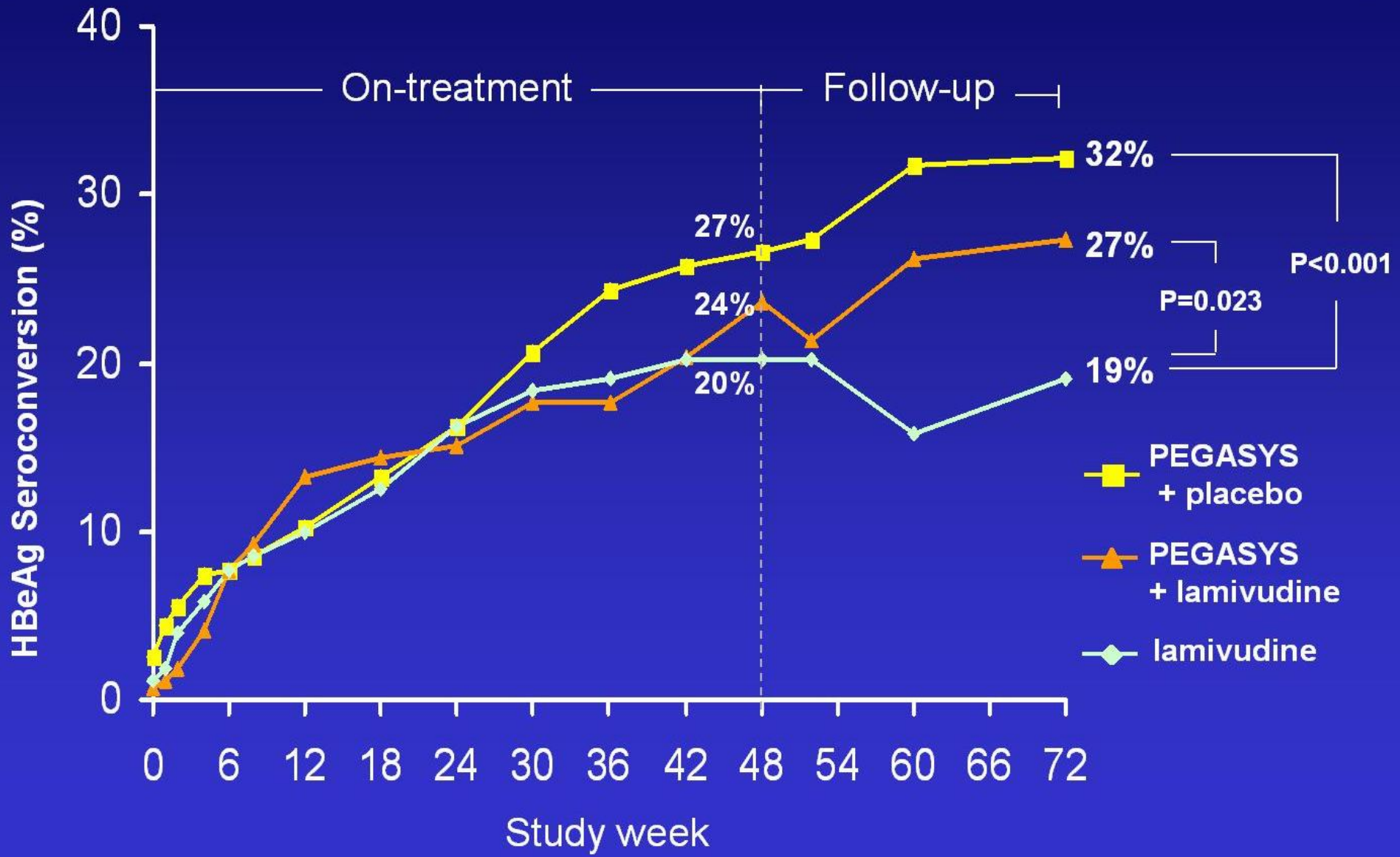
IFN-α 2a



Pegylated IFN-α 2a



HBeAg Seroconversion Rates Over Time

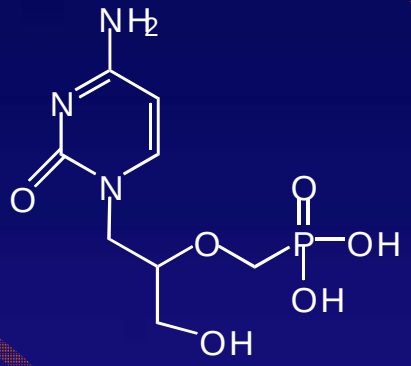


Nucleoside/Nucleotide Analogues

