Chronic Viral Hepatitis

It's closer than you think

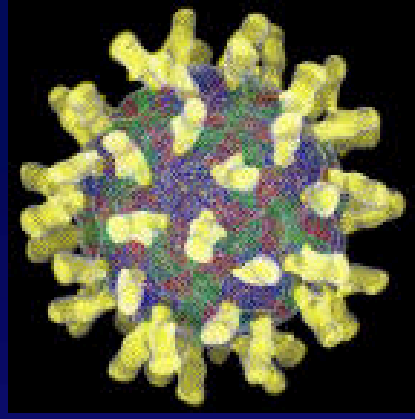
Dr Ed Gane
NZ Liver Transplant Unit

Viral Hepatis is a Global Problem

- **1 in 3 people have had previous hepatitis**
- **1 in 12 have active chronic viral hepatitis**
  - »180 Million have chronic hepatitis C
  - »400 million have chronic hepatitis B
- **Significant health burden**
  - »>1 million deaths per annum
  - »Unemployment
  - »Stigmatisation
  - »discrimination
- **In 2011, all 193 member states in WHO passed resolution recognising chronic viral hepatitis as a global health issue.**

Chronic Hepatitis B

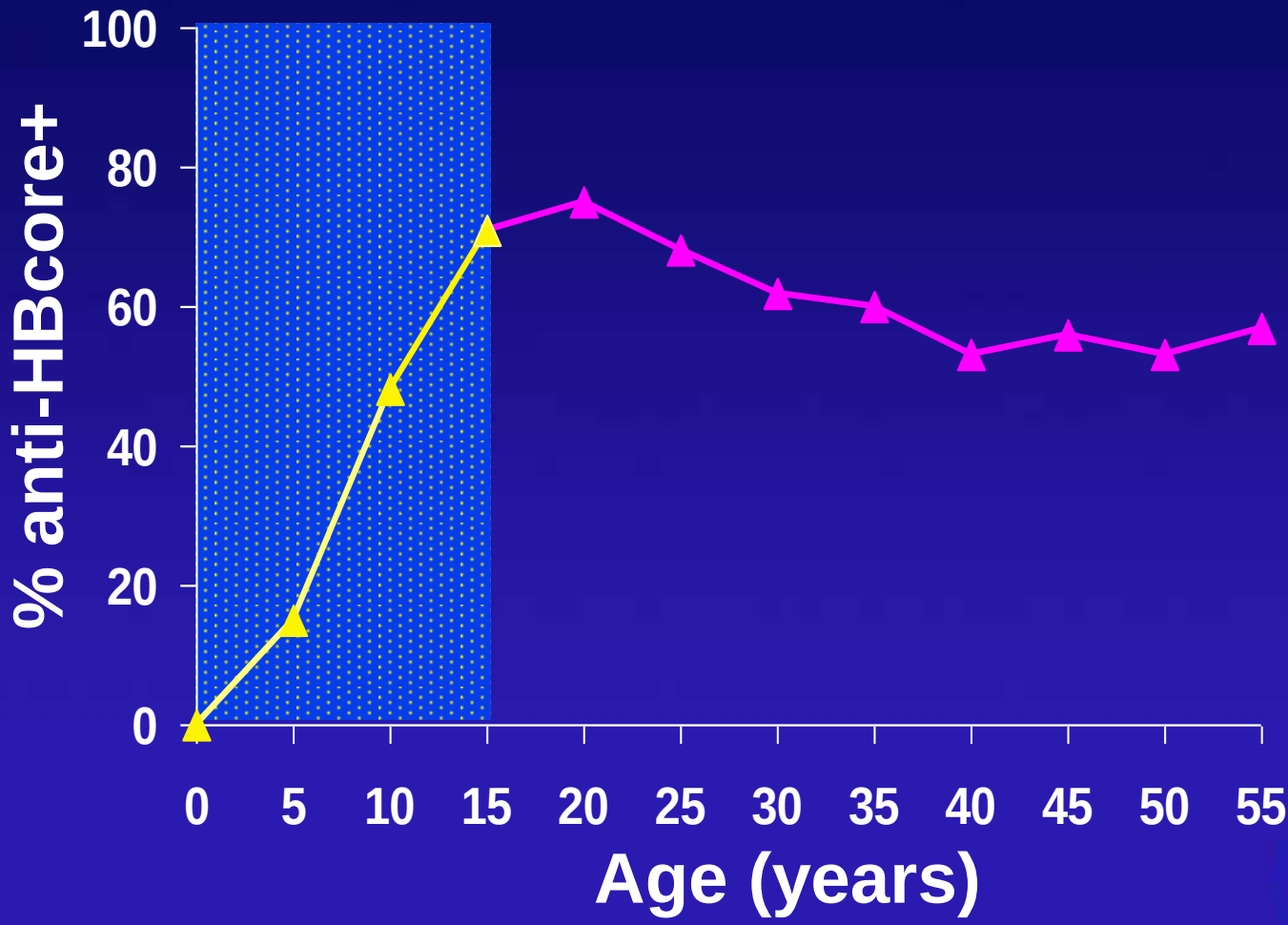
Hepatitis B



- Double stranded DNA virus
- 10^{12} viruses made each day
- $>10^{12}$ virus/ml blood
  - »Transmitted via blood, body secretions
  - »High risk of sexual transmission
  - »High risk of vertical transmission
- Vaccine available, cheap, >99% effective

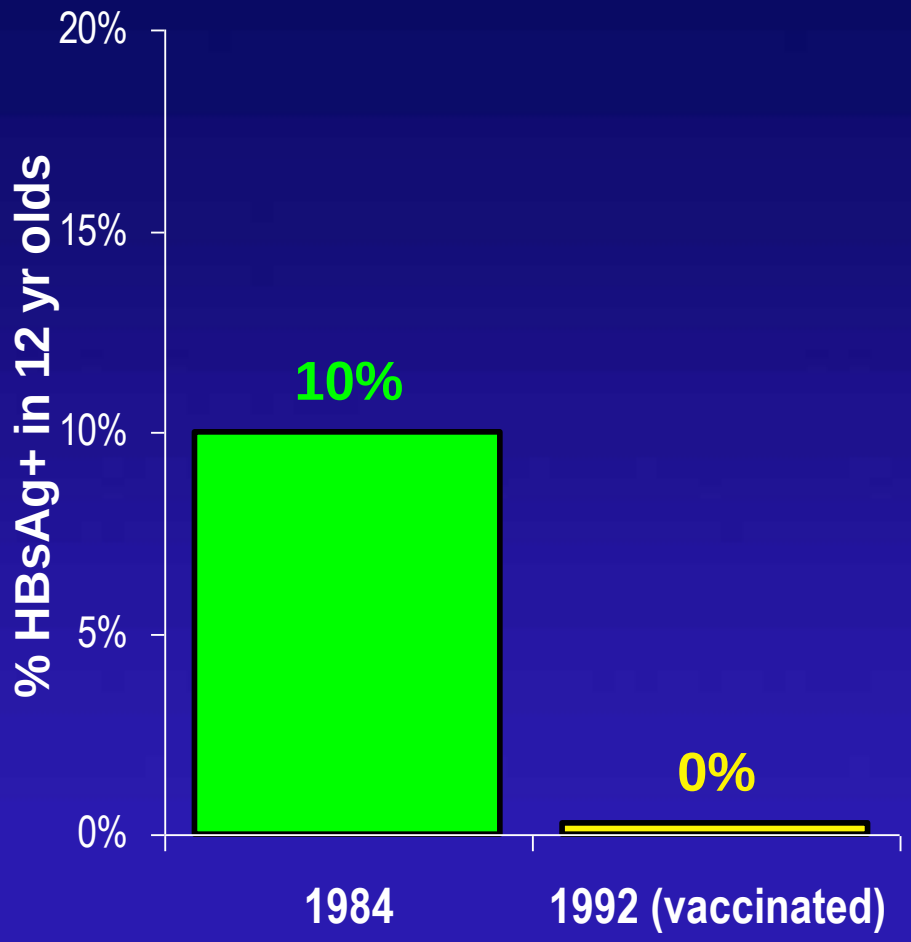
Mode of HBV Transmission in NZ Early Horizontal not Vertical

