Chronic Hepatitis B
What every GP should know

Prof Ed Gane
NZ Liver Unit

Case 1

- 55 Yr old Tonga male
  - Well but dad died of liver cancer
  - LFTs: **ALT 85**, GGT 60; ALP 75; bilirubin 12

What next?

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  - Well but dad died of liver cancer
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- HBsAg +
- HBeAg neg

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- **HBV DNA 6,500,000 IU/mL**

What next?

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  - LFTs: **ALT 85**, GGT 60; ALP 75; bilirubin 12
- HBsAg +
- HBeAg neg
- **HBV DNA 6,500,000 IU/mL**
- **Referred to Hospital**
- **Fibroscan ➡ cirrhosis**

Treat?

Case 2

- 35 Yr old European male
  - 2 weeks malaise, anorexia
  - Now dark urine, RUQ abdo pain,
  - Previously well, no family history
  - LFTs: **ALT 1600**, GGT 160; ALP 95; bilirubin 122
- New partner Chinese tertiary student who has strong family history of liver cancer

What next?

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- **Anti-HAV IgM neg**
- **Anti-HCV neg**
- **HBsAg neg; anti-HBs neg**

What next?

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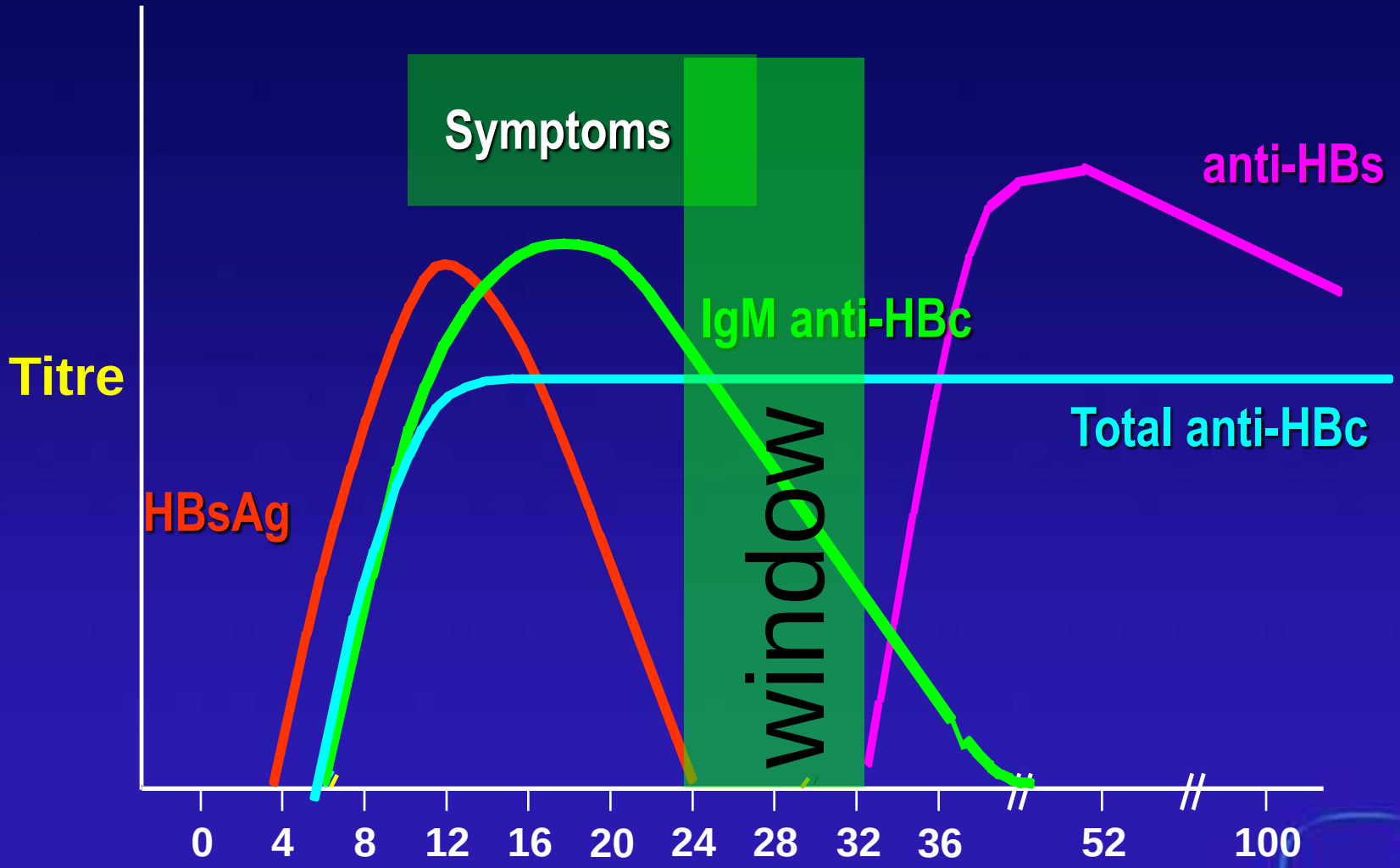
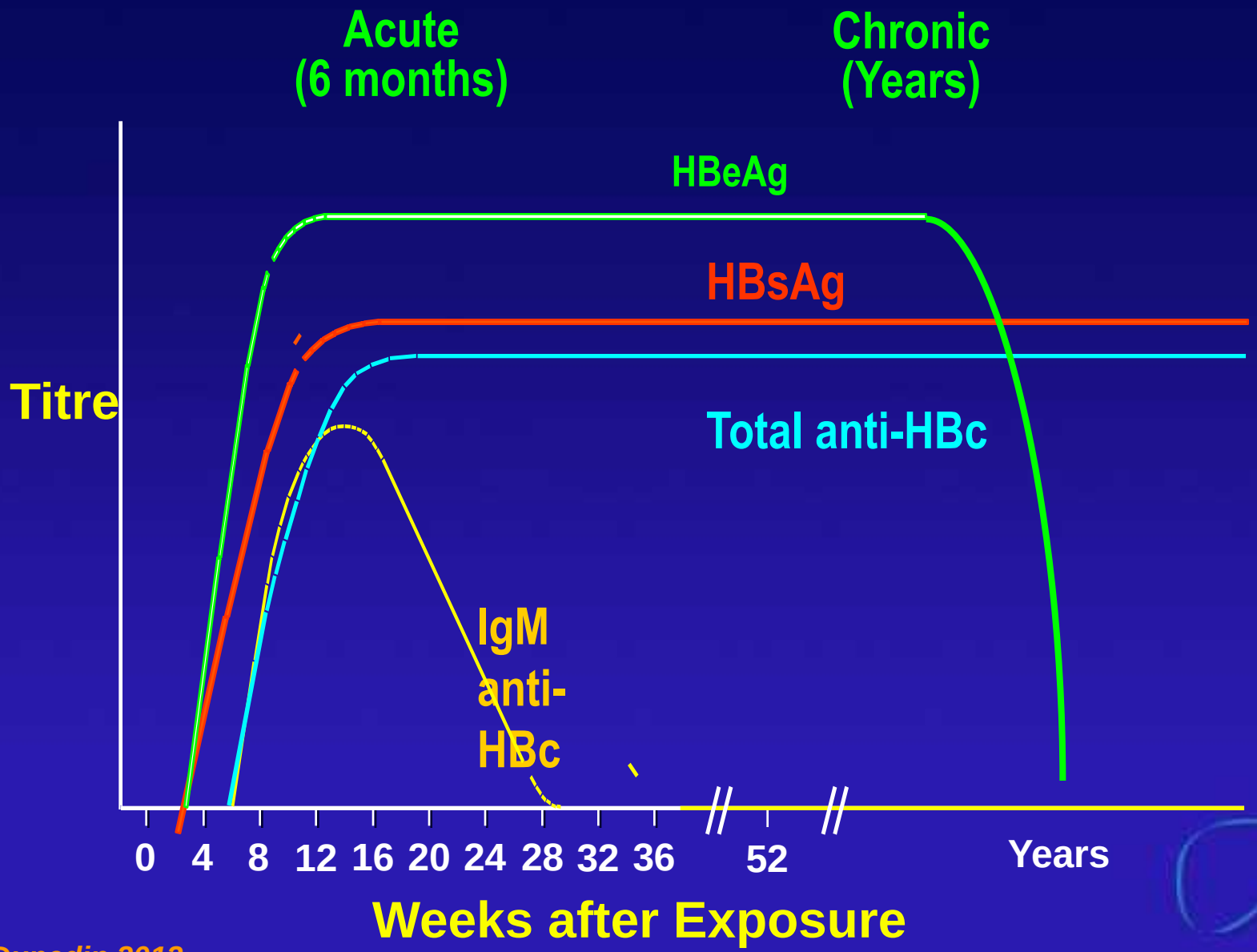
- **Anti-HAV IgM neg**
- **Anti-HCV neg**
- **HBsAg neg; anti-HBs neg**
- **Anti-HBcore IgM ++**

Diagnosis of Acute Hepatitis B



Diagnosis of Chronic Hepatitis B

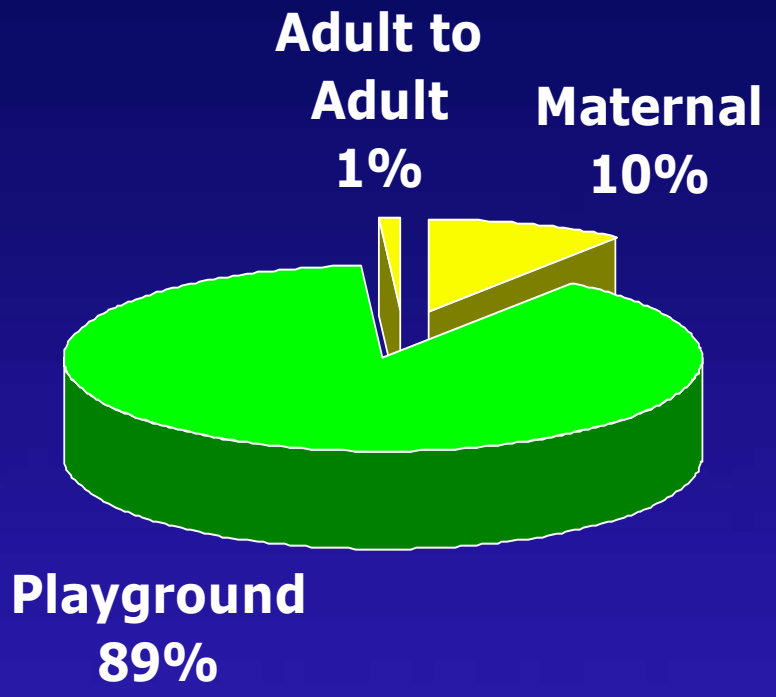


	ACUTE HBV		
	early	window	late
HB_sAg	+	±	–
anti-HBs	–	–	±
HB_eAg		–	±
anti-HBe	–	–	±
anti-HB_cIgM	+ +	+ +	+ +
anti-HB_cIgG	–	–	+
Serum ALT	>5x ULN		
HBV DNA	+	+/-	+/-

	ACUTE HBV			CHRONIC HBV	
	early	window	late	eAg+	eAg -
HB_sAg	+	±	–	+	+
anti-HBs	–	–	±	–	–
HB_eAg		–	±	+	
anti-HBe	–	–	±	–	+
anti-HB_cIgM	+ +	+ +	+ +	–	–
anti-HB_cIgG	–	–	+	+	+
Serum ALT	>5x ULN			>ULN	
HBV DNA	+	+/-	+/-	+ +	+ +

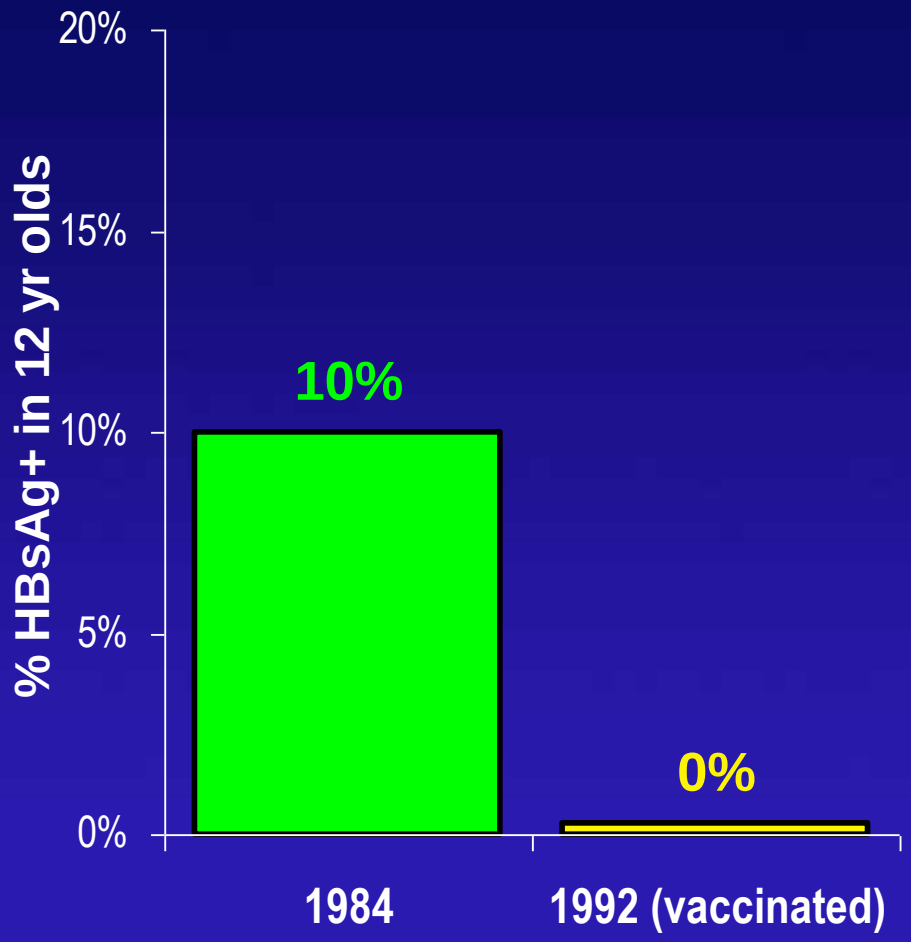
	ACUTE HBV			CHRONIC HBV		IMMUNE	
	early	window	late	eAg+	eAg -	past HBV	vaccine
HB_sAg	+	±	–	+	+	–	–
anti-HBs	–	–	±	–	–	+/-	+/-
HB_eAg		–	±	+		–	–
anti-HBe	–	–	±	–	+	+	–
anti-HB_cIgM	+ +	+ +	+ +	–	–	–	–
anti-HB_cIgG	–	–	+	+	+	+	–
Serum ALT	>5x ULN			>ULN		< ULN	
HBV DNA	+	+/-	+/-	+ +	+ +	–	–