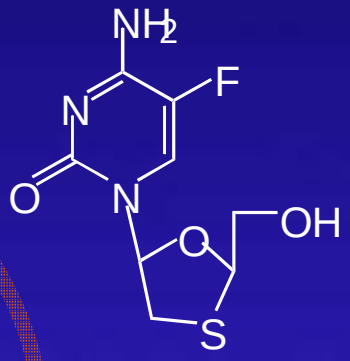
(a) Purine Analogues

Entecavir

Adefovir

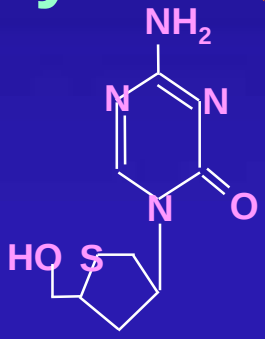


Tenofovir



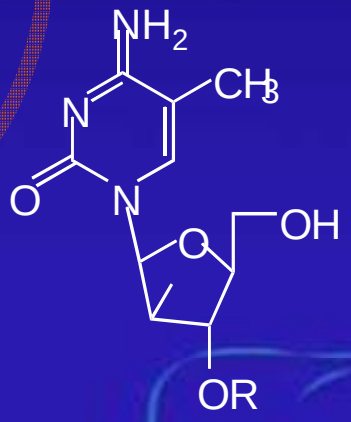
Emtricitabine