- **Kawerau School Survey 1984**



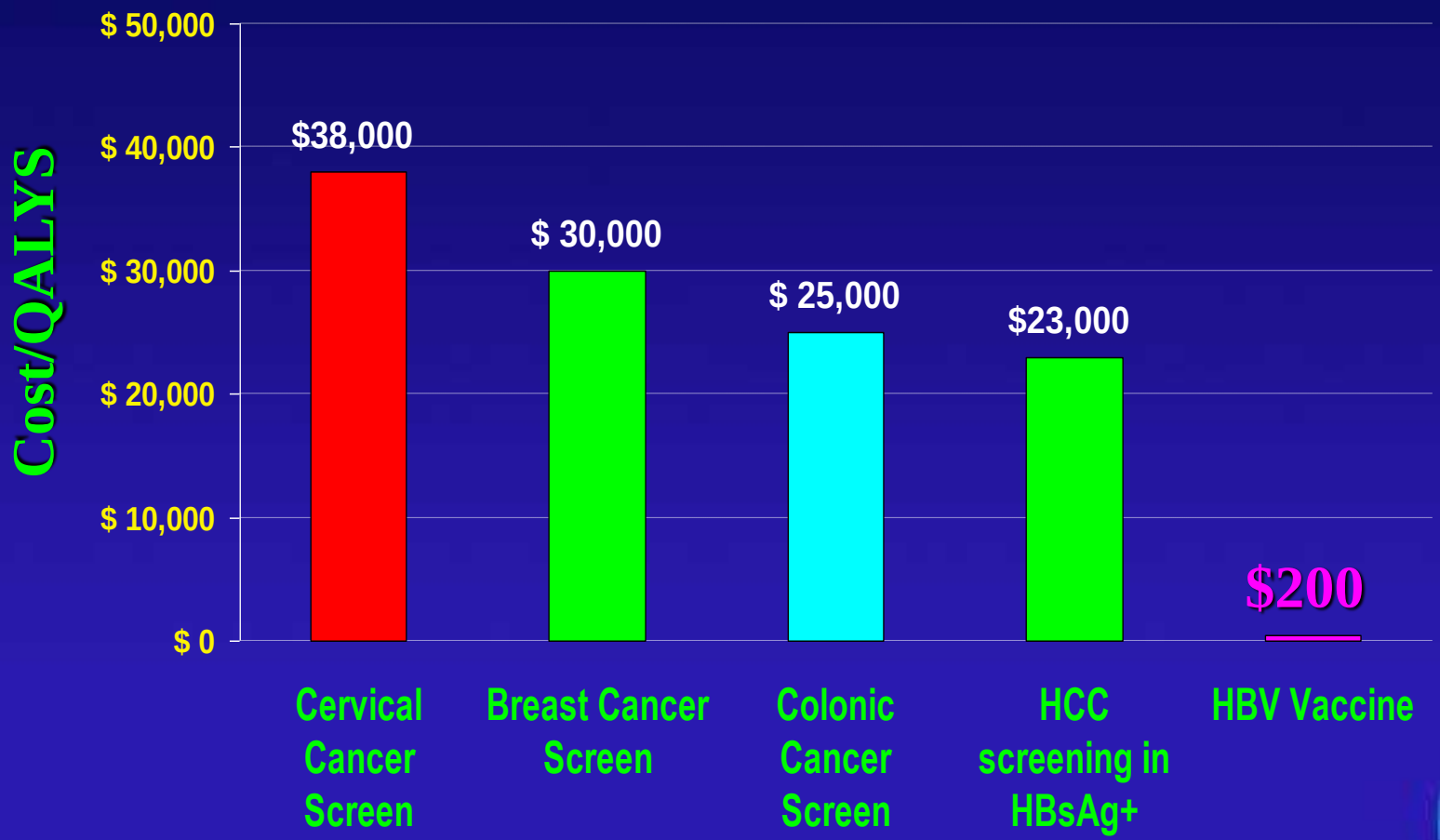
Milne A et al. *I J Epidem* 1987; 16: 84-90