Route of acquisition of Chronic HBV infection in NZ



- Vaccine available, cheap, >99% effective

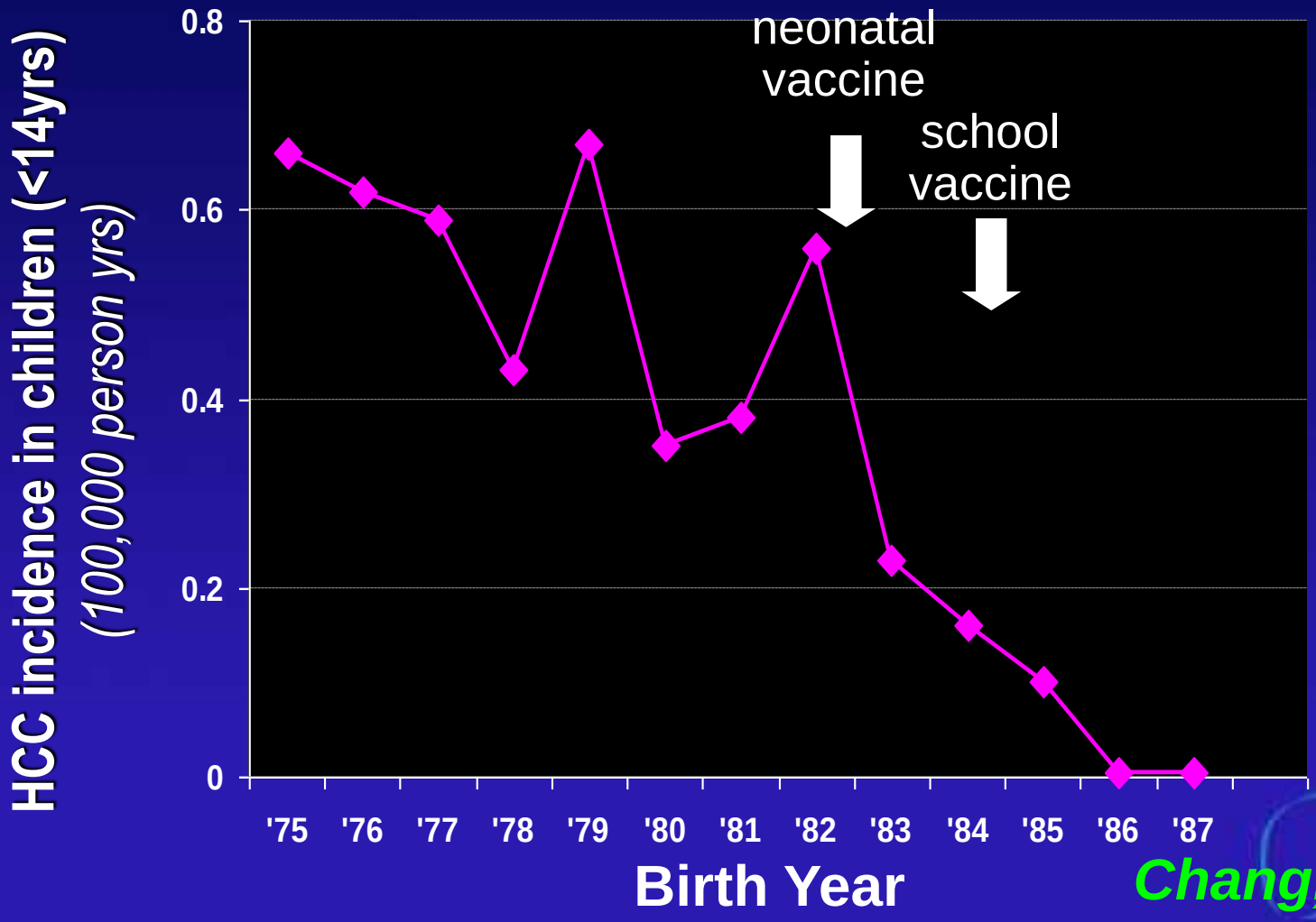
Control of HBV in New Zealand Neonatal Vaccination Program (1987)