(b) Pyrimidine Analogues



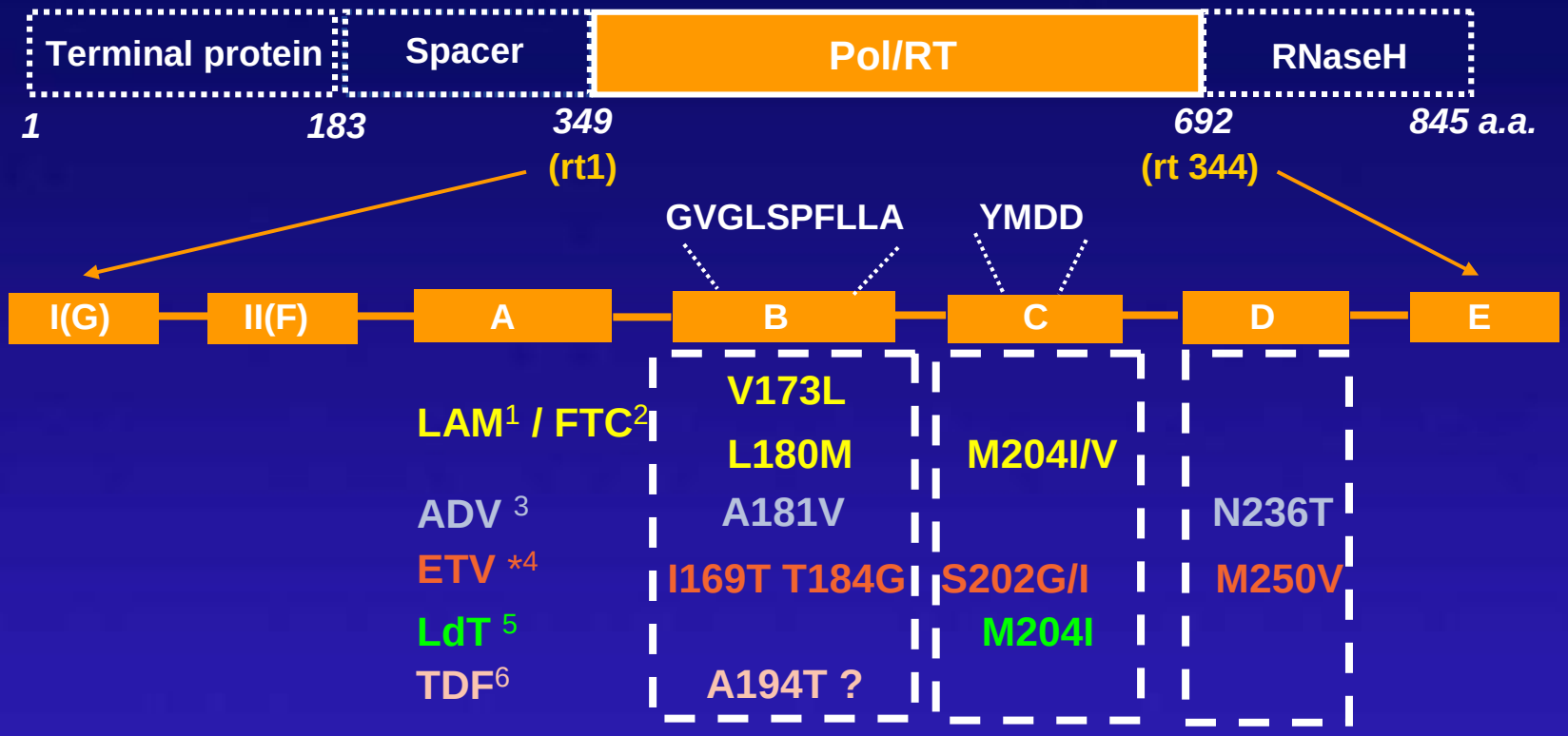
Lamivudine

Telbivudine



Valtorcitabine

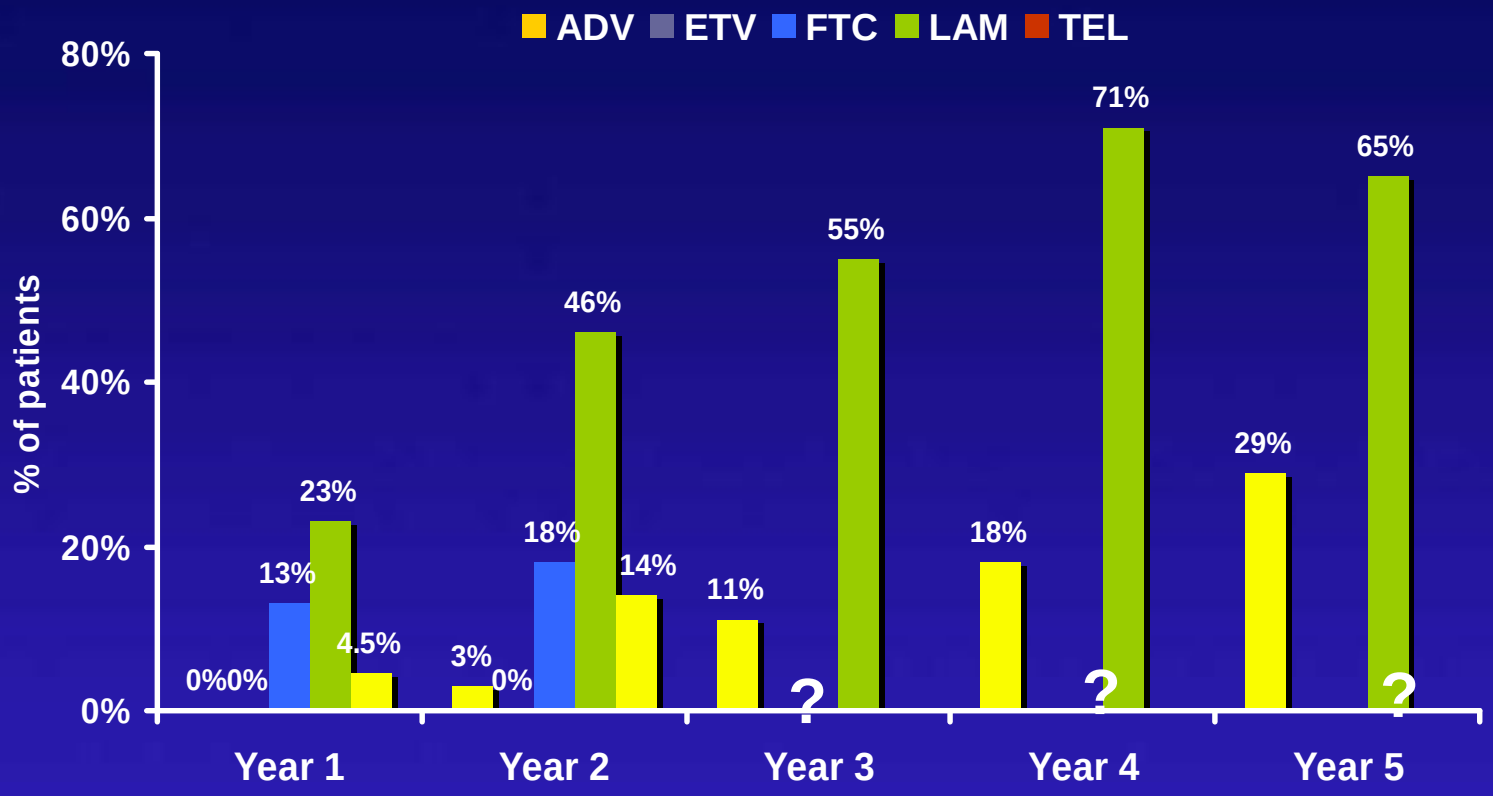
Identified mutations associated with drug resistance



