

Viral Hepatitis

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Viral Hepatitis



- **HAV**
- **HBV**
- **HCV**
- HDV
- HEV
- Other viral: CMV, EBV, HSV
- Unknown



Hepatitis A

Hepatitis A



- Transmitted via the faecal-oral route
 - Faecally contaminated food or water
- Worldwide distribution
- Most common cause of viral hepatitis
- Causes **acute infection** only
 - Asymptomatic → fulminant hepatitis

Hepatitis A



- Diagnosis
 - Prodromal symptoms
 - Jaundice
 - Abdominal tenderness and liver enlargement
 - ALT elevated
 - HAV IgM antibody positive
- Symptoms resolve in majority after 2 months
- Prevention
 - Public and personal health measures
 - Vaccination



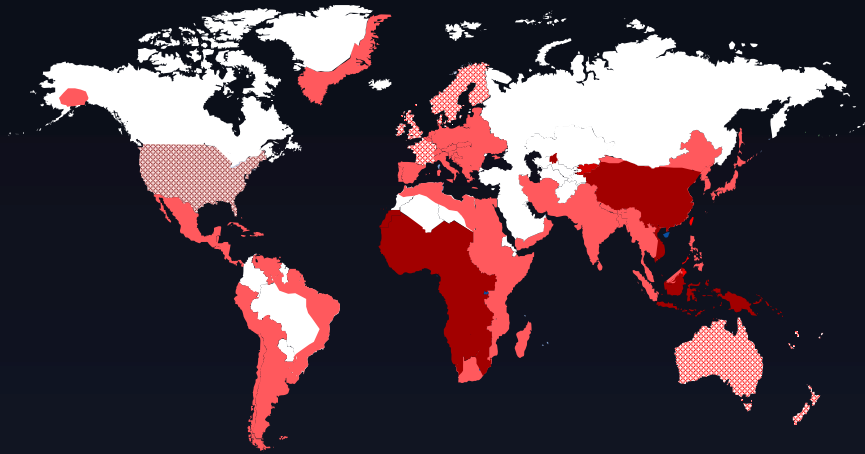
Hepatitis B

Global Importance of Hepatitis B Virus



- Hepatitis B virus (HBV) is one of the world's most common infectious agents
- Serious global public health problem
- One third of world's population (~2 billion) have been infected with HBV
- Estimated 350 million people (~5% of world's population) have chronic HBV infection
- 25-40% (75-160 million) die of cirrhosis or liver cancer

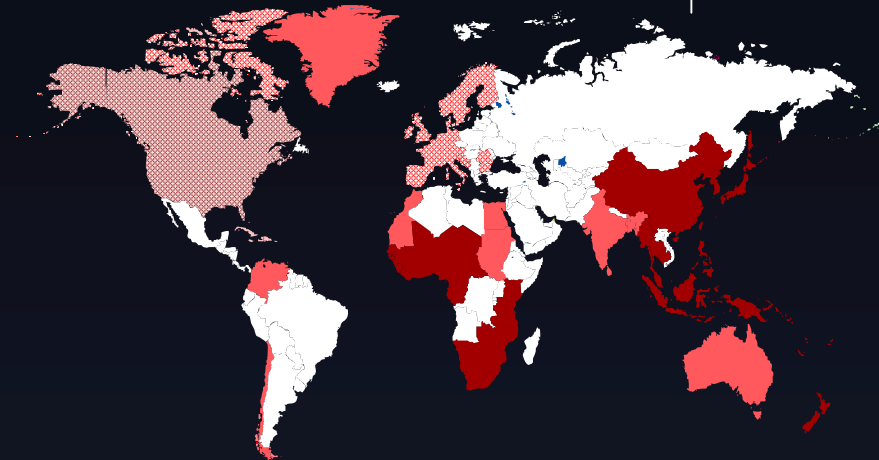
Worldwide Prevalence of HBV and Incidence of HCC



World prevalence of HBV carriers

HBsAg carriers-prevalence

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



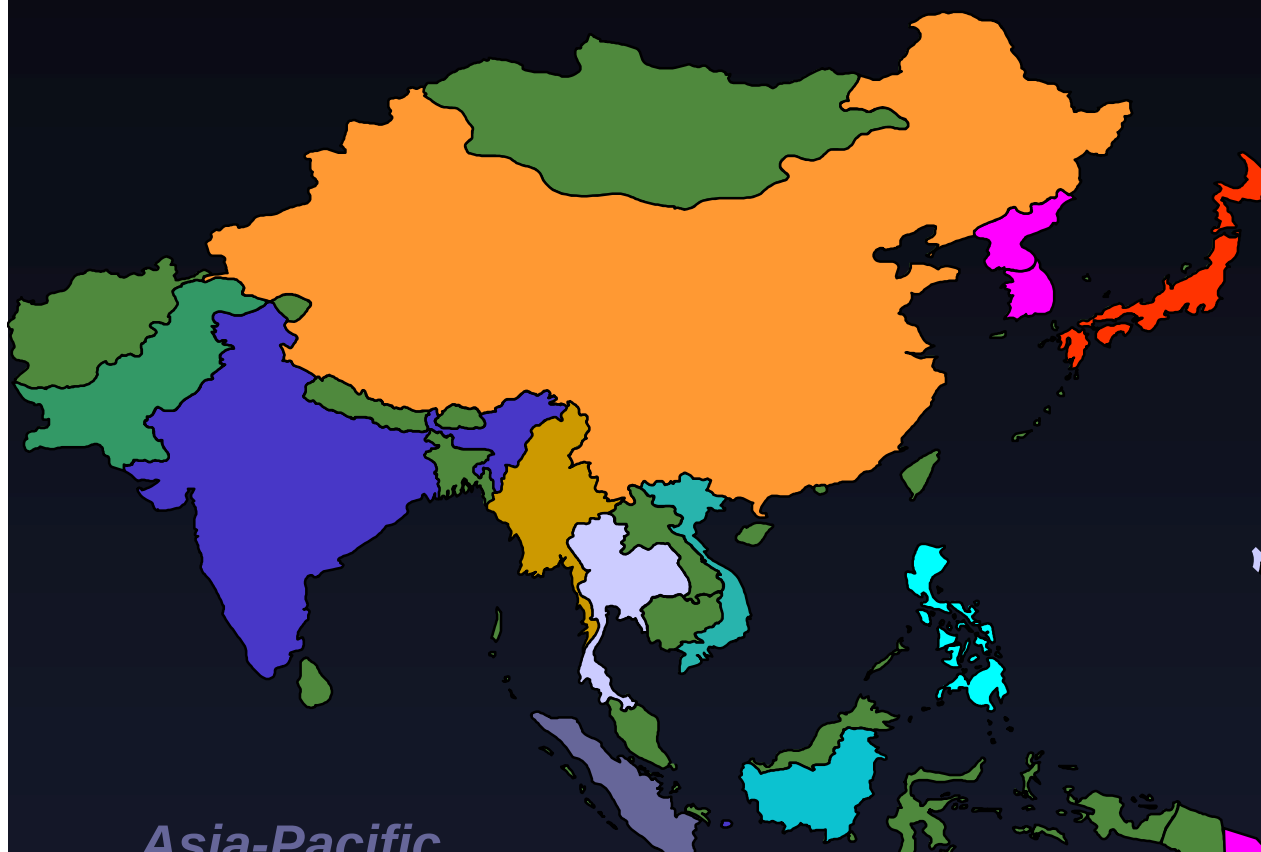
Annual incidence of primary HCC

Cases/100,000 population

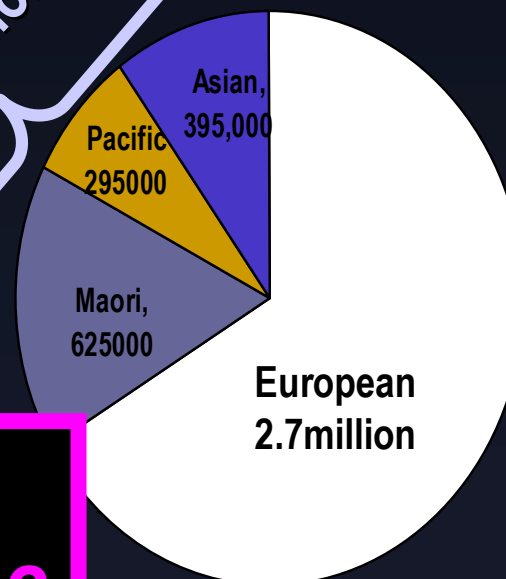
-  1–3
-  3–10
-  10–150
-  Poorly documented