Lucas et al. *NZ Med J* 1994; 107:266-8

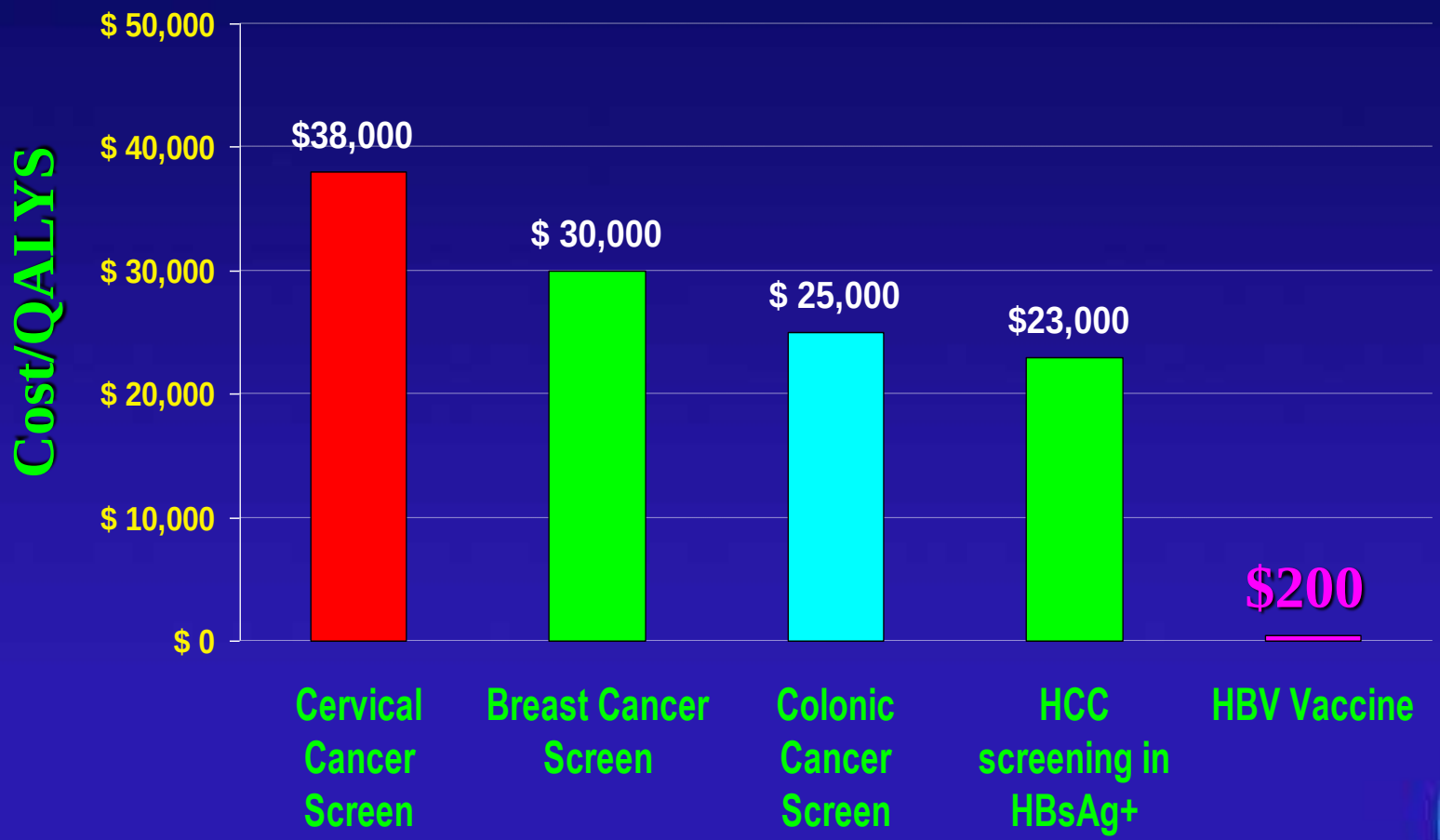
Prevention of HBV-related Hepatoma

Vaccination in Taiwan



Chang,1997

HCC Surveillance in Chronic HBV Infection
Cost-Effectiveness Comparison

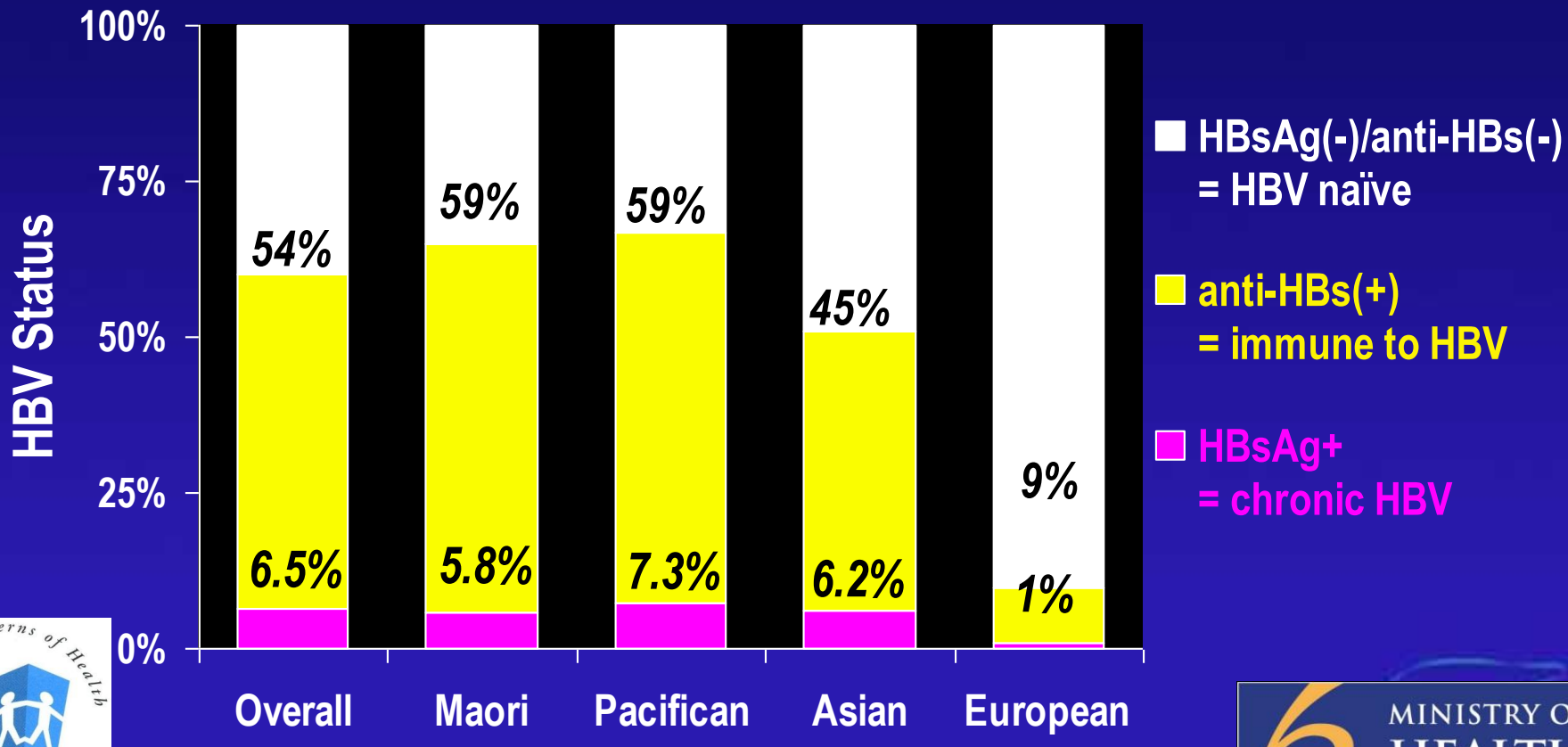


National HBV Screening Programme

Target Maori, Pacific and Asians >15 yrs

- 177,292 screened July 1999 - July 2002

⇨ 11,300 HBsAg+ identified

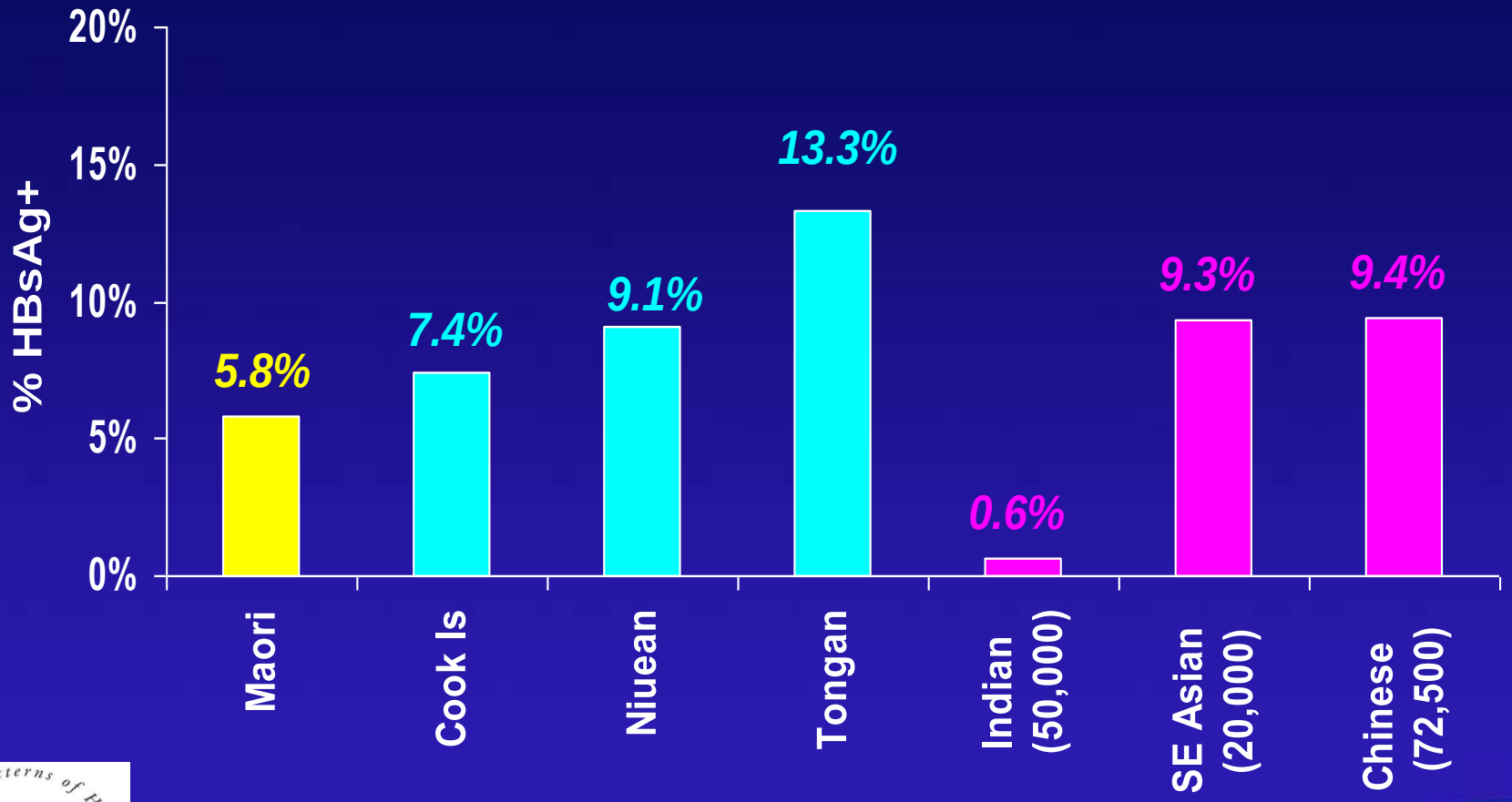


Tracing Patterns of Health
THE HEPATITIS FOUNDATION

edin 2012

MINISTRY OF HEALTH
MANATŪ HAUORA

National HBV Screening Programme
Prevalence according to Ethnicity



Tracing Patterns of Health
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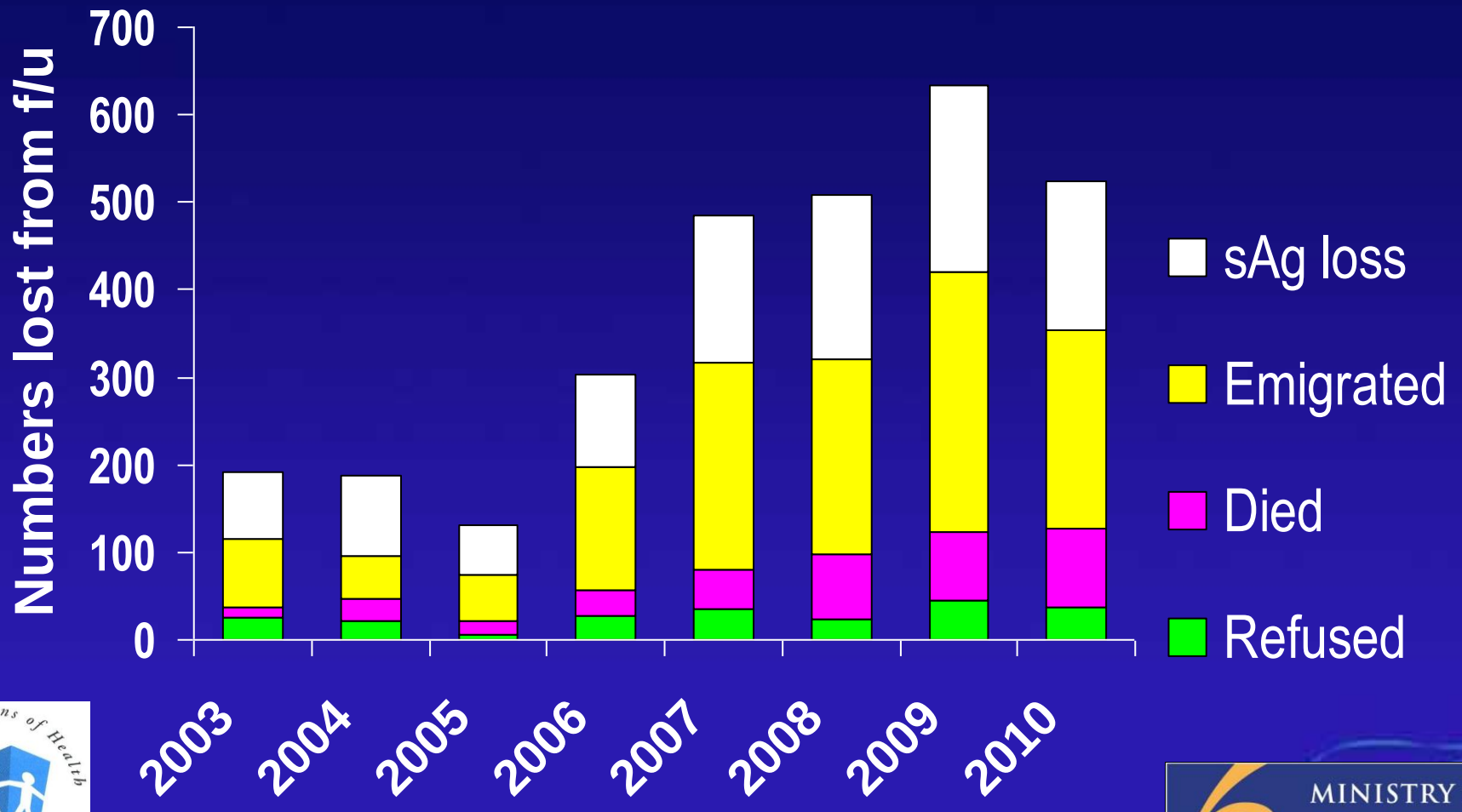
MINISTRY OF HEALTH
MANATŪ HAUORA

National HBV Screening Programme

- 2000-02: MoH-funded screening programme
  - Enrolled 11,300 HBsAg+
- Since 2002: MoH surveillance programme
  - Lost 3100 from original cohort
  - Gained 4100 from opportunistic screening
  - Currently 12,234 enrolled

National HBV Screening Programme
Lost from Surveillance Programme



Tracing Patterns of Health
The Hepatitis Foundation

edin 2012

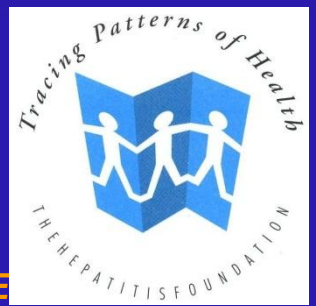
MINISTRY OF HEALTH
MANATŪ HAUORA

National HBV Screening Programme
What is the future?

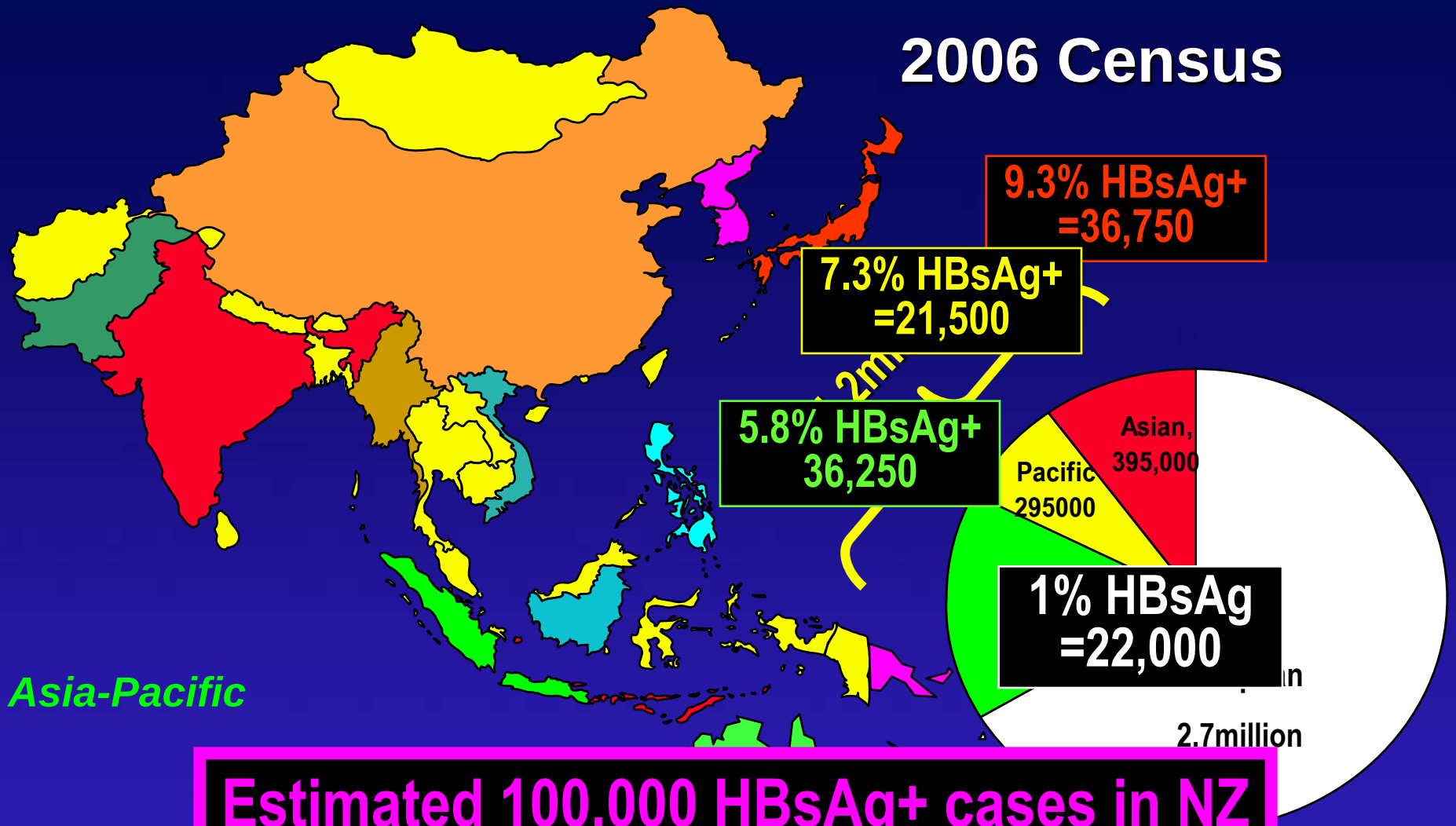
- Estimated 100,000 New Zealnders have HBV
- Only 12,000 in the Surveillance Programme
- Need to increase screening and follow-up
  - ➡Target Maori, Pacific Islanders and Asians