Childhood Vaccination in NZ reduces incidence of HBV infection



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

Childhood Vaccination is the most cost-effective health intervention



What about those already infected? National Screening Programme 2000-2

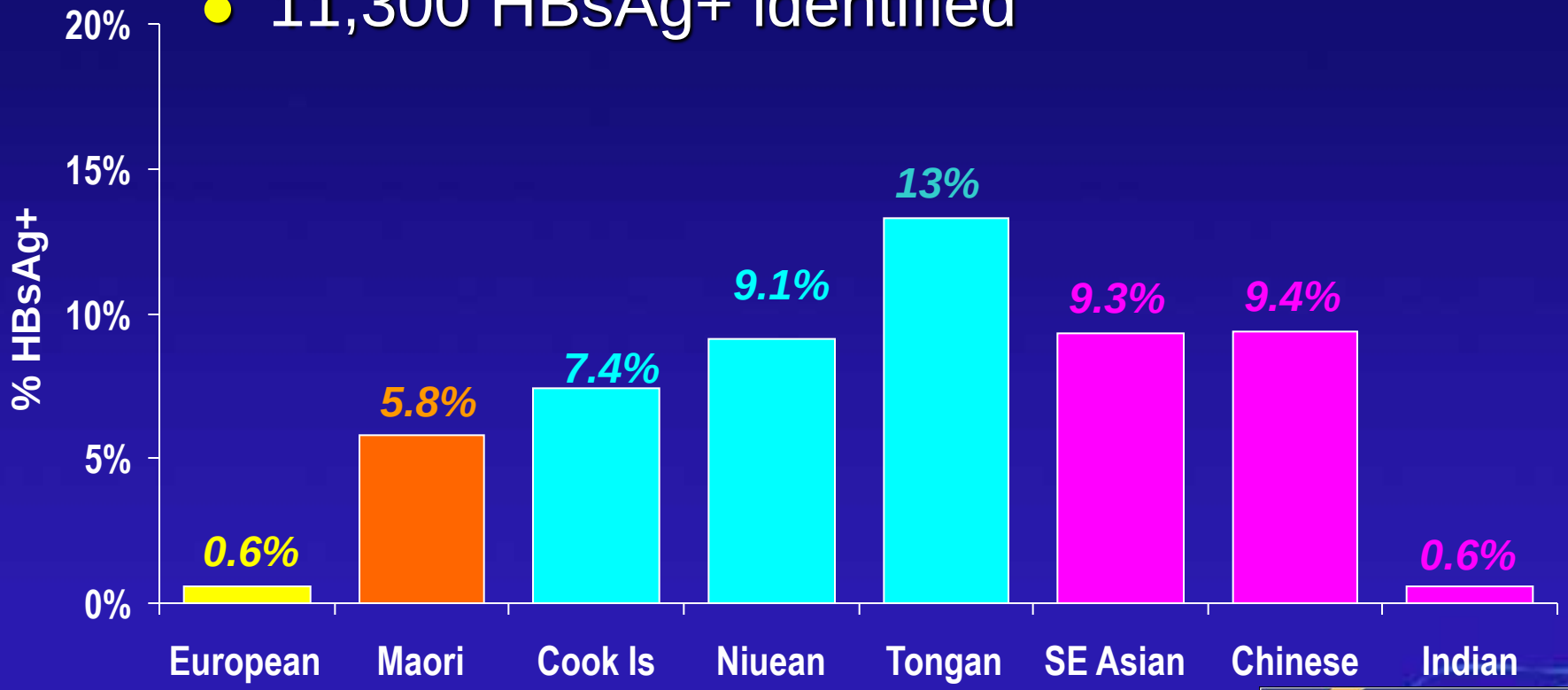
TARGET POPULATION

- **Asian, Pacific Islander, Maori**
  - *rates= 10x European*
- **≥15 years old**
  - *neonatal vaccination since 1987*
- **North Island only**
  - *90% population*
  - *rates= 10x South Island*