Impact of HBV in NZ



1.2million



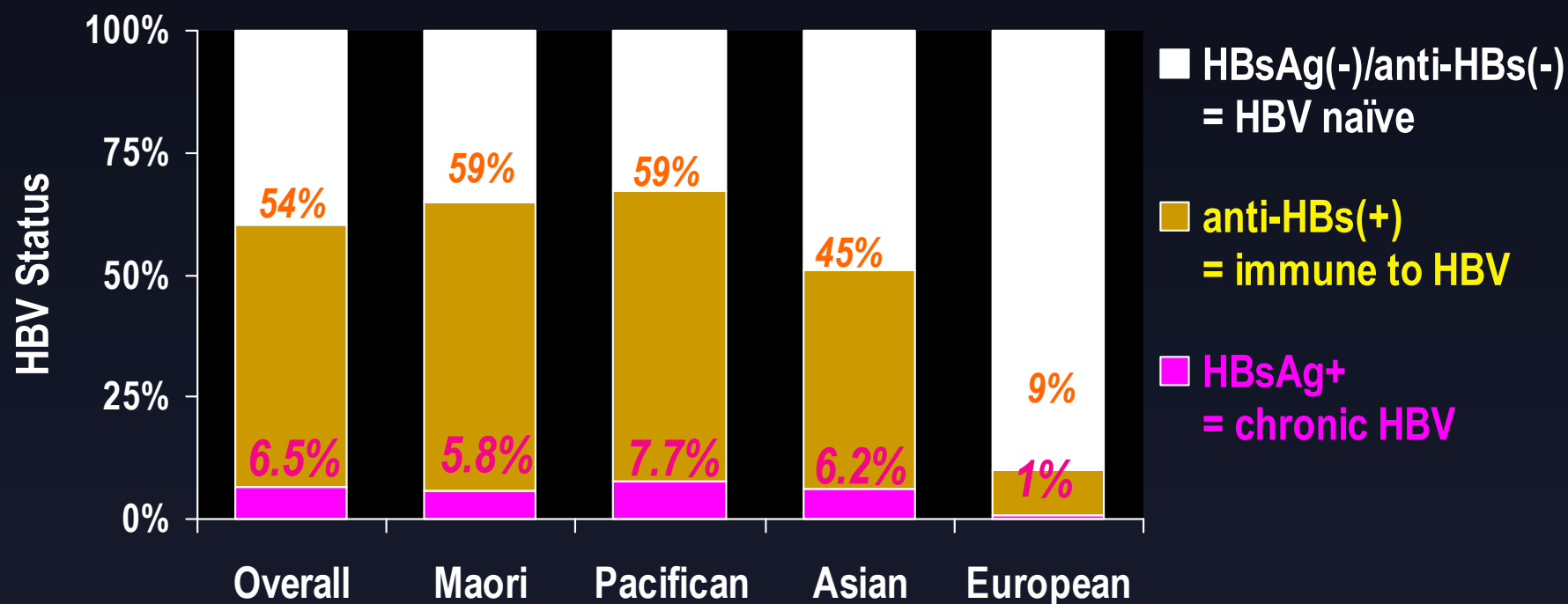
**Estimated 90,000 HBsAg+
living in New Zealand in 2006**

National HBV Screening Programme



177,292 Screened (July 1999 - July 2002)