1. GPs ➡opportunistic screening

2. Reopen National Screening Program
- ➡Demonstrate need
- ➡Demonstrate benefits of screening



Demonstrate Need



Estimated 100,000 HBsAg+ cases in NZ

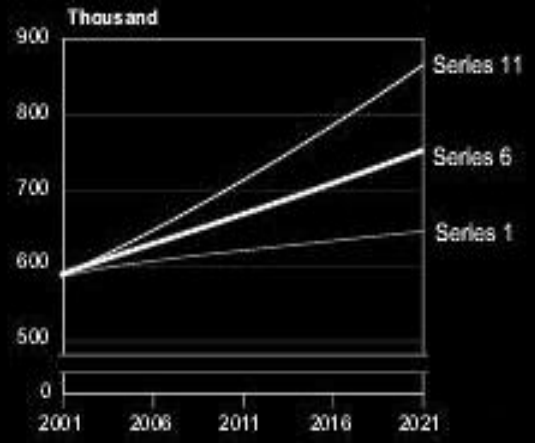
➡>60,000 cases NOT YET DETECTED

*(assumed **NO** childhood infections since 1987)*

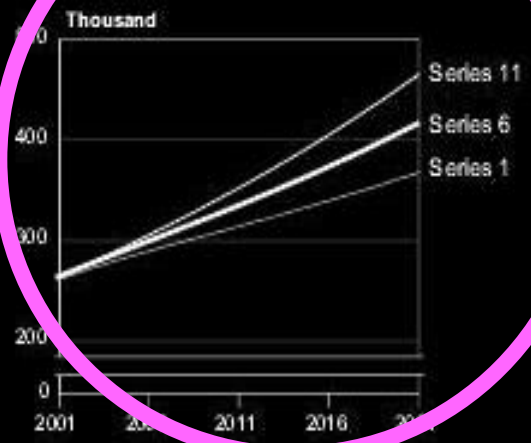
The HBV population is NOT declining

Projected Ethnic Populations 2001-'21

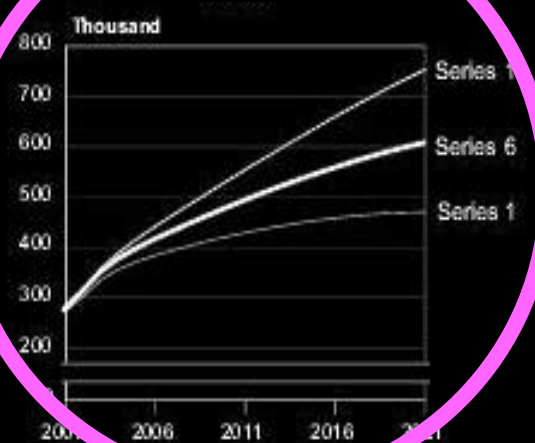
(i) Maori



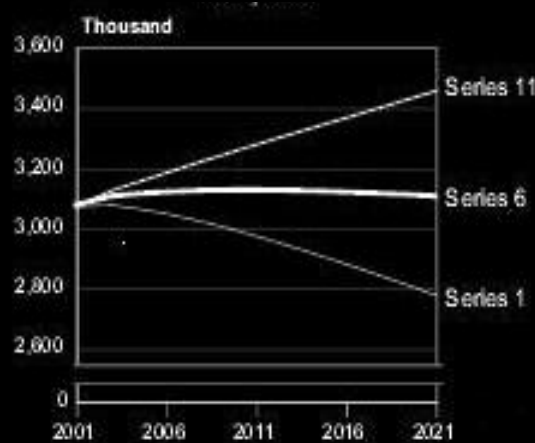
(ii) Pacific



(iii) Asian



(iv) European

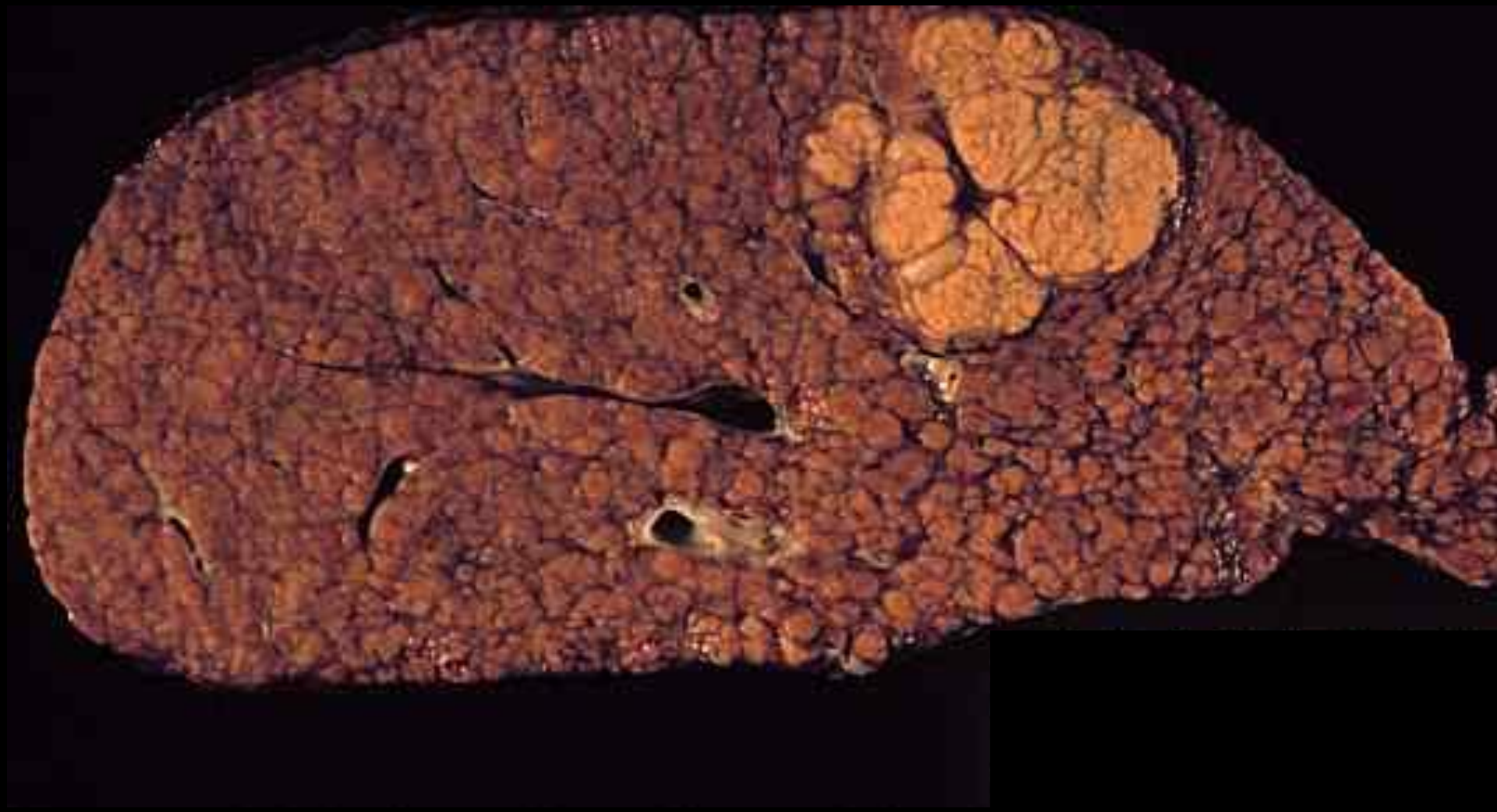


http://www.stats.govt.nz/products-and-services/Articles/pop-proj-Jun07.htm

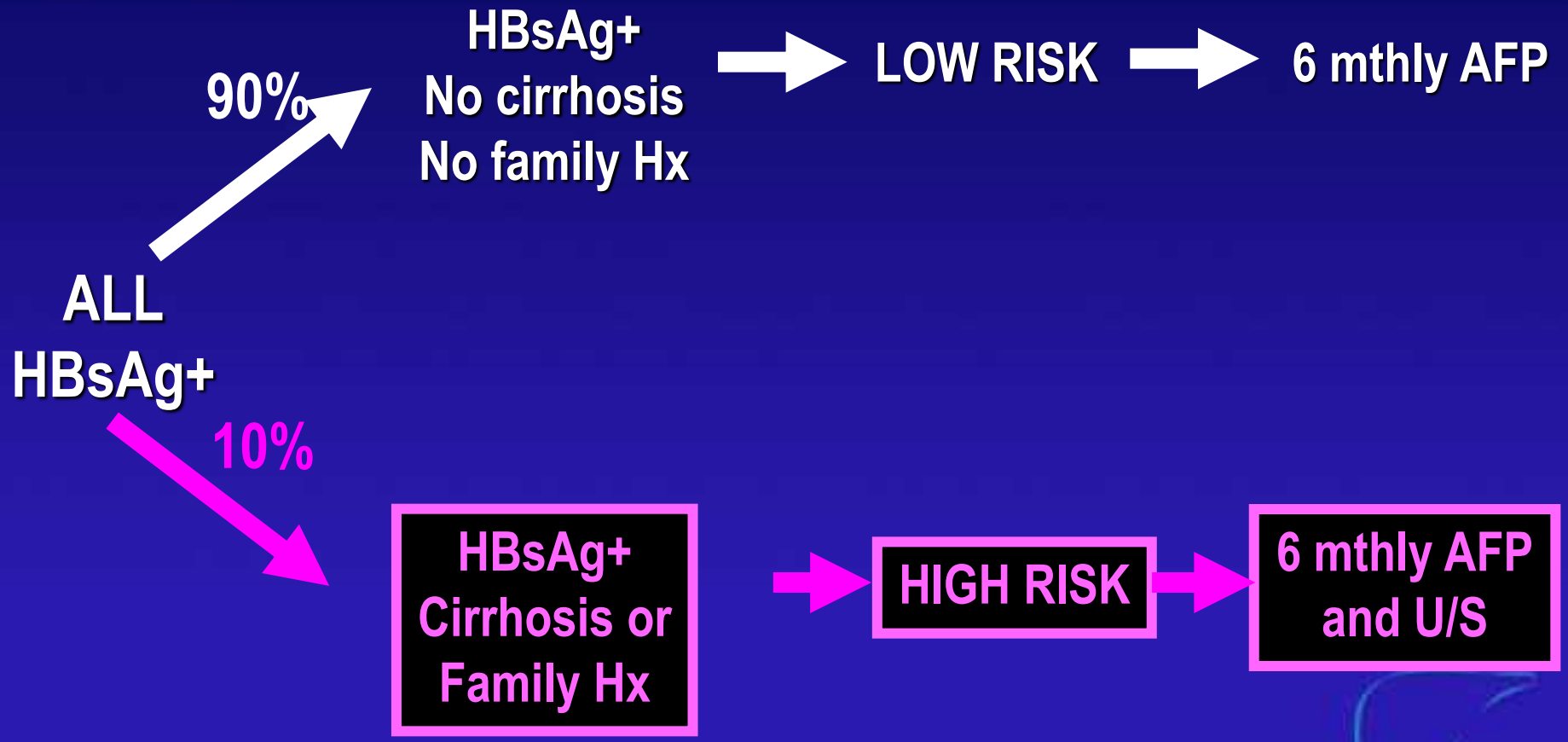
Re-open National Screening
Demonstrate Benefit

- All HBsAg+ offered 6 monthly surveillance for chronic hepatitis and liver cancer (HCC)
  - Safe, effective surveillance tests (AFP, ALT)
  - Effective treatments available
    - HCC ⇨ ablation/resection
    - Chronic hepatitis ⇨ antiviral therapy
  - Do treatments improve survival?

National HBV Surveillance Improves survival



National HBV Follow-up Programme
Surveillance for Hepatoma



National HBV-HCC Surveillance Programme
Outcomes to date (2002-2010)

Patients in the NZ HBV Screening Program

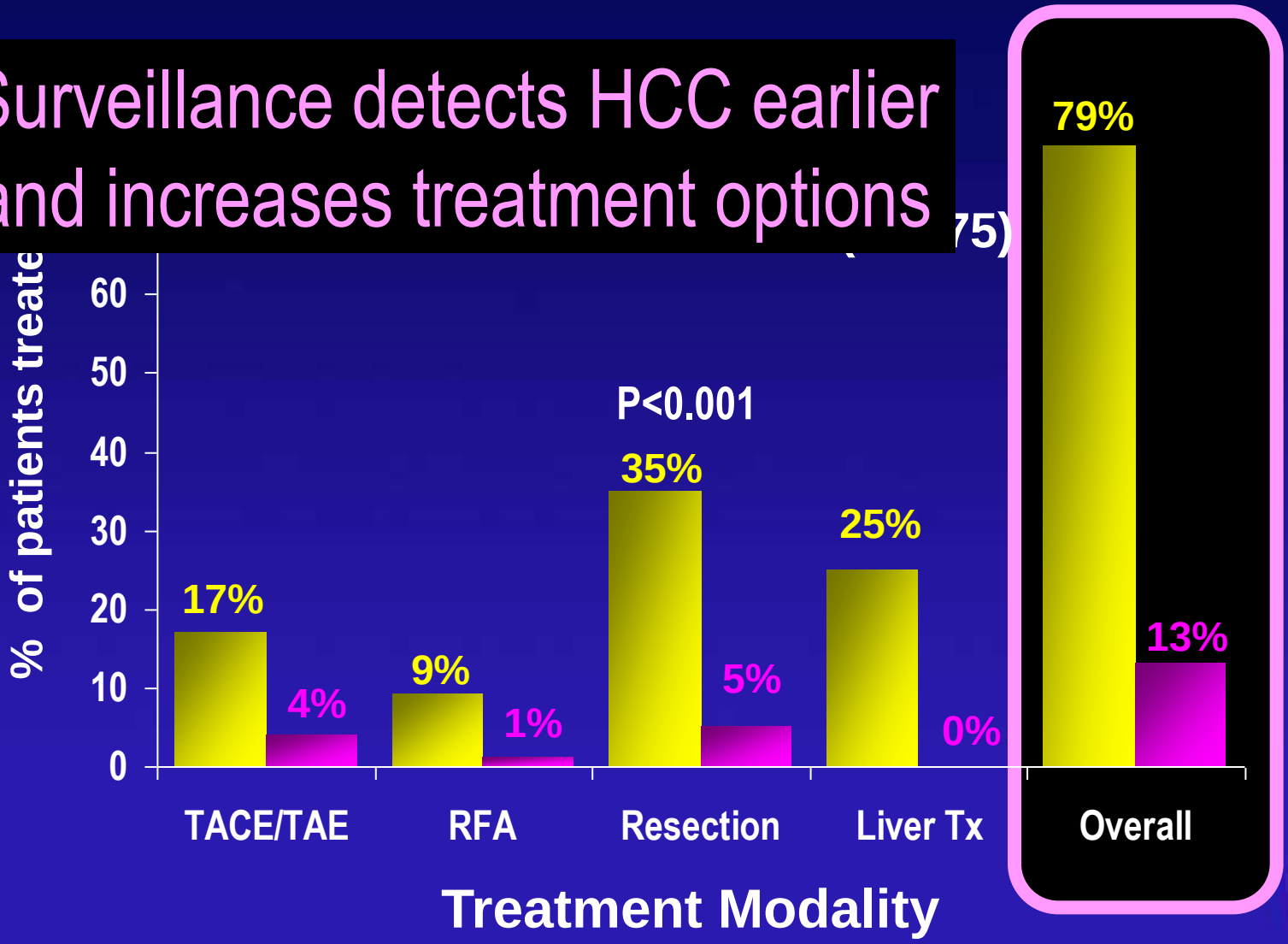
→ 190 HCCs
- Detected at screening visit
- Detected between visits

Patients NOT enrolled in HBV Screening Program

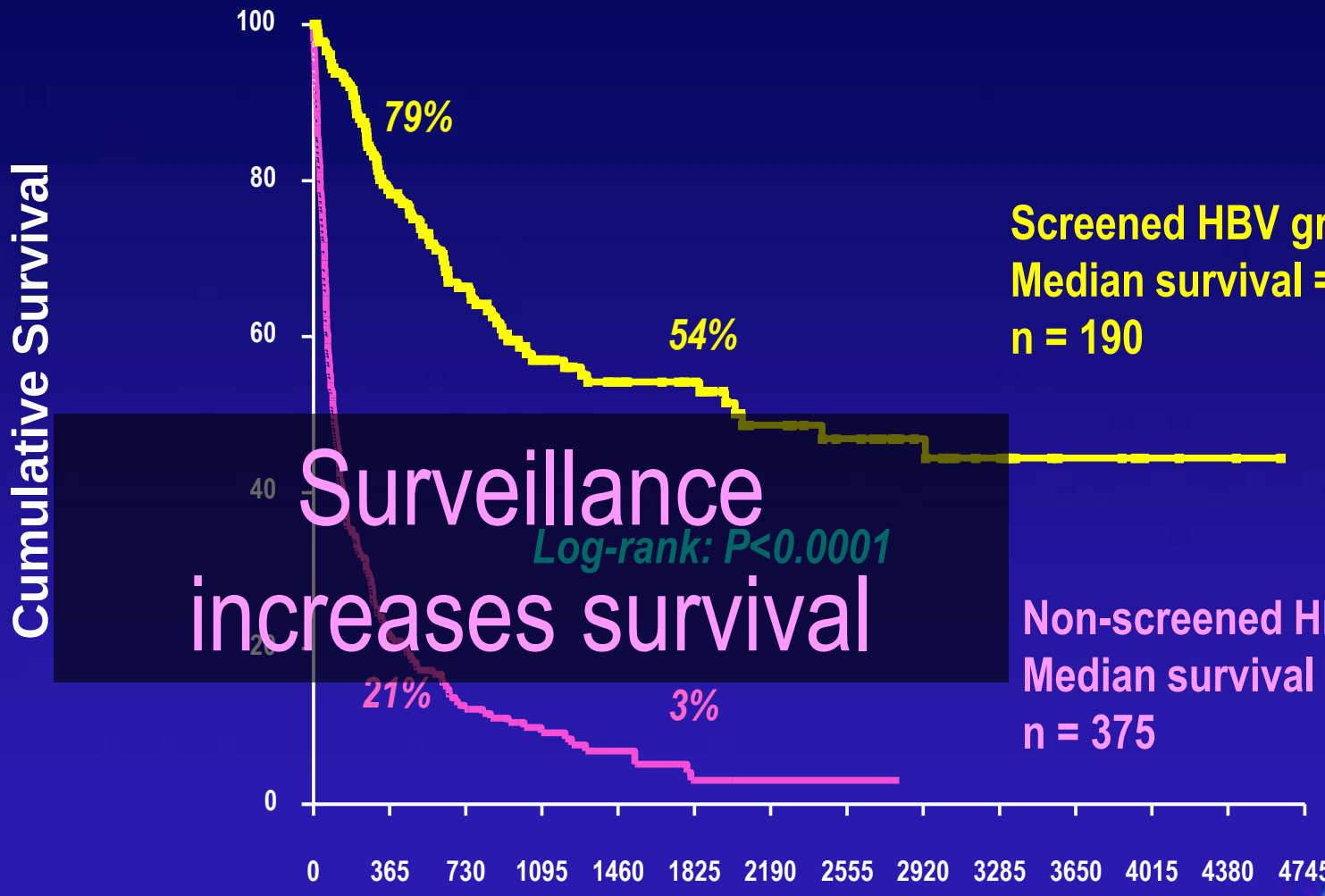
→ 375 Non-screened HCCs
- All symptomatic