➡ Total to be screened= 566,000

National HBV Screening Programme
Prevalence according to Ethnicity

- 177,292 screened July 1999 - July 2002
- 11,300 HBsAg+ identified



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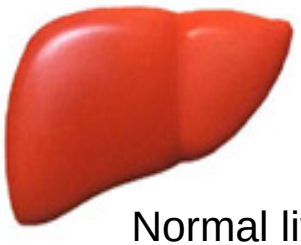
Clinical background
CHB infection has severe consequences

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

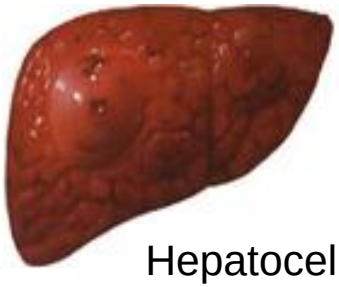


Normal liver

Chronic hepatitis

Cirrhosis

End-stage liver disease



Hepatocellular carcinoma(HCC)

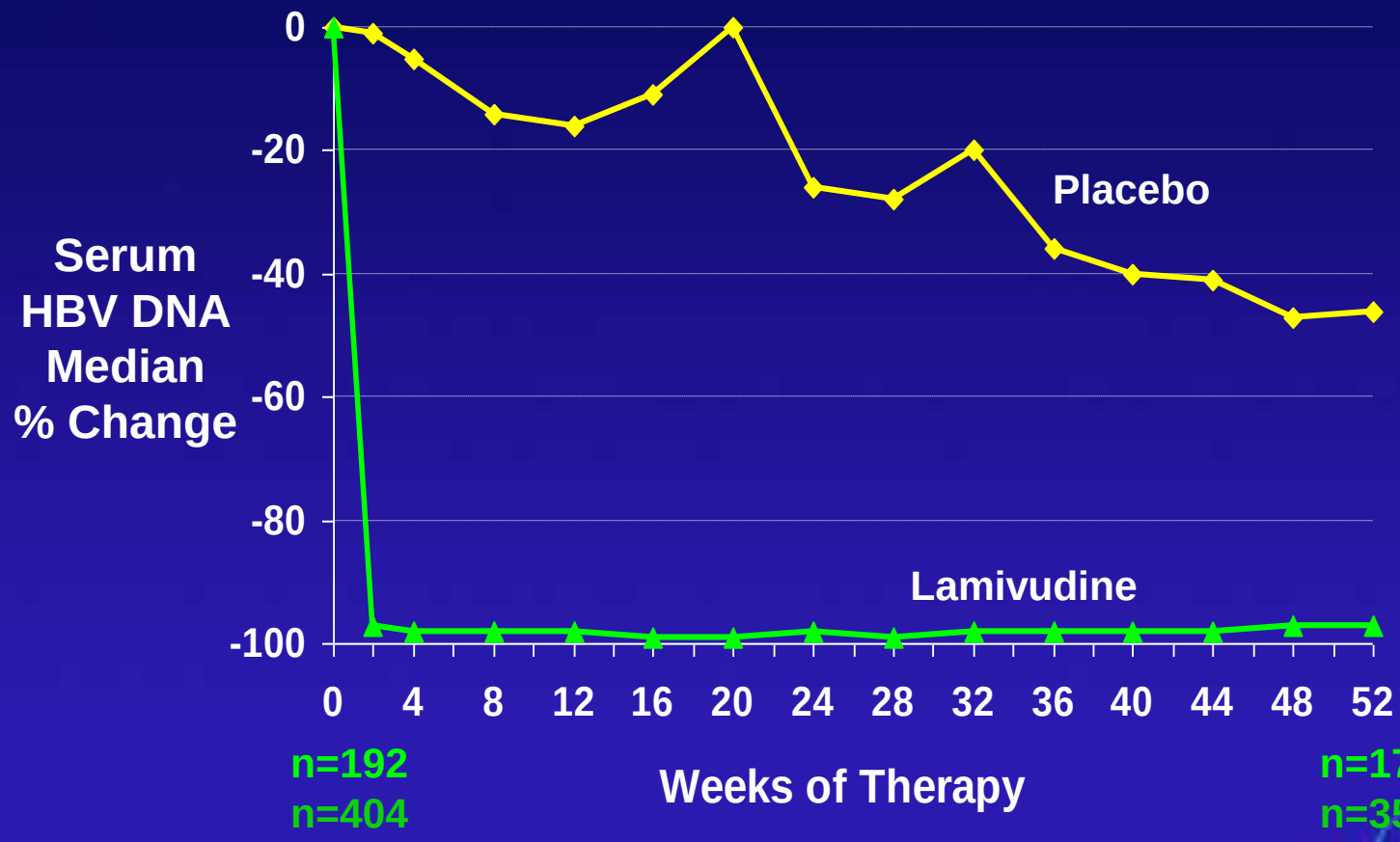
Chronic inflammation and increasing liver damage over time (average 10 -15 years)