⇒ 11,300 HBsAg+ identified



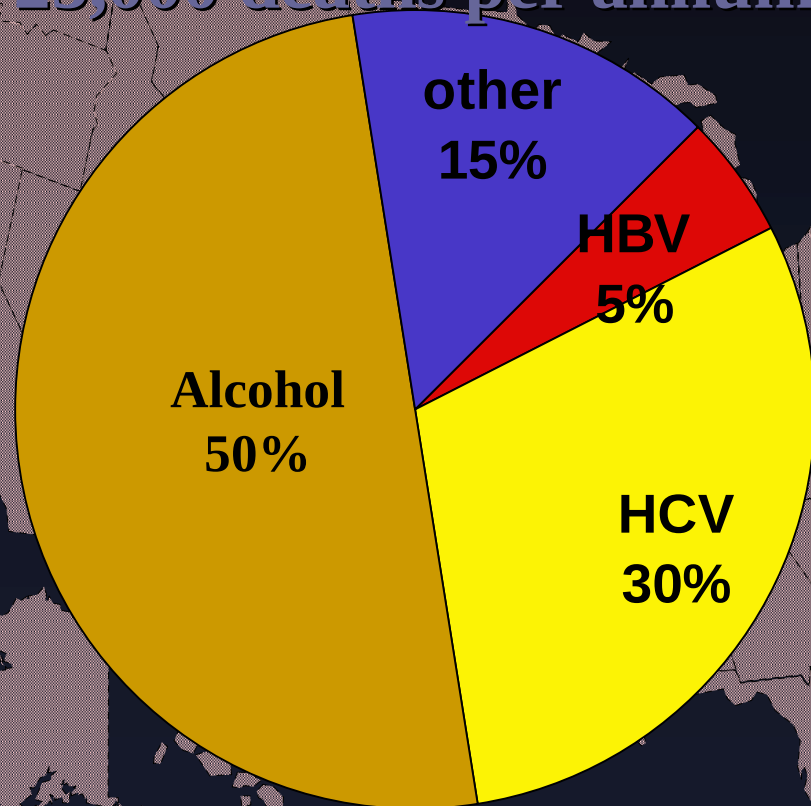
End-Stage Liver Disease in New Zealand

Liver-Related Mortality



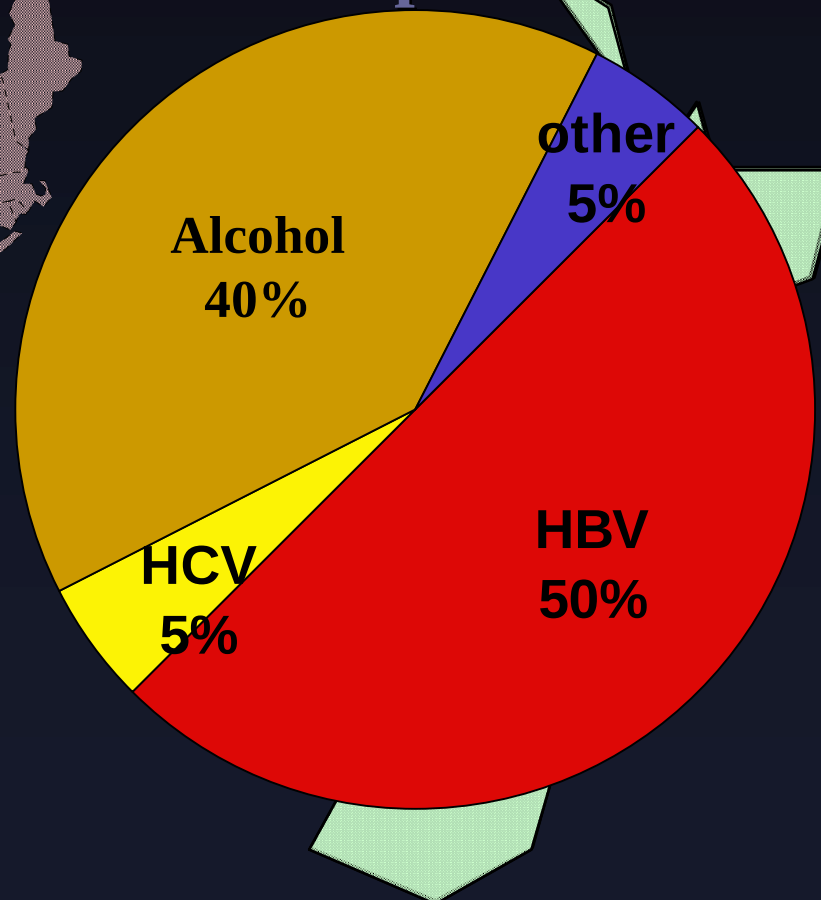
USA

25,000 deaths per annum



New Zealand

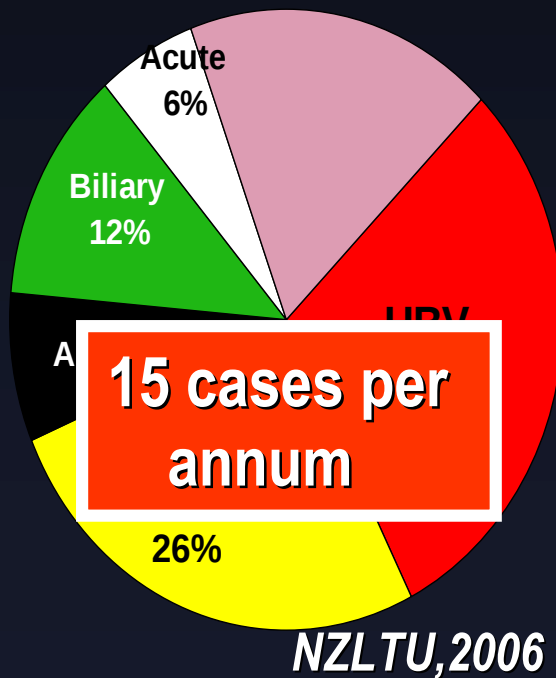
300 deaths per annum



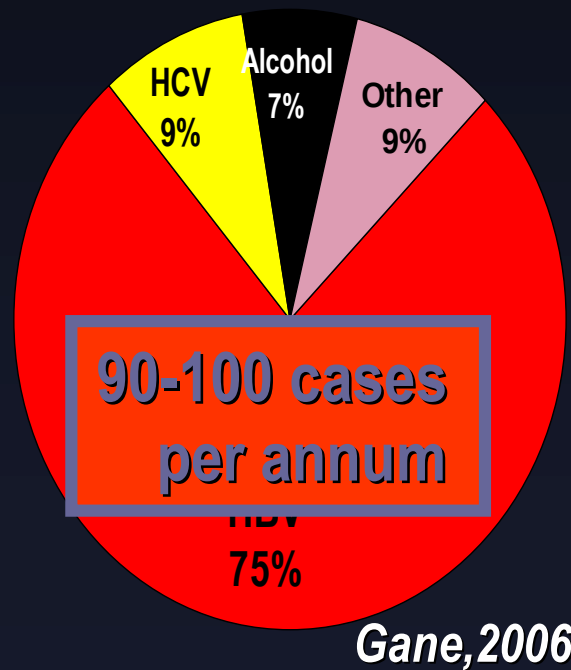
Impact of HBV Infection



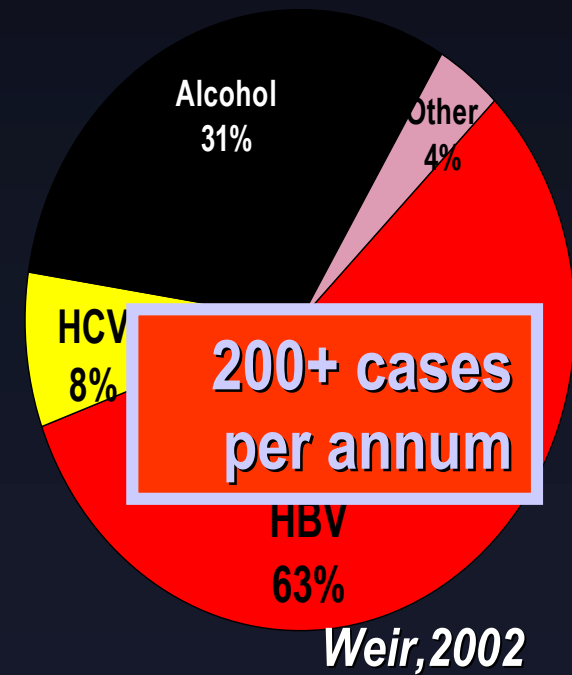
Liver Transplant
1998-2006
(n=290)



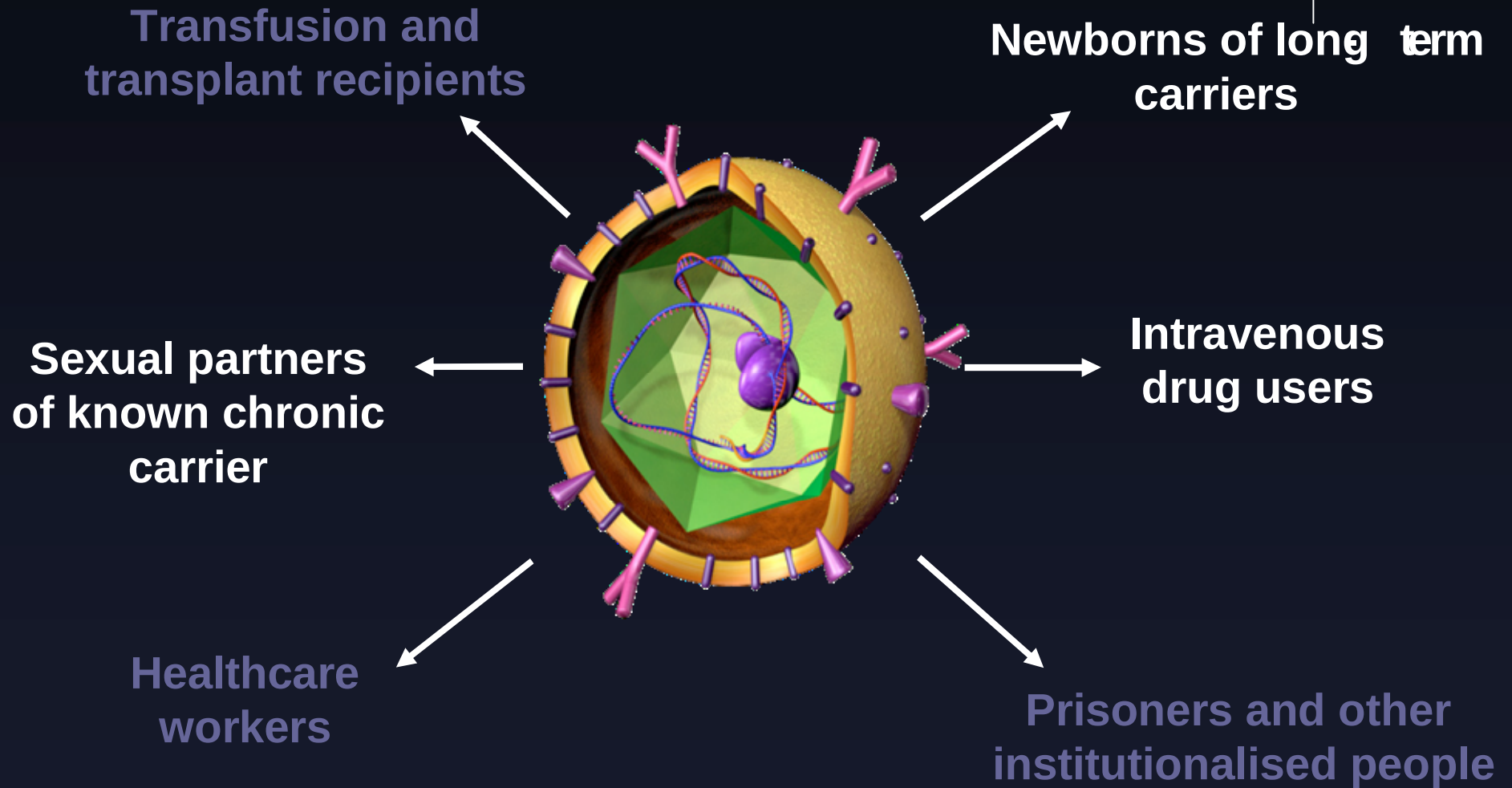
Hepatoma Clinic
2000-2006
(n=544)