Surveillance in HBV increases chance of curative treatment for HCC

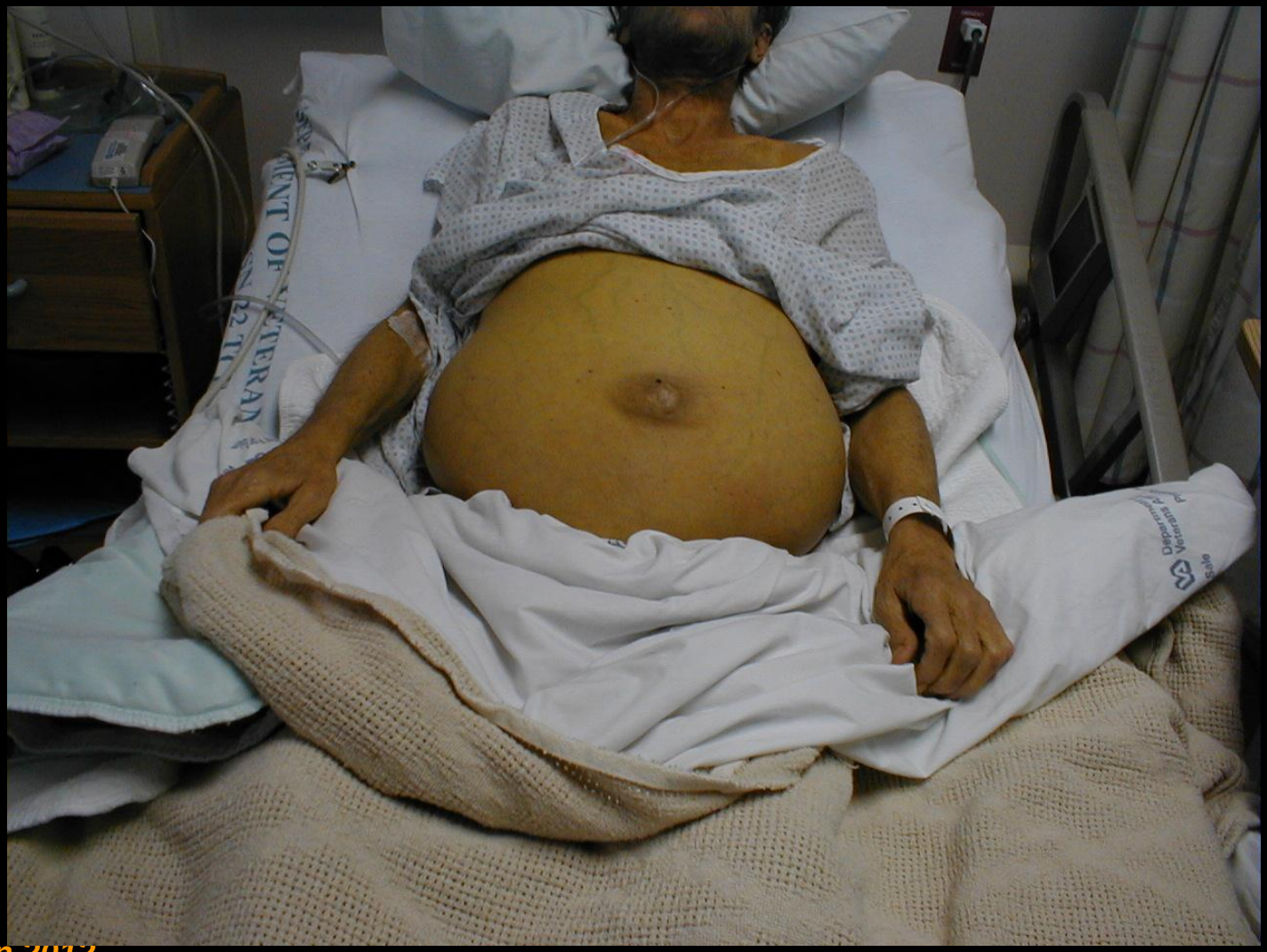
Surveillance detects HCC earlier and increases treatment options



Surveillance in HBV increases survival

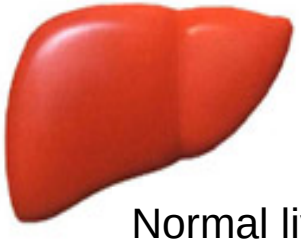


National HBV Surveillance Improves survival



Clinical background
CHB infection has severe consequences

CHB is a long-term disease – liver damage occurs progressively over time (usually several years)

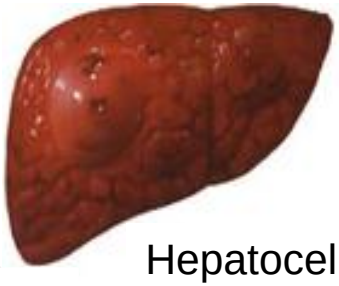


Normal liver

Chronic hepatitis

Cirrhosis

End-stage liver disease



Hepatocellular carcinoma(HCC)

Chronic inflammation and increasing liver damage over time (average 10 -15 years)

Aim of therapy: Prevent progression to cirrhosis, end-stage liver disease, HCC and death

Roche

cobas®
Life needs answers

Goals of treatment in CHB: APASL Consensus Statement 2005

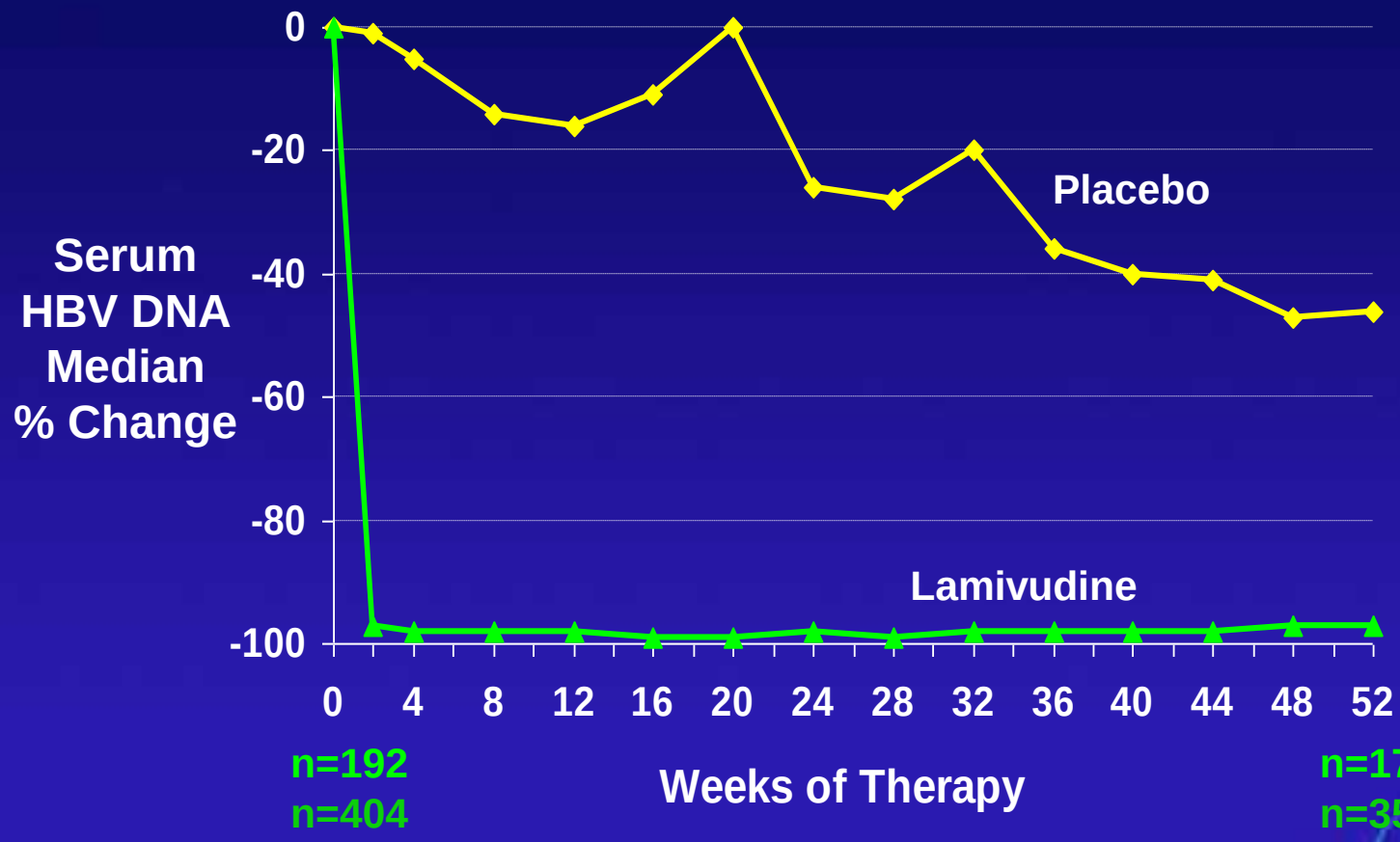
"The ultimate long-term goal is prevention of cirrhosis, decompensation and HCC, and prolong survival.

Sustained viral suppression is the key to the reduction or prevention of hepatic injury and disease progression.

Therefore, the primary goal of treatment for chronic hepatitis B is to eliminate or permanently suppress HBV….. "

Liaw YF et al. Liver Int 2005

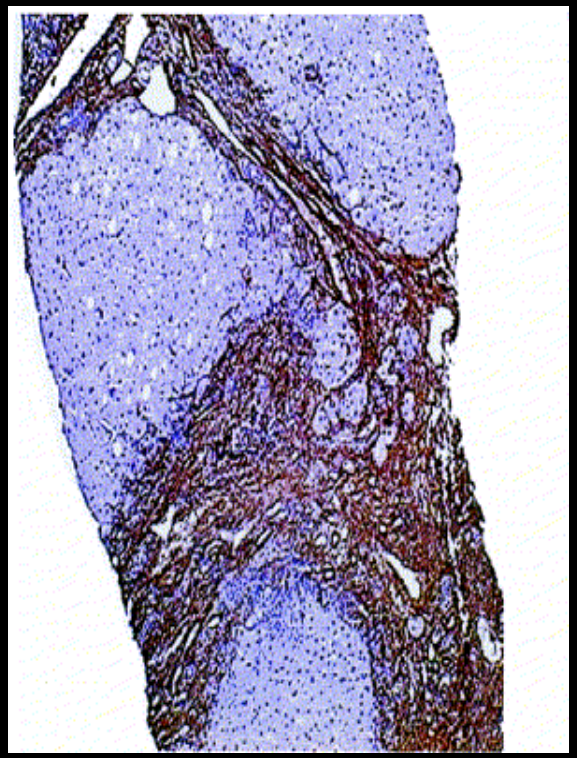
Virological Response
Lamivudine Phase III Data