** All ETV resistance requires background YMDD mutations*

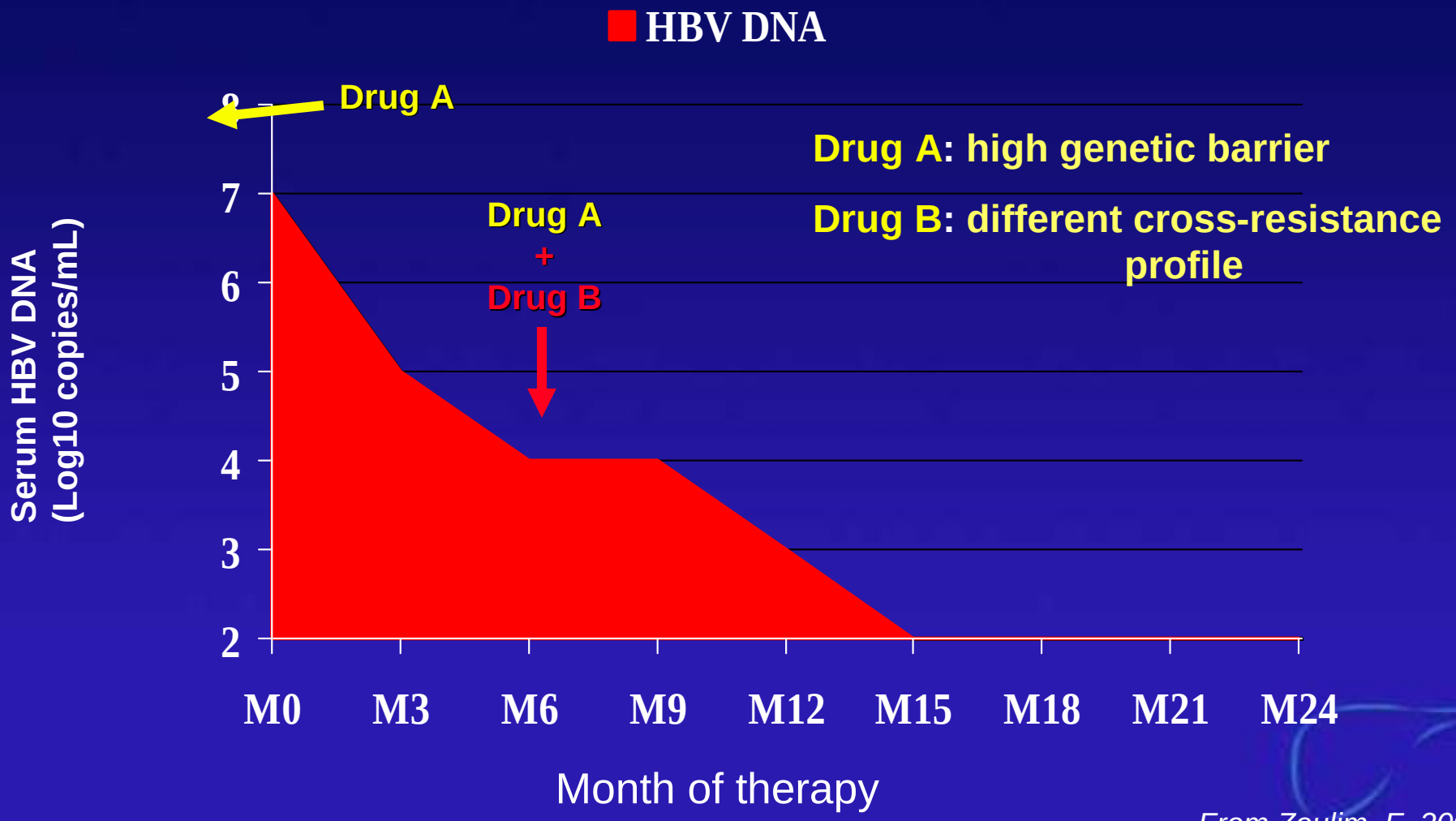
1. Allen *et al. Hepatology* 1998;27:1670–7; 2. Gish *et al. J Hepatol* 2005;43:60–6;
3. Qi *et al. J Hepatol* 2004;40(Suppl 1):20–1; 4. Tenney *et al. AAC* 2004;48:3498–507;
5. Lai *et al. Gastroenterology* 2005;129:528–36; 6. Sheldon *et al. Antivir Ther* 2005;10:727–34