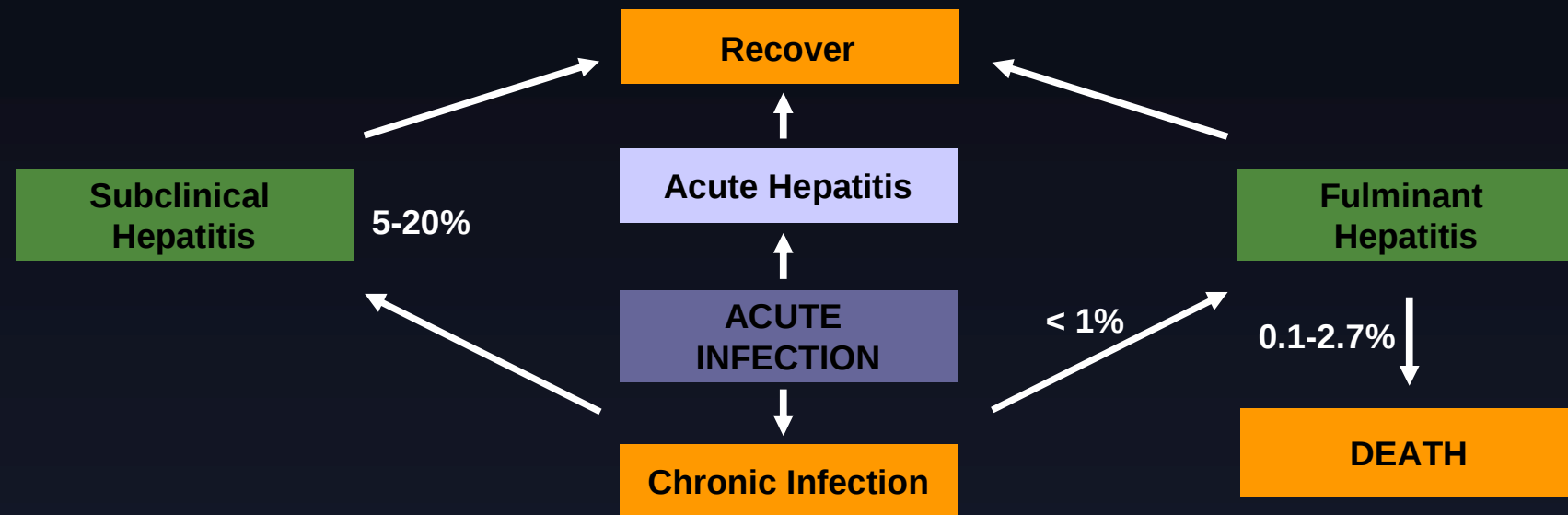
Liver-related Mortality
1999



Transmission of Hepatitis B Infection



Outcomes of Acute HBV Infection



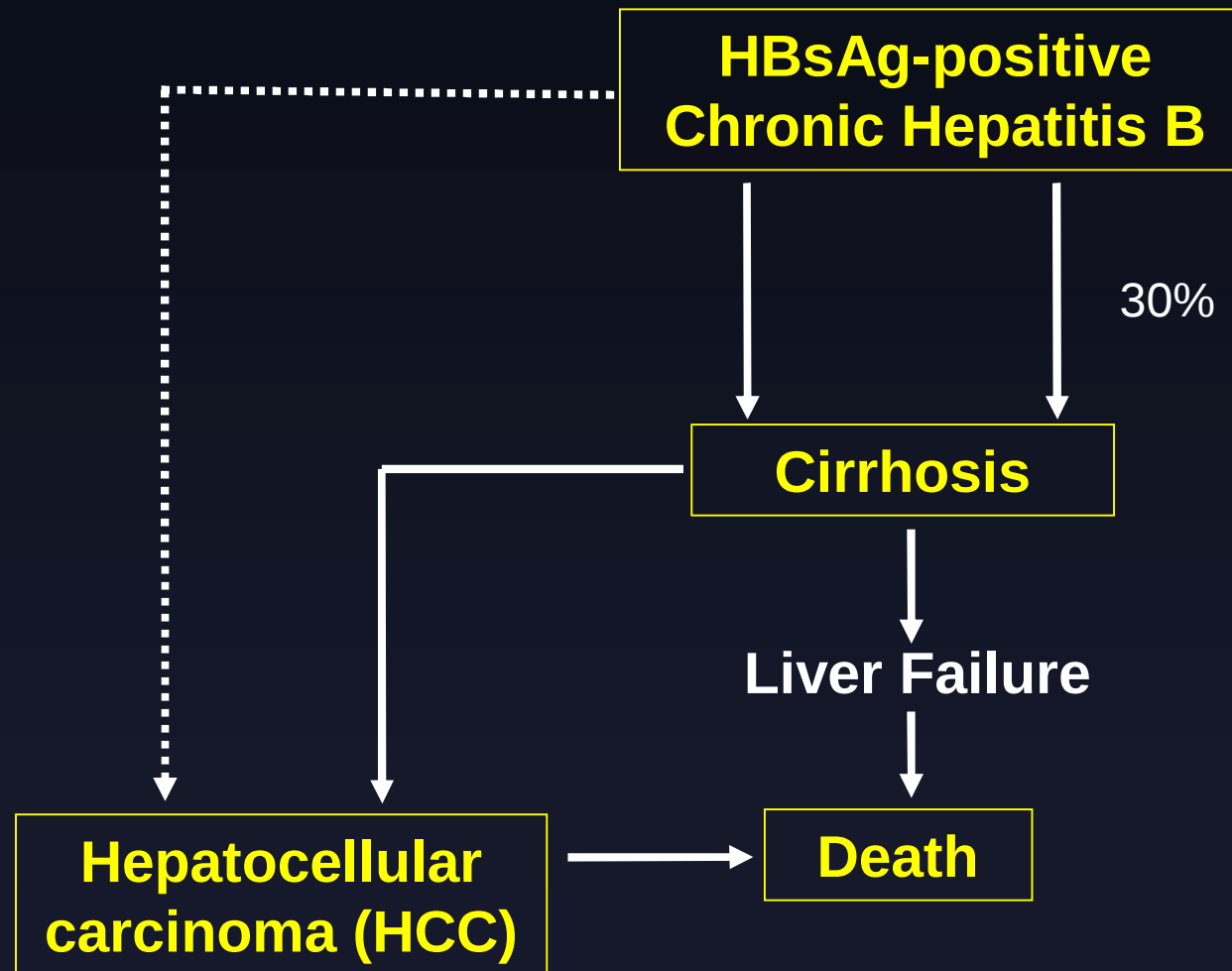
Risk is Related to Age at Infection

Outcome	Neonates, %	Children, %	Adults, %
Chronic carrier	90	20	< 5
Recover	10	80	> 95

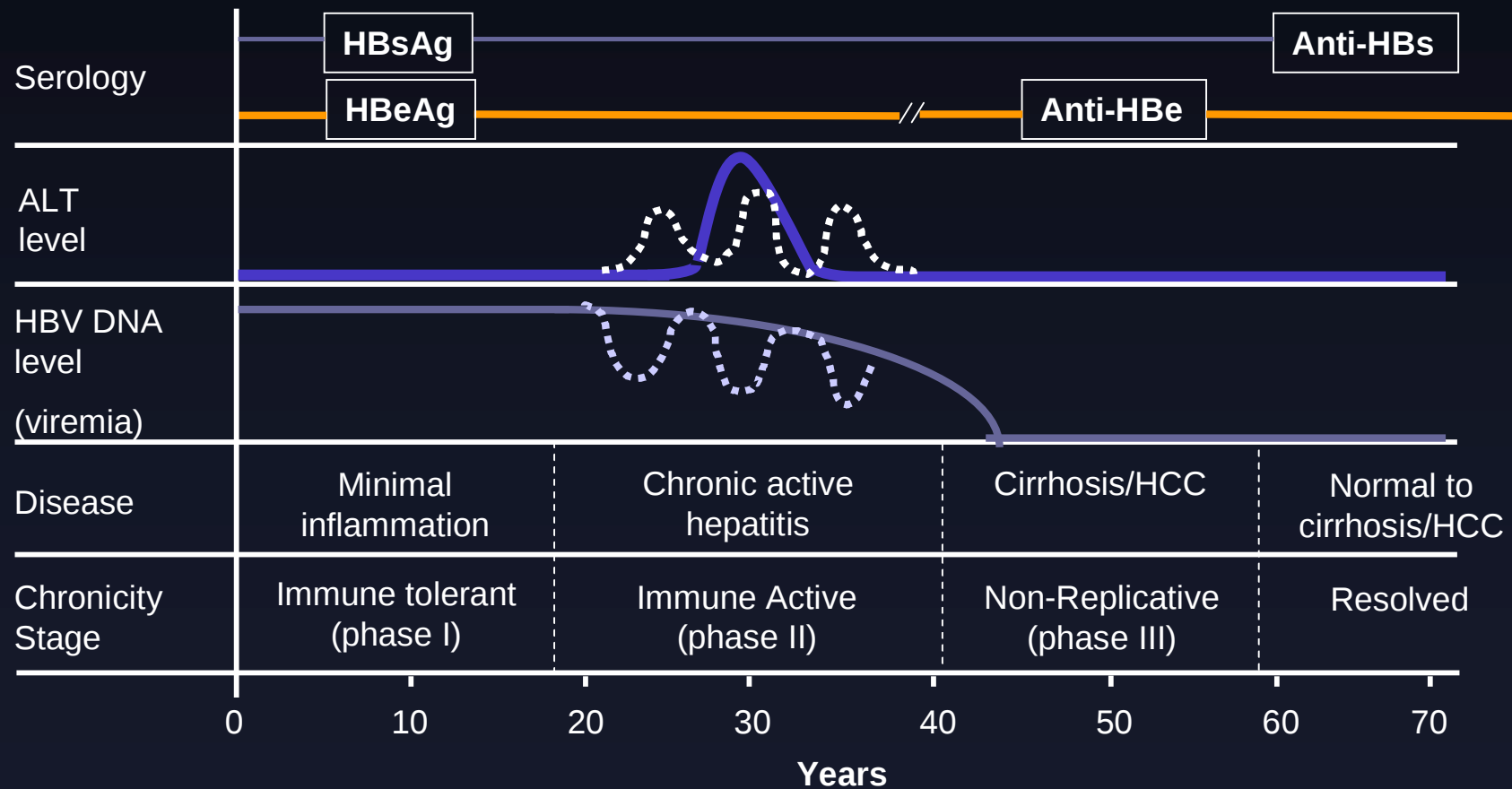


**They are all healthy
carriers!**

Chronic hepatitis B has serious long-term consequences



Natural History of Chronic HBV Infection



Initial Evaluation of HBV Carriers (HBsAg+)



- History and examination
- Assess risk factors (coinfection)
- Alcohol use
- Family history of HBV and HCC
- Physical findings of cirrhosis

Investigations

- Liver disease activity
- Liver fibrosis/cirrhosis
 - INR, albumin, bilirubin
- Serologic and virologic markers
- Screening for HCC (AFP and ultrasound)



Is HBV Serology Confusing??