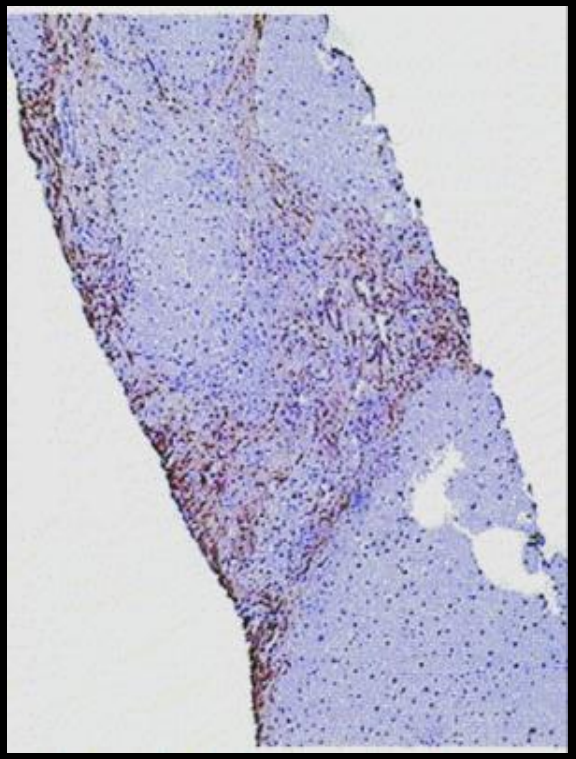
Lai, NEJM, 1998

Treatment in HBV prevents and reverses Cirrhosis

Pre-treatment
Cirrhosis



After 3 years Lamivudine
Mild Fibrosis

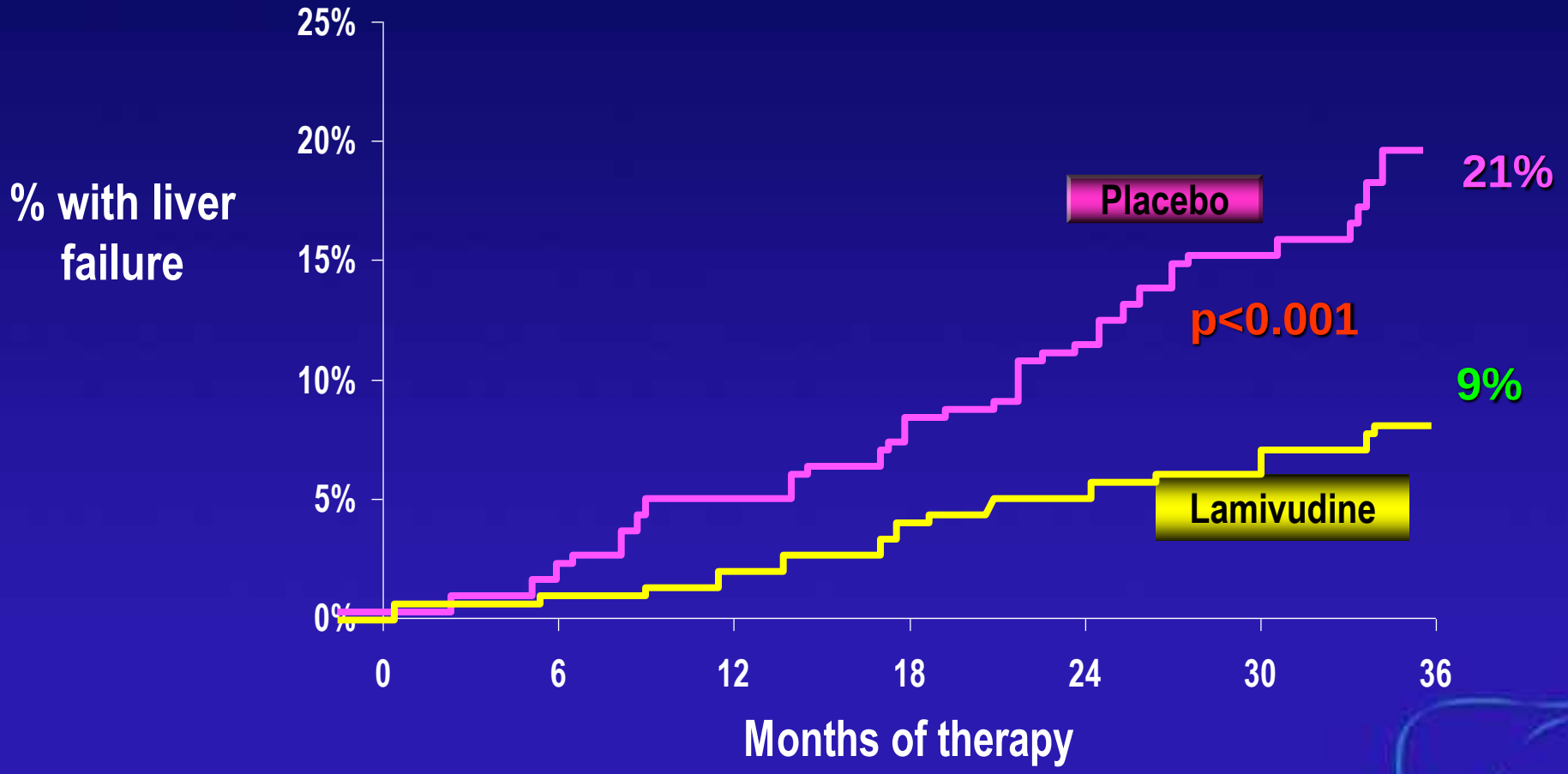


Dienstag,2003

Viral Suppression with Lamivudine may prevent Liver Failure

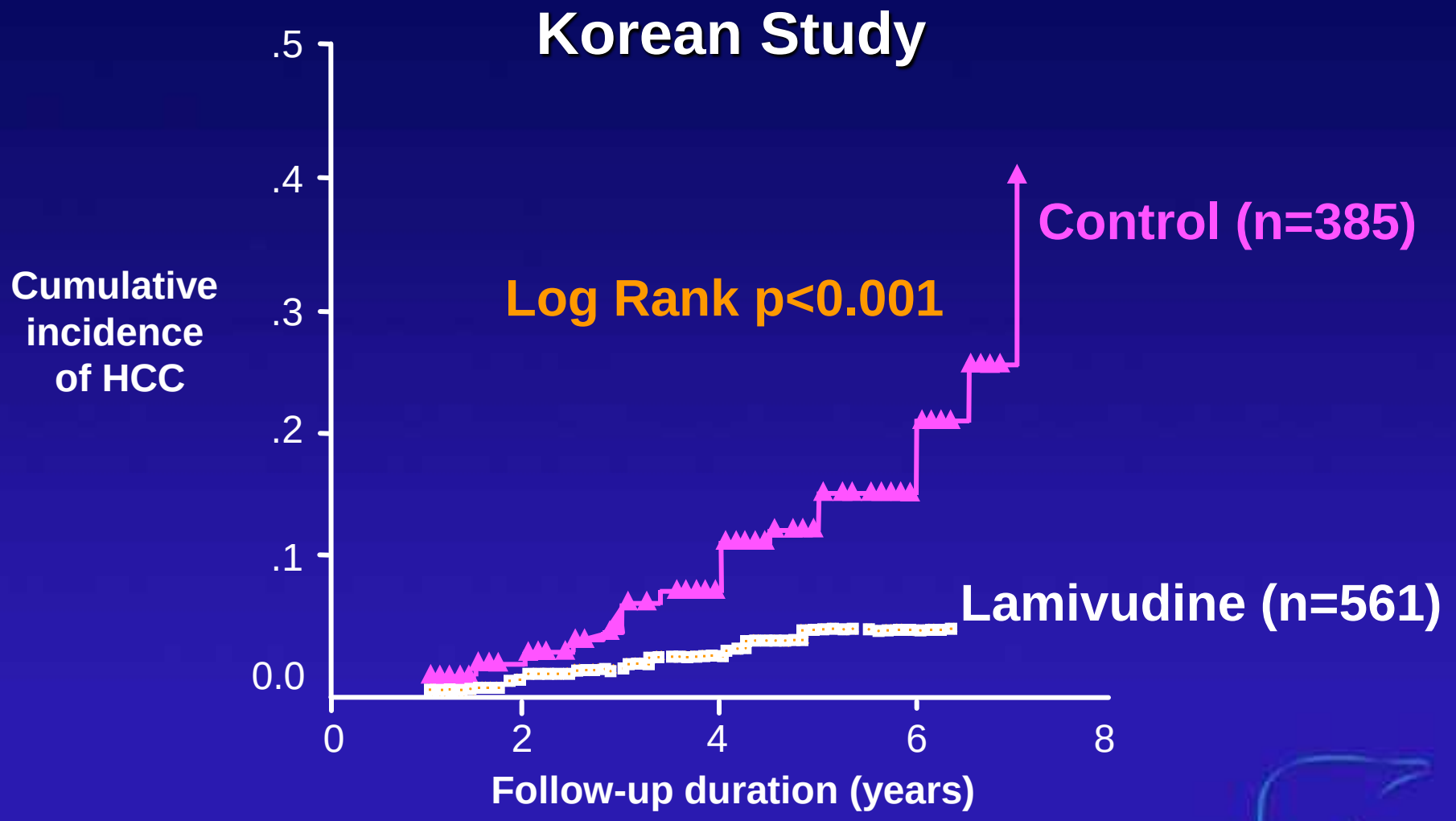
Cirrhosis Asian Lamivudine Multicenter study

RCT of 651 Pts with compensated HBV-cirrhosis



Liaw YF. *NEJM.* 2004;351:1521-1531.

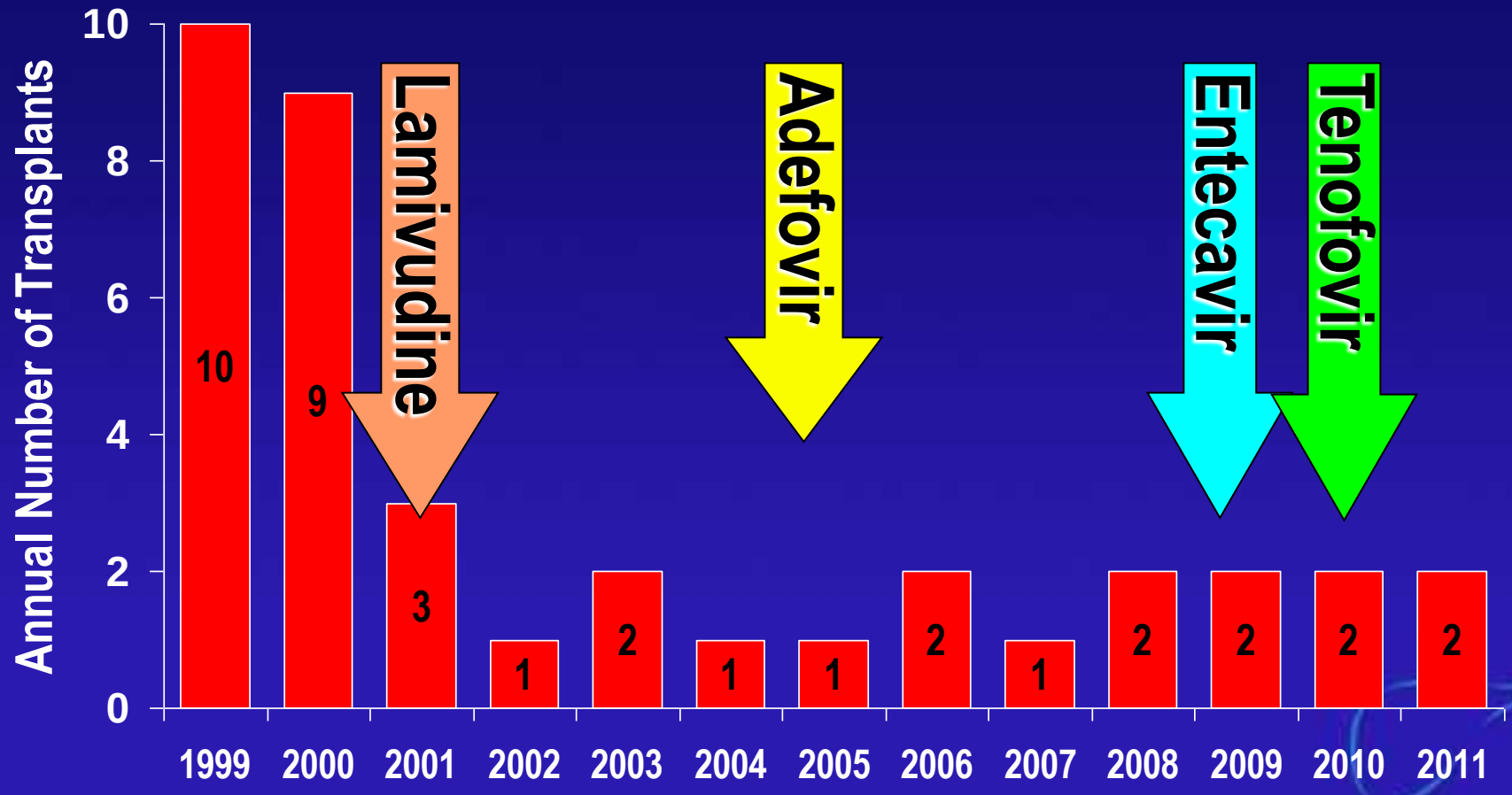
Viral Suppression with Lamivudine may prevent Hepatocellular Carcinoma



Eun JR et al. *J Hepatol* 2010; 53: 118-25

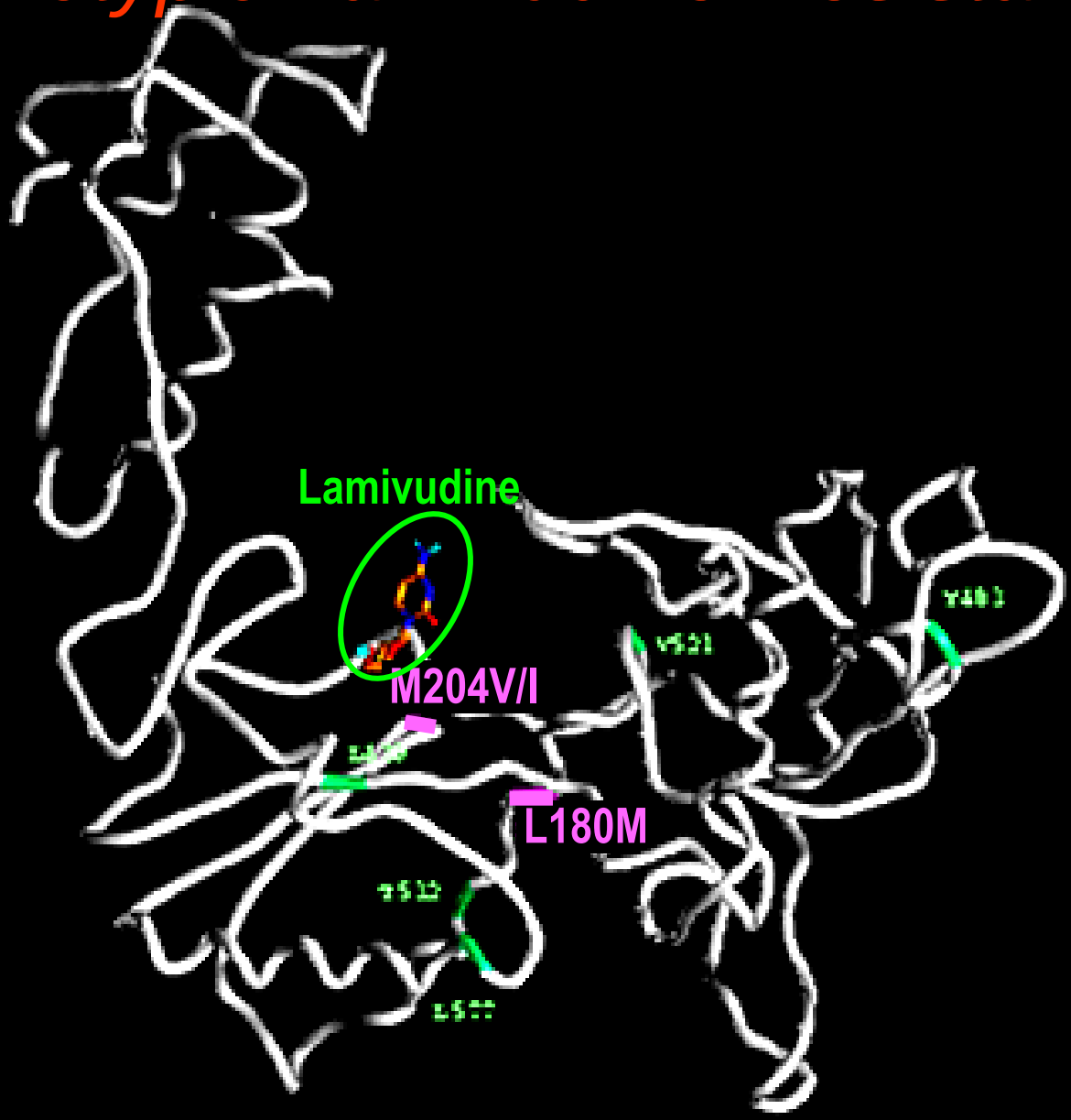
Viral Suppression with Lamivudine may prevent Liver Transplantation