Incidence of Resistance in Treatment-naïve Patients Over Time



Lai et al. Clin Infect Dis. 2003;36:687-96; Lok et al Gastroenterology 2003; 125 : 1714-1722; Zoulim et al J Viral Hepatitis 2006;13:278-288; Hadzyiannis et al NEJM 2005; 352 : 2673-2681; Chang et al. NEJM 2006; 351: 1001-1010; Lai et al NEJM 2006; 354: 1011-1020; Lai et al Abstract # 91, AASLD 2006. Colonno R et al. Abstract #110, AASLD 2006.

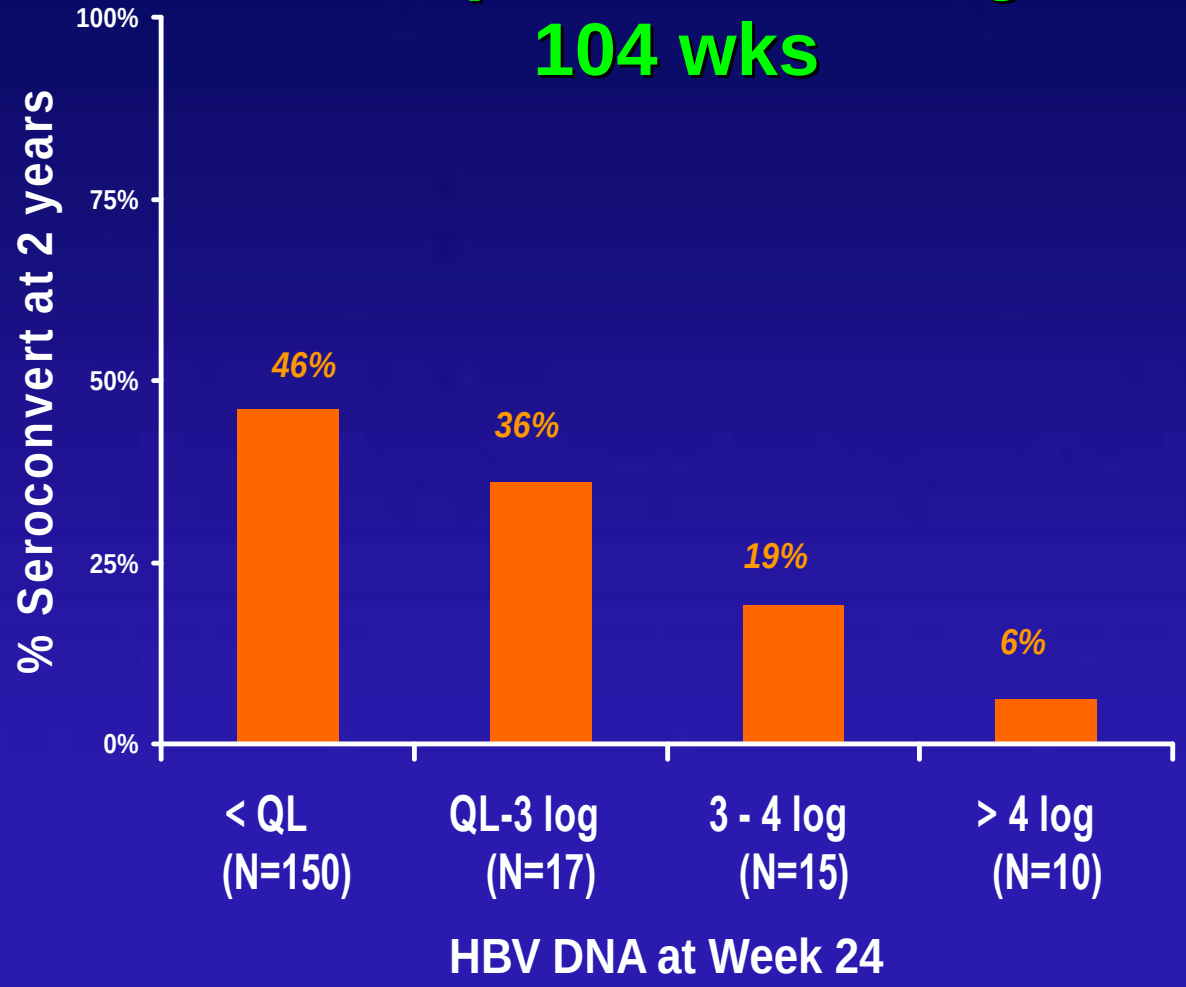
Very Early Add-on Therapy to Keep Viral Load as Low as Possible