HBV Serology



- sAg determines carrier status
- eAg determines replication and infectivity
- cAb confirms natural infection
- sAb confirms immunity
- HBV DNA (viral load) measures infectivity and replication

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)

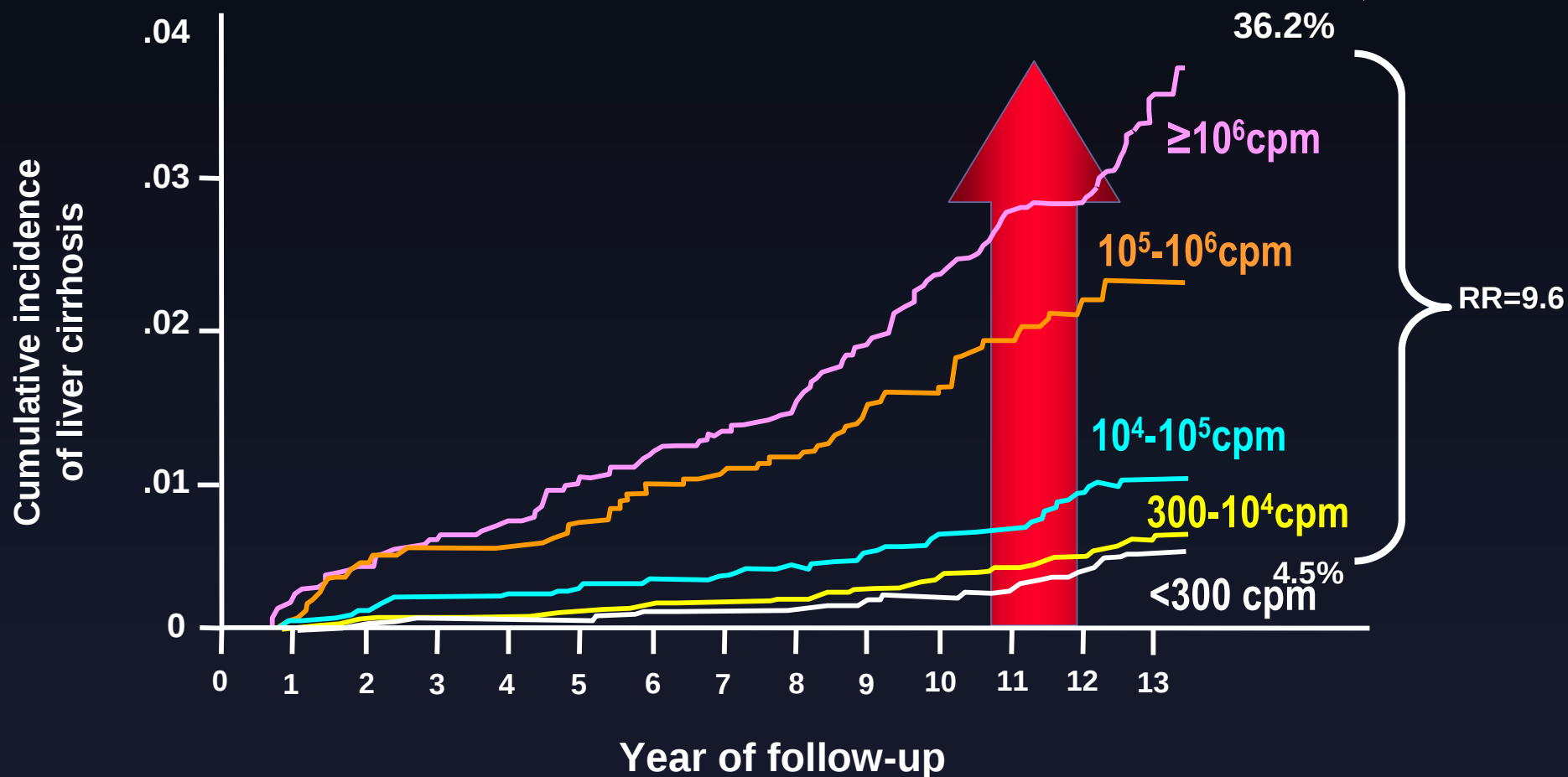
Baseline HBsAg+
(n=9800)

Baseline HBV DNA
(n = 3851)

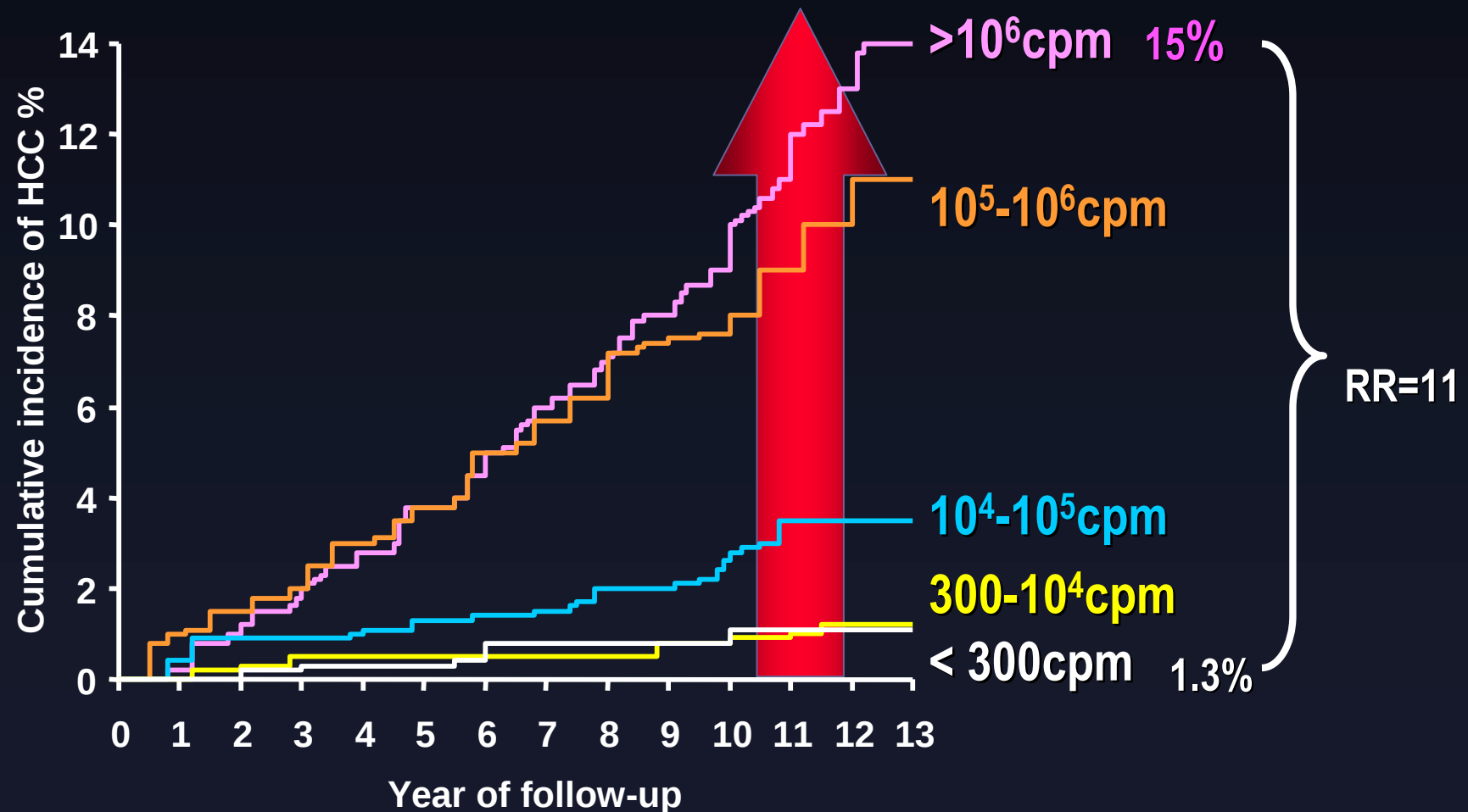
Follow-up analysis
For Cirrhosis/HCC
(n = 3774)