Transplants for Decompensated CHB



NZLTU data 1999-2011

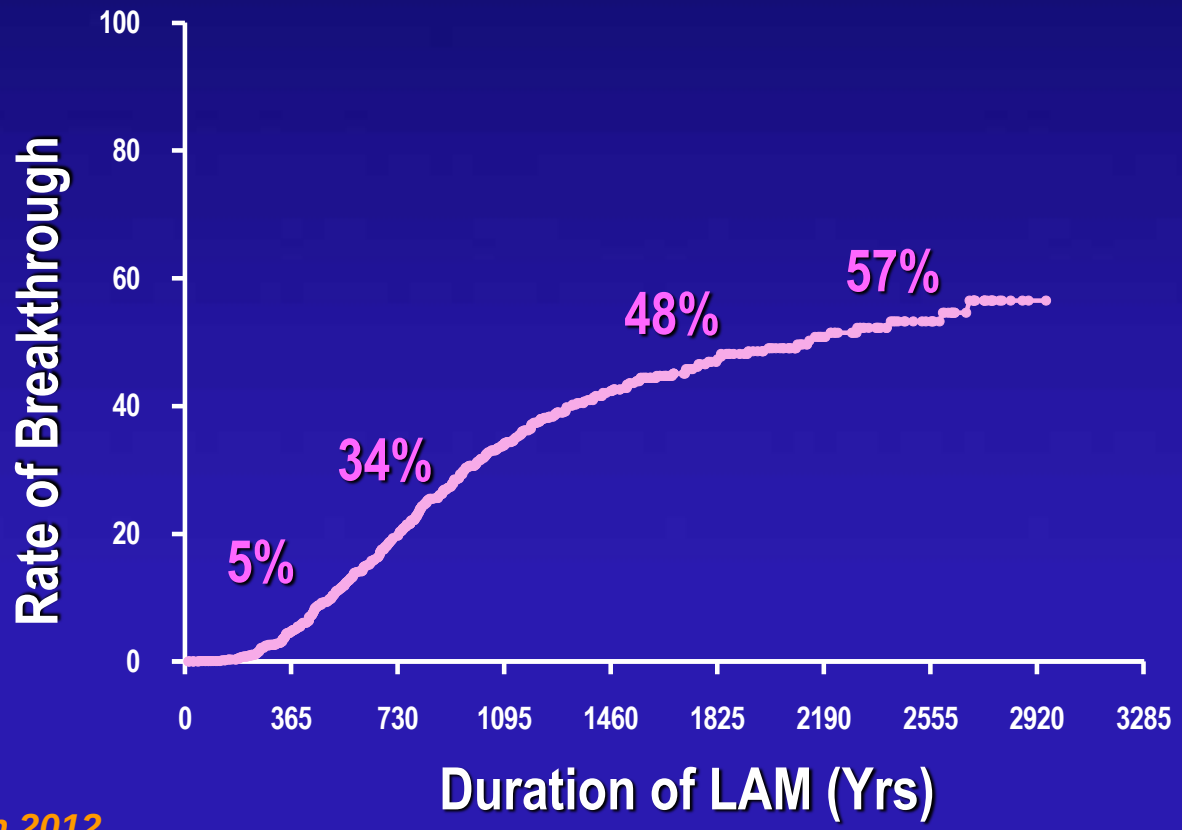
Genotypic Lamivudine Resistance



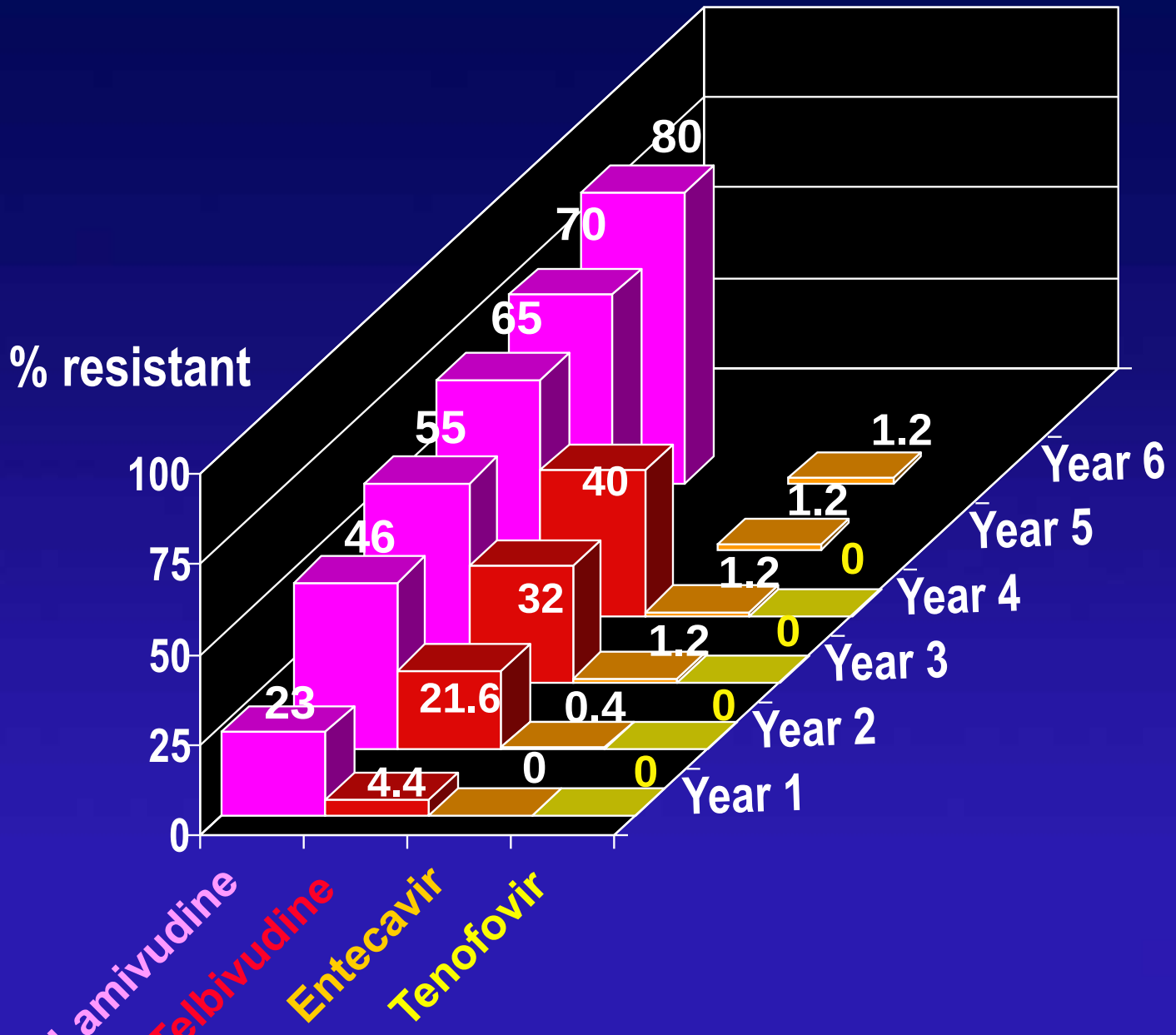
Lamivudine in NZ
Auckland HBV Clinic (1999-2009)

1254 treated with Lamivudine

- **F/U 35 months (0-90)**
- **3 monthly ALT and HBV DNA**
- **Breakthrough in 422 (↑DNA >1 log)**



Resistance to Nucleoside Analogues



Management of CHB in NZ
Summary

- **>100,000 New Zealanders have chronic HBV**
  - »>10,000 New Zealanders have HBV-cirrhosis
  - »200 die each year from HCC/liver failure
- **Suppression of HBV with antiviral therapy prevents disease progression and reverses liver cirrhosis**
- **Current treatments (entecavir, tenofovir) are safe and 100% effective and fully funded for life**
- **Life-long antiviral therapy prevents disease progression and reverses liver cirrhosis**
- **Earlier diagnosis and treatment will prevent liver cancer, liver failure, transplant and death**

Management of CHB in NZ
Challenges

- < 25% all HBsAg+ patients have been recruited into regular follow-up
- <5% all active CHB receive antiviral Rx
- Most cases of liver cancer and cirrhosis present late with symptoms of advanced disease, when therapeutic options are limited and survival poor (<3 months)
- Outcomes can only be improved from earlier diagnosis and surveillance

The National HBV Programme & Hepatitis Foundation of NZ

The Story So Far?