From Zoulim, F. 2006

Degree of Early Viral Suppression Predicts HBeAg seroconversion with Telbivudine

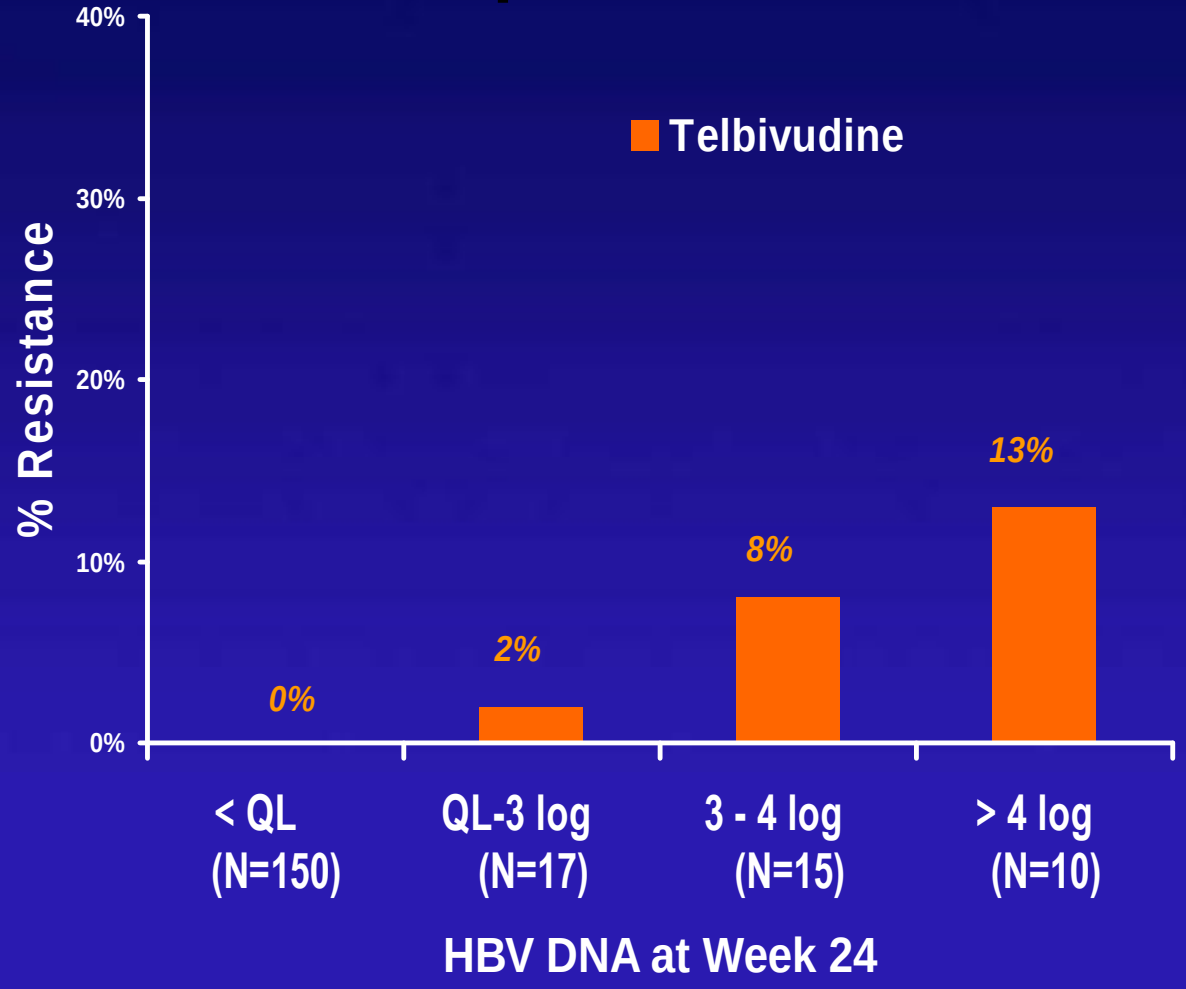
- Wk 24 viral load predicts HBeAg conversion at 104 wks