June 2004:
43,993 PYs follow-up

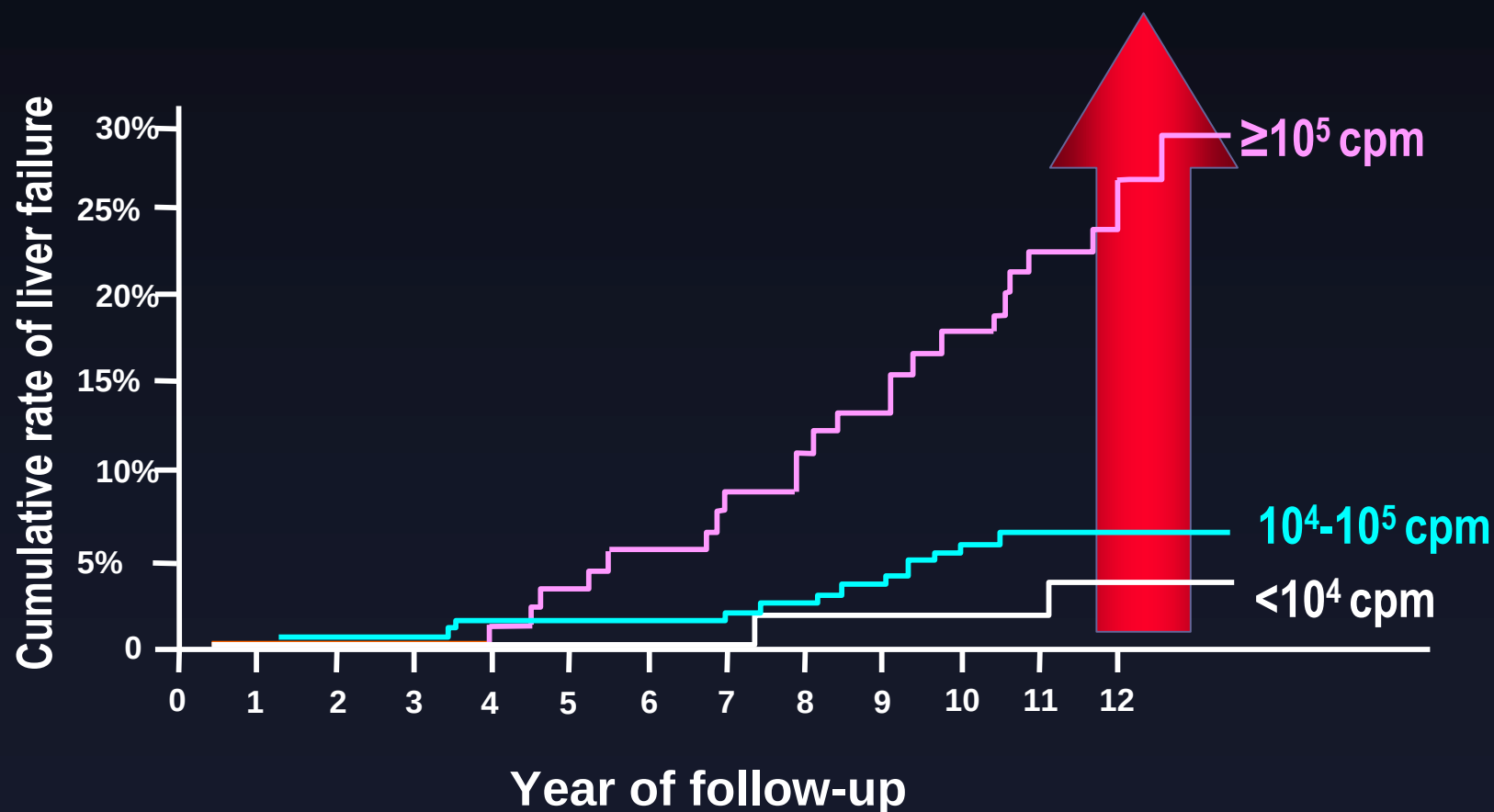
Higher viral loads are associated with increased rate of cirrhosis



Higher viral loads are associated with increased rate of hepatoma

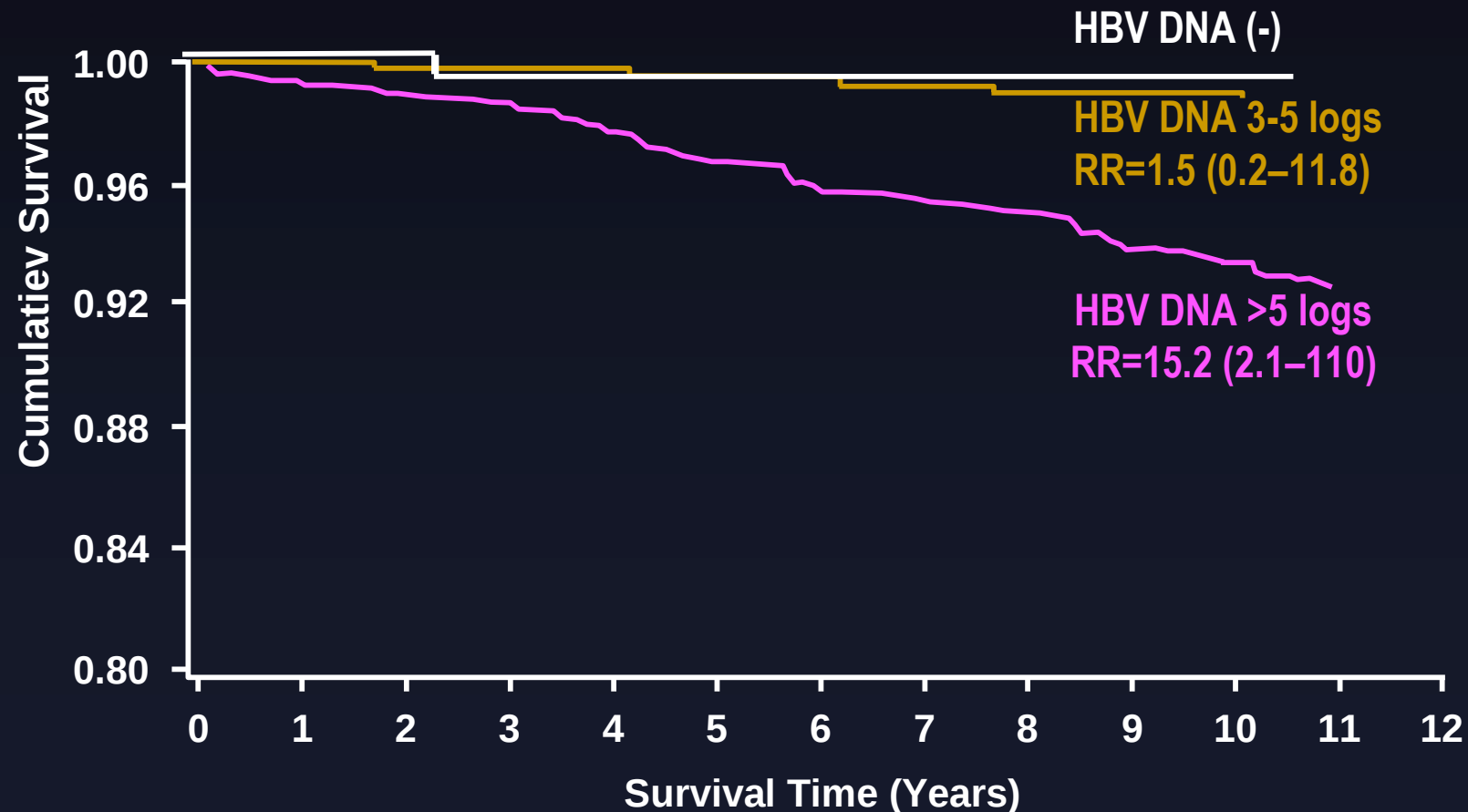


Higher viral loads associated with increased rate of liver failure



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

Higher viral loads associated with increased liver-related mortality



Chen G et al., Am J Gastro, 2006

Indications for Treatment of Chronic HBV



- Patients with active liver disease:
 - Abnormal liver function tests (AST, ALT)
 - HBeAg positive and $> 10^5$ HBV DNA
 - HBeAg negative and $> 10^4$ HBV DNA
 - Biopsy if HBV DNA $< 10^4$ with $\uparrow$ ALT
 - Treat if active hepatitis (biochemical or histologic)

Objectives of Treatment



- **Viral suppression**
 - Reduction or loss of serum HBV DNA
- **Immune system activation**
 - Development of antibodies against HBV
- **Reduction/cessation of liver injury**
 - Normalisation of liver function
 - Improvement in liver histology
- **Prevention of complications**
 - Cirrhosis, liver failure, hepatoma
- **Improve survival**

Current approaches to treatment of chronic hepatitis B



Drug types

- Anti-viral agents
 - Lamivudine
 - Adefovir dipivoxil*
- Immunomodulators
 - Interferon- α