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

Roche

cobas®
Life needs answers

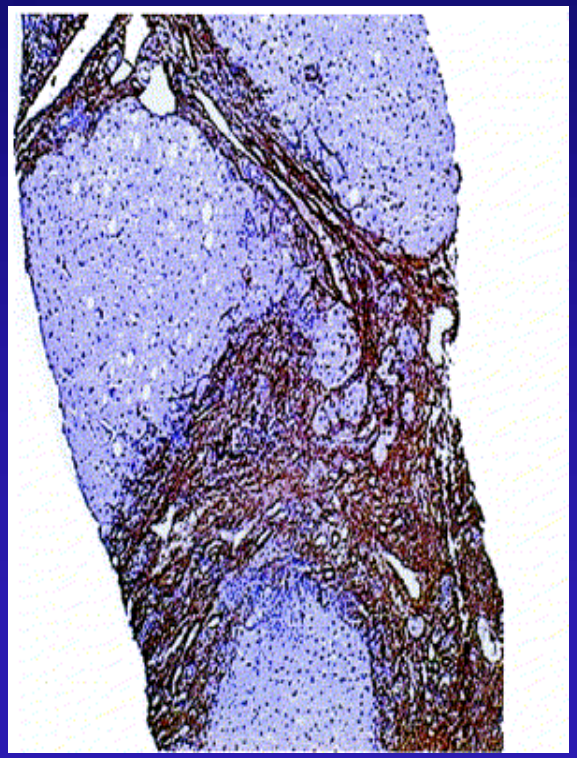
Virological Response
Lamivudine Phase III Data



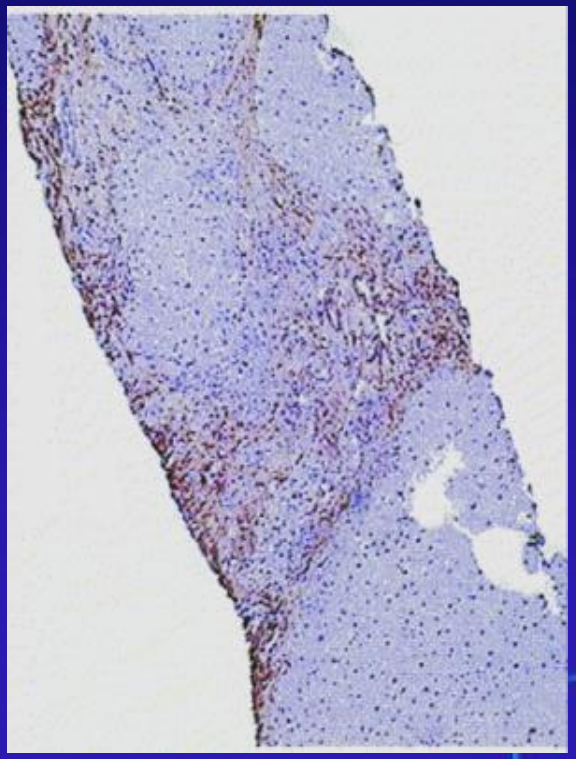
Lai, NEJM, 1998

Viral Suppression Improves Histology
(ii) Regression of Fibrosis