MINISTRY OF HEALTH
MANATŪ HAUORA

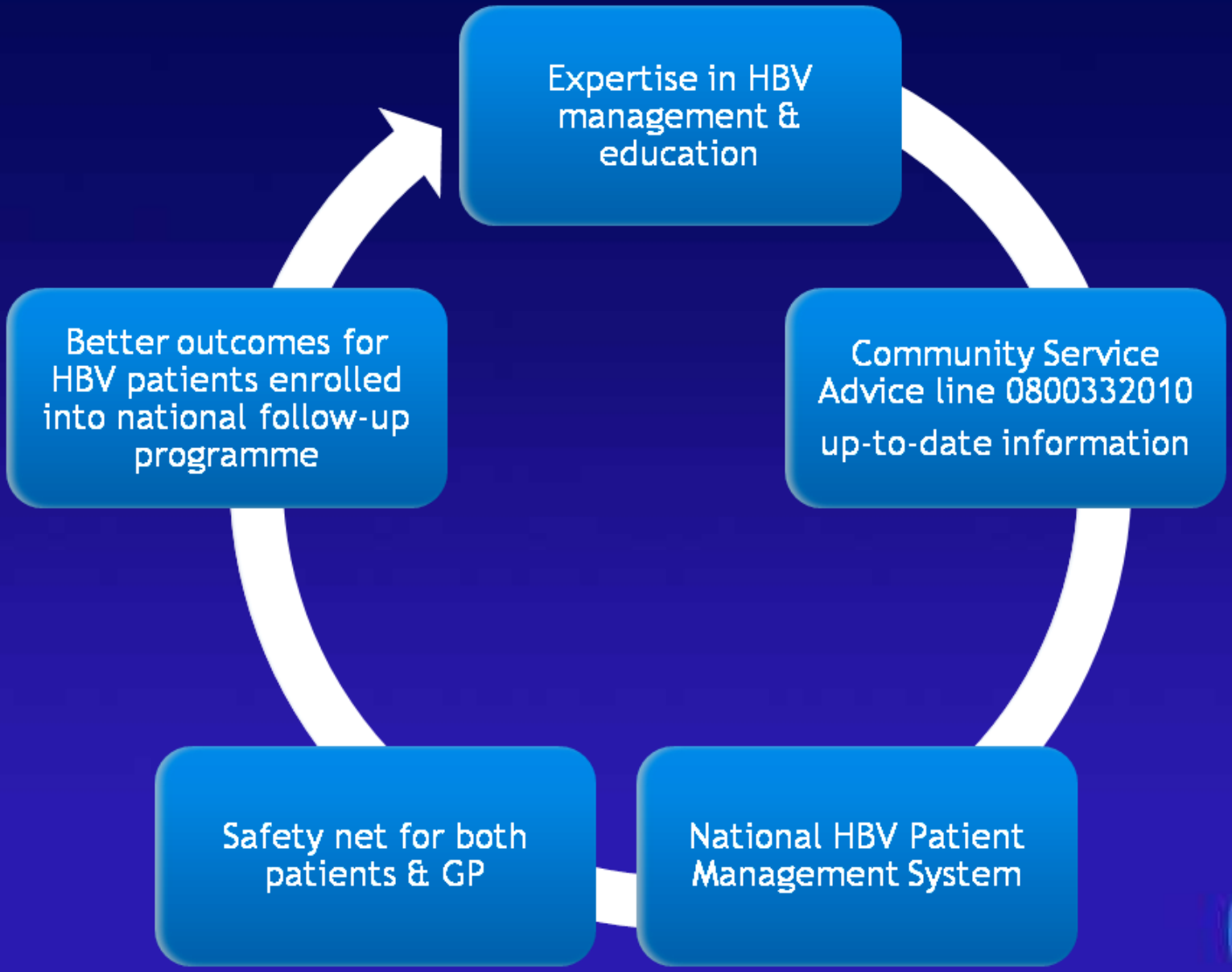
GP CME Dunedin 2012

Tracing Patterns of Health
THEHEPATITISFOUNDATION

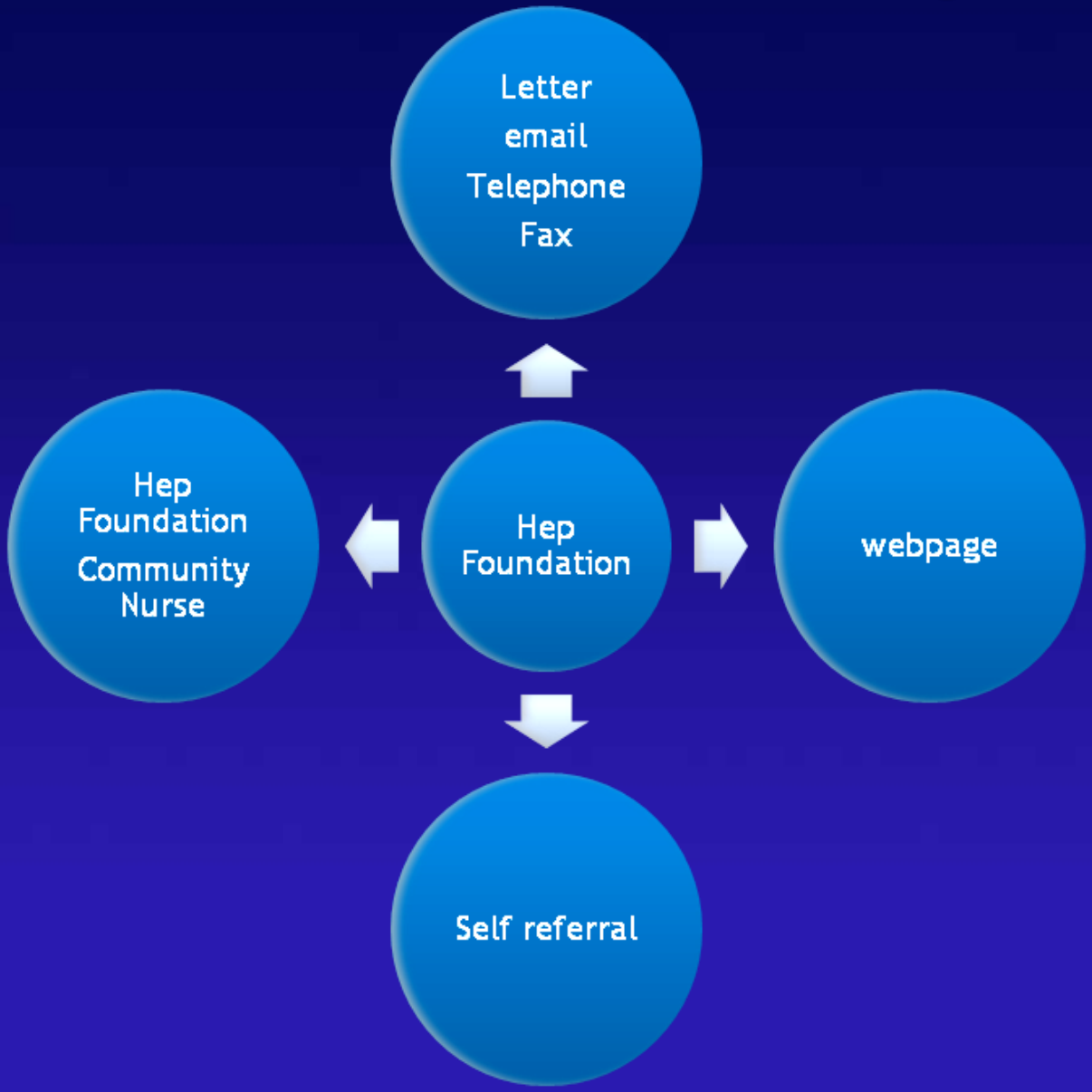
History so far

- Established 30 years ago
- Charitable Trust
- Offices in Whakatane and Tauranga
- Community nurses in Auckland, Northland, Wellington and Eastern BOP
- Largest HBV follow-programme globally
- Employs 22 staff
- Works in partnership with the NZ Liver Unit
- >12,000 clients in long-term follow-up

Why use the Hepatitis Foundation?



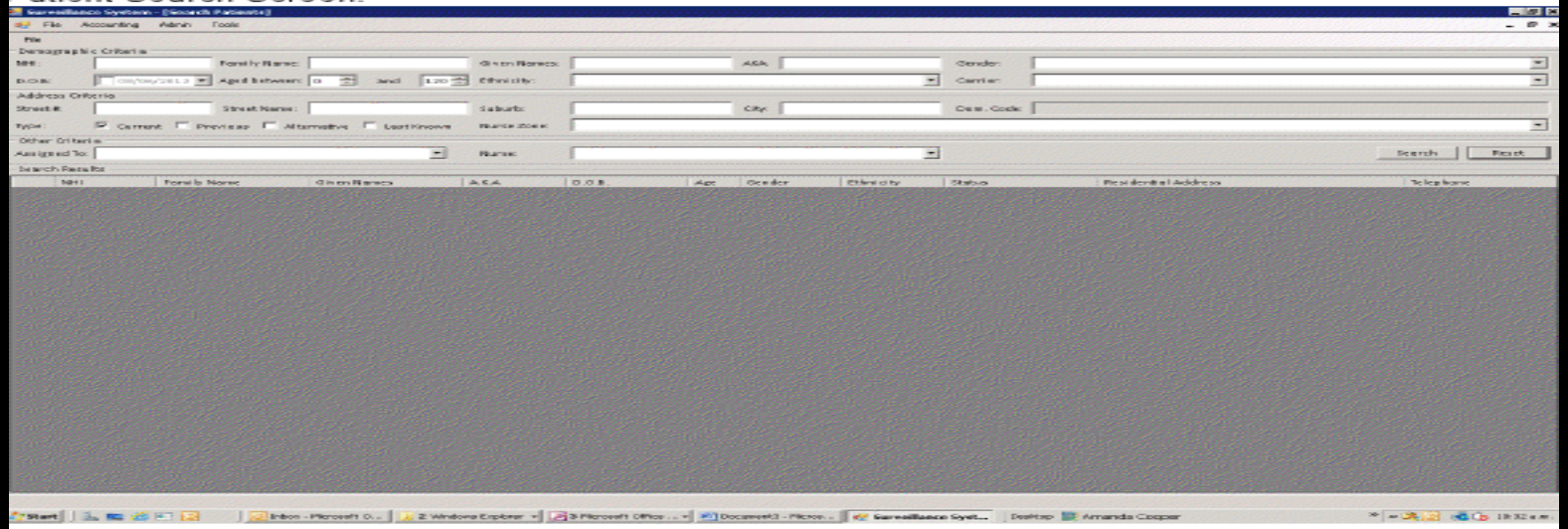
How to refer from Primary Care



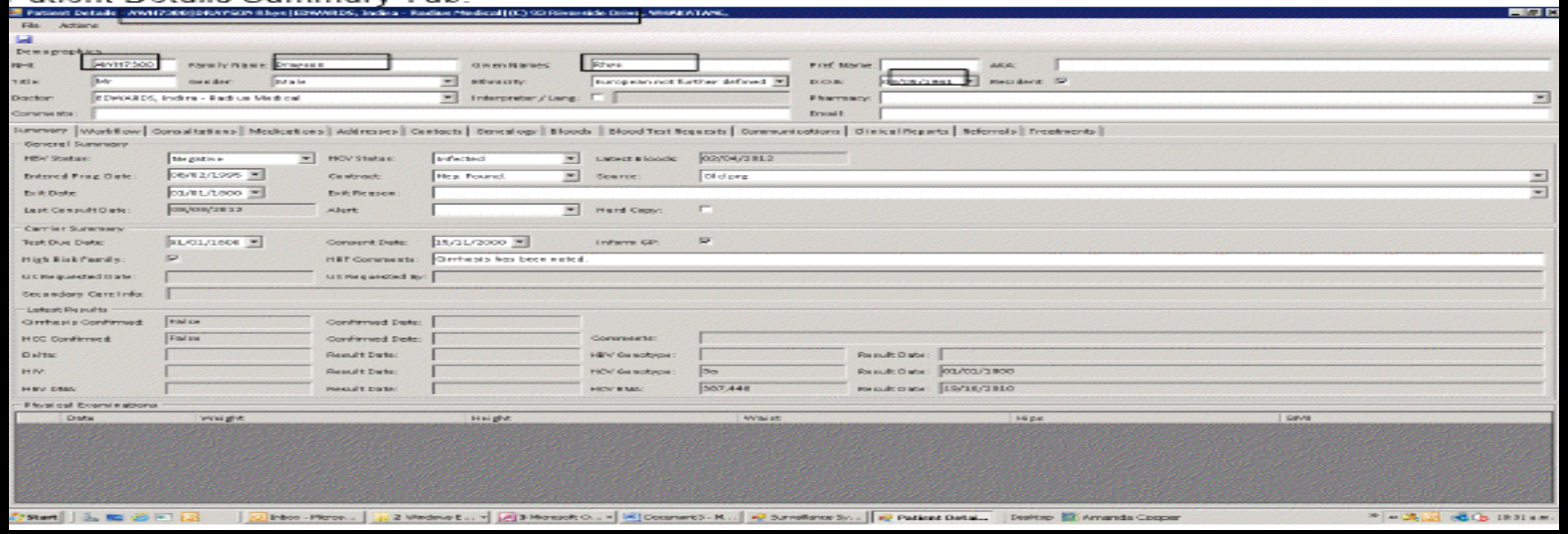
National HBV Surveillance Program

- Contracted to Hep Foundation since 2002
- Still GP-based but community nurse available to chase repeated nonresponders to recall
- Facilitated collection
  - » Preprinted blood forms/HepBFree stickers
- Central database (updated SQL)
  - » ↑ Efficiency
  - » ↑ Quality assurance;
  - » ↑ GP access

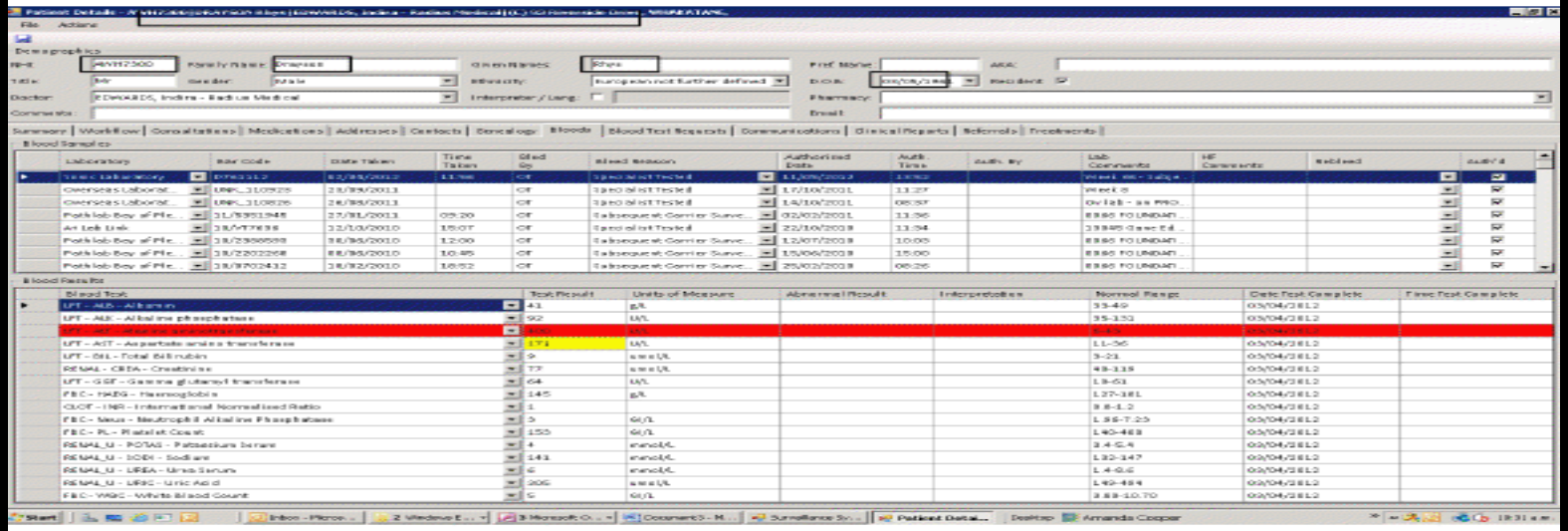
Patient Search Screen:



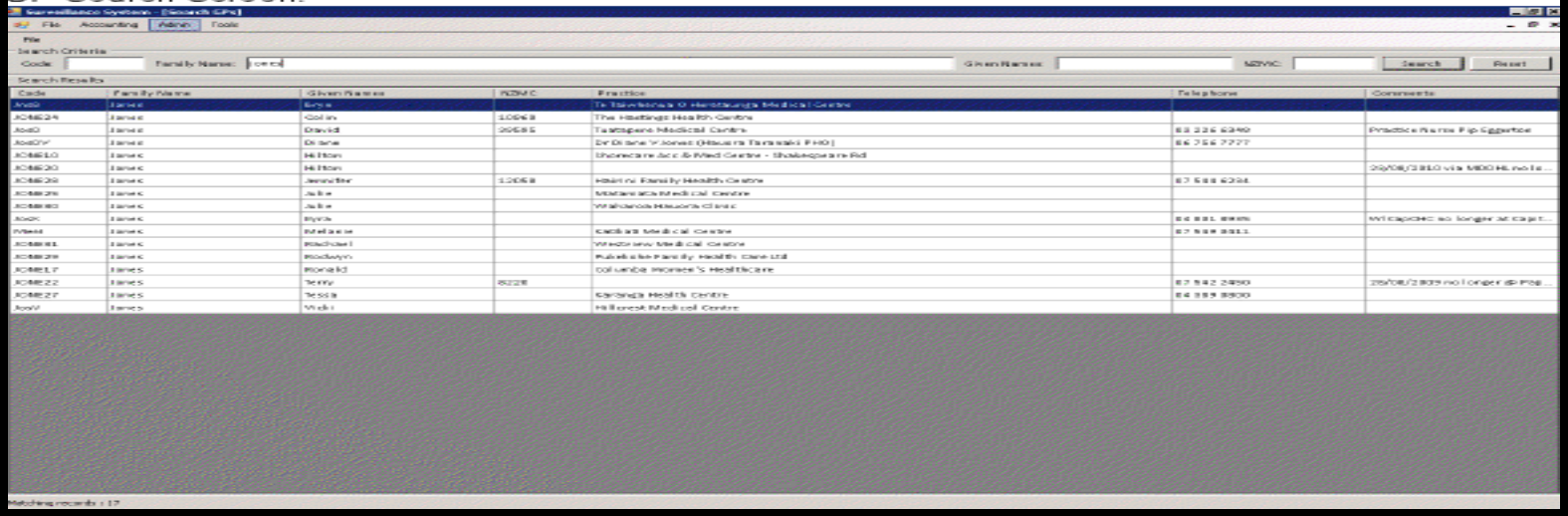
Patient Details Summary Tab:



Patient Blood test results tab:



GP Search Screen:



viral HEPATITIS

AUCKLAND 2012

8TH AUSTRALASIAN CONFERENCE

10–12 September 2012

SkyCity Convention Centre – Auckland, New Zealand

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Supporting the HIV, Viral Hepatitis and Sexual Health Workforce

www.hepatitis.org.au