Treatment duration

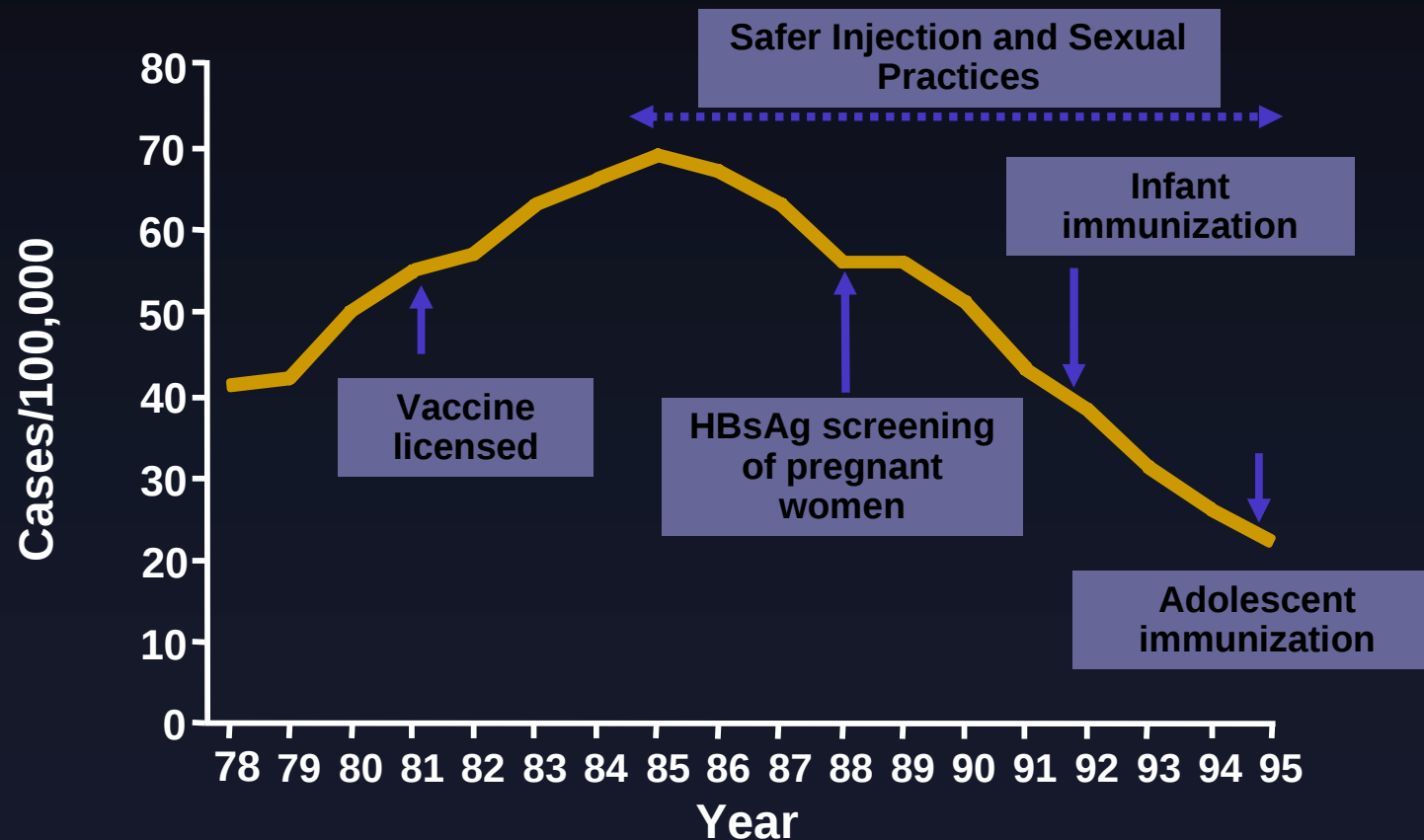
- Continuous long term
- Finite course
- Undefined: dependant on response



Vaccination for Hepatitis B

Reducing the Burden of Chronic HBV

Incidence of Acute Hepatitis B: United States, 1978-1995



Annual Incidence of Liver Cancer in Children Aged 6-15 Years



Age at Diagnosis	Before Program Cohort (1974-1984), Incidence per 100,000	After Program Cohort (1984-1986), Incidence per 100,000
6	0.46	0.00
7	0.53	0.15
8	0.48	0.31
9	0.61	0.00
Total	0.52	0.13*

*P < .001 for comparison between birth cohort.
Vaccination program in effect since July 1984

Infants who do not receive vaccination



Up to 9 out of 10 babies born to infected mothers will end up **being carriers for the rest of their lives**, if they do not get the shots.



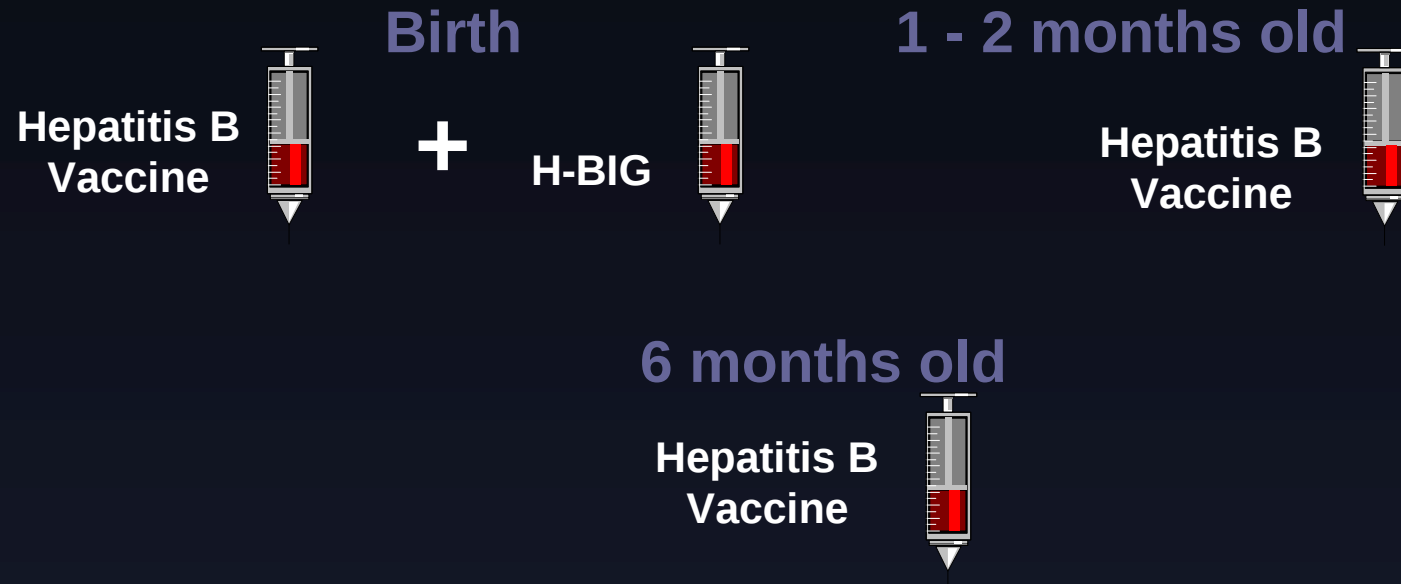
Babies who end up as carriers have a **1 out of 4 chance of dying** from liver problems.



19 out of 20 babies who get the shots will be protected for life!

Baby Shots for Hepatitis B

if the mother has Hepatitis B

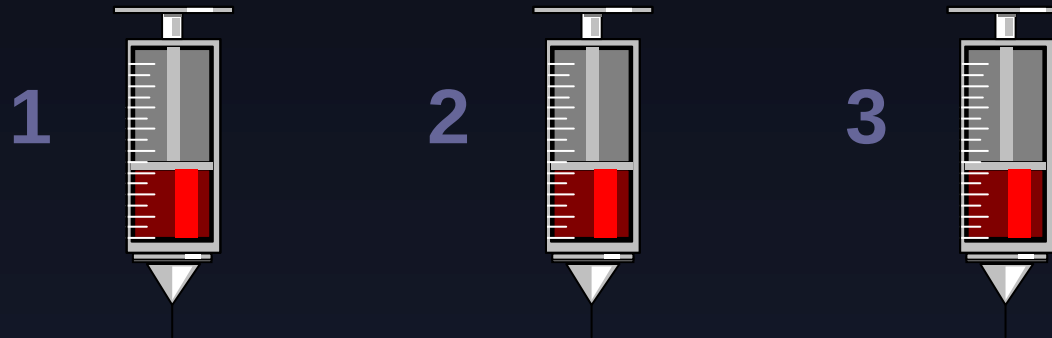


Infants who receive **all 3 shots**, plus **H-BIG**, have a 95% chance of being cured from hepatitis B for life.

Hepatitis B can be prevented!



If you have never had hepatitis B,
you can get 3 shots . . .

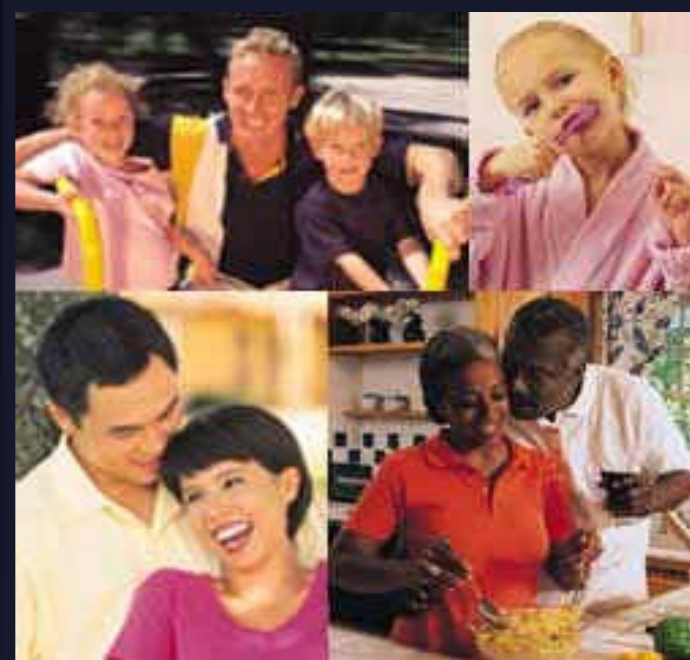


. . . and get long lasting protection.