Di Bisceglie et al., AASLD 2006

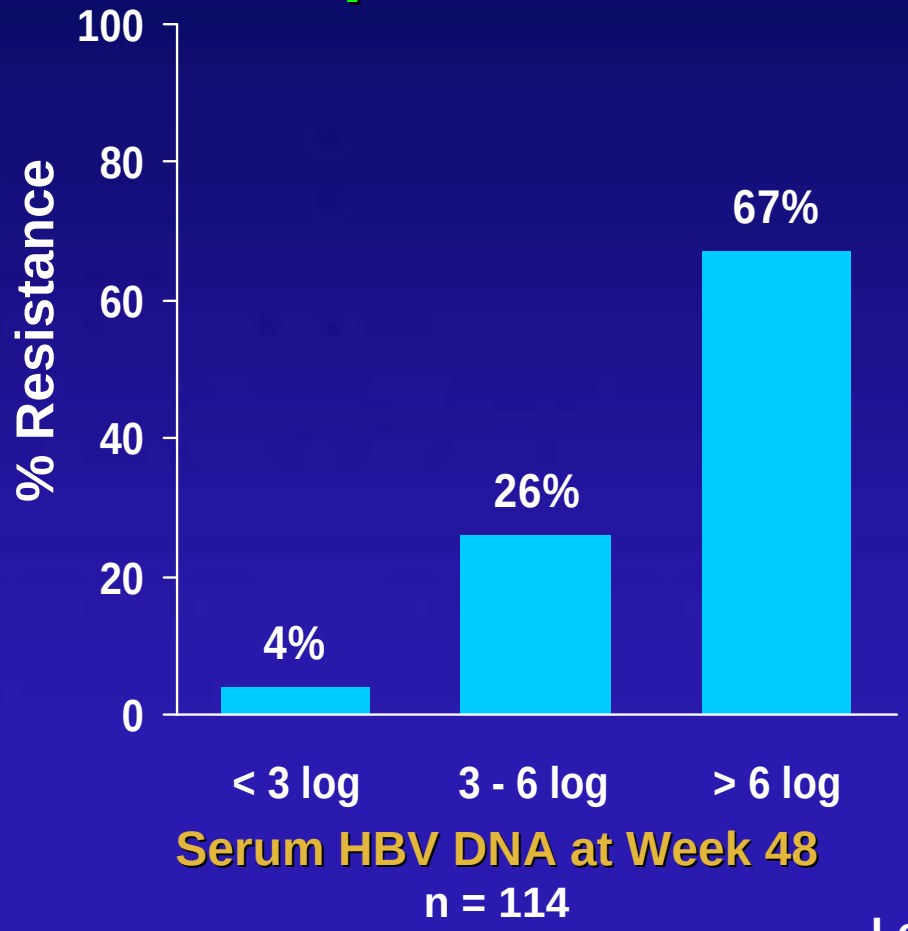
Degree of Early Viral Suppression Predicts Virologic Breakthrough with Telbivudine

- Wk 24 viral load predicts resistance at 52wks



Degree of Early Viral Suppression Predicts Virologic Breakthrough with Adefovir

- Wk 48 viral load predicts resistance at 144 wks



Locarnini *J. Hepatology 2005*

Conclusion

- HBV is a New Zealand Problem
  - » Identifying all carriers
- Refer patients with known HBV
  - » Surveillance is necessary
- Treatment is available
  - » Prevents disease progression