Should relatives/partners be tested for HBV?



- Since hepatitis B virus can be passed to them, they should be tested to see if they have this virus in their bodies.
- If they do not have the hepatitis B virus, they should get the shots to protect themselves.



Issues Related to HBV Vaccination



- Poor or non-response to vaccination
 - Strategies to maximize likelihood of response
- Durability of vaccine response
 - Need for booster vaccinations?
- Missed opportunities for vaccination
 - Especially among adults at risk



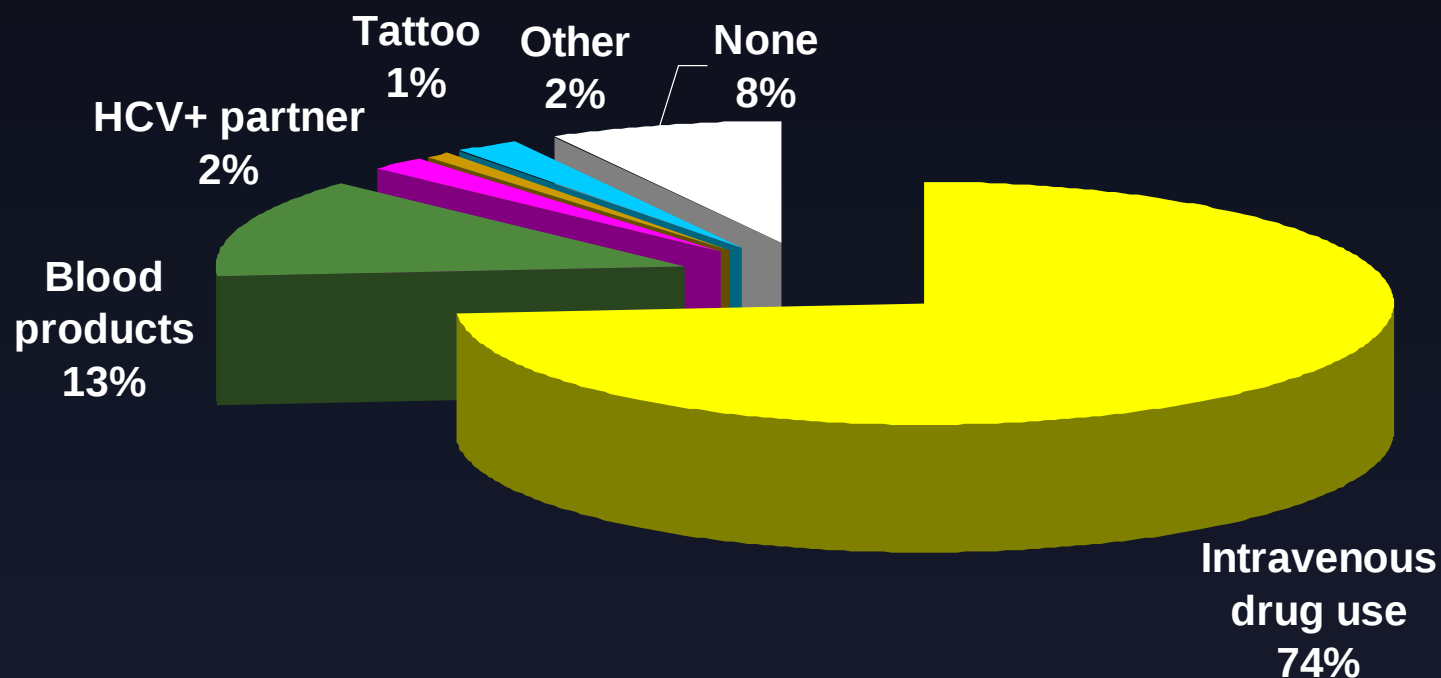
Hepatitis C

HCV infection

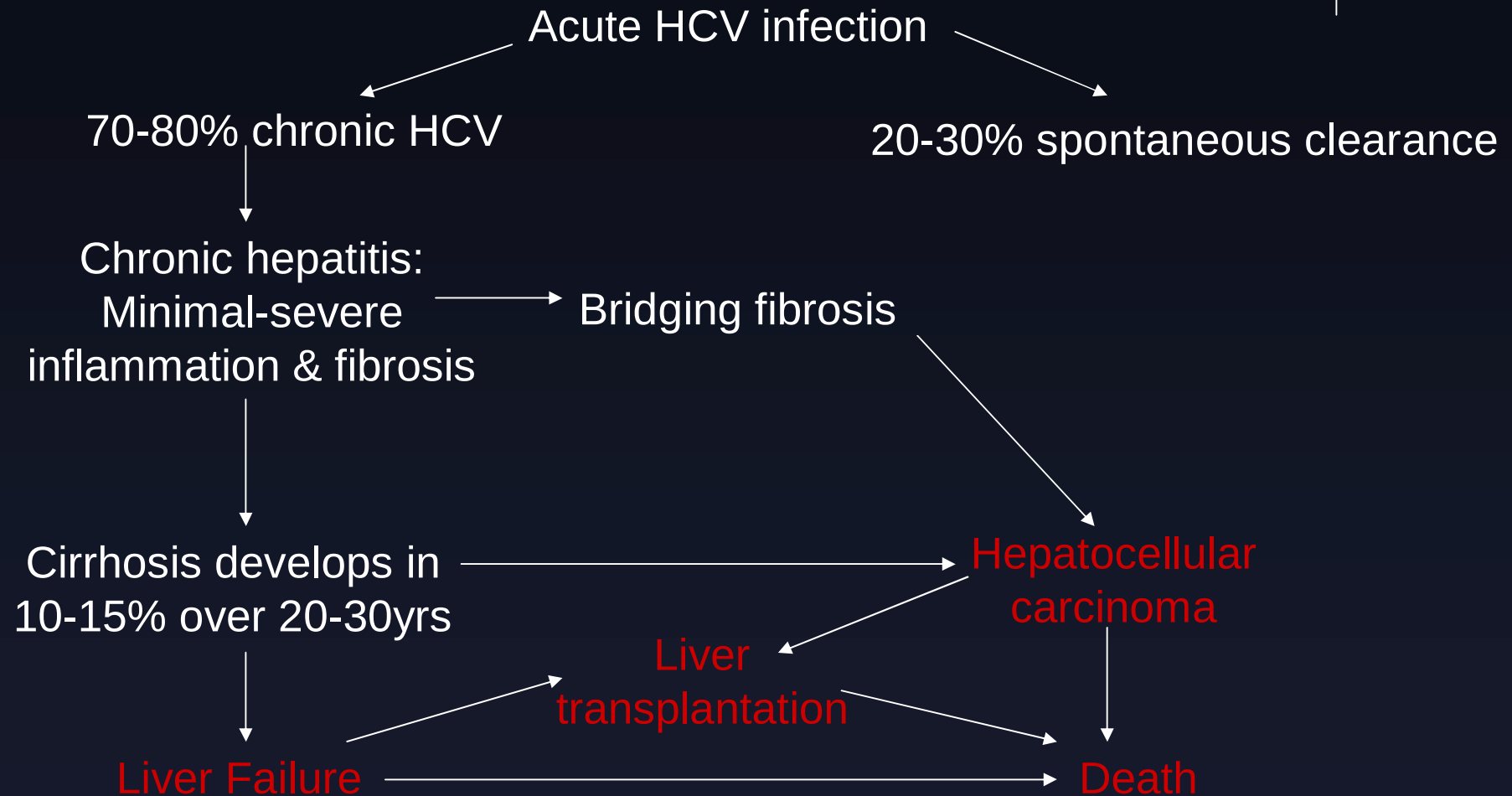


- 25,000 New Zealanders have HCV infection
- Most are young, ex-IDU
- 9% are cirrhotic at presentation
- ↑↑ referrals to Hepatitis Clinics
 - ↑ detection
 - *awareness of risk factors*
 - ↑ demand for treatment
 - *more effective therapies*
- HBV still main cause of end-stage liver disease in NZ BUT ↑↑ HCV-ESLD over next decade

Risk factors for HCV exposure



Natural History of Hepatitis C



Management



- Diagnosis
 - HCV IgG antibody positive
 - HCV RNA positive
- Determine genotype
 - 1 & 4 'hard to treat': 12 months, 55% cure rate
 - 2 & 3 'easy to treat': 6 months, 80% cure rate
- Treatment
 - Pegylated interferon +ribavirin

Conclusion



- HBV and HCV are New Zealand problems
- Refer patients
 - Surveillance for HCC is necessary
- Treatment is available
 - Prevents disease progression
- HBV vaccine is highly effective
 - Reduces incidence HBV
 - Reduces rates of liver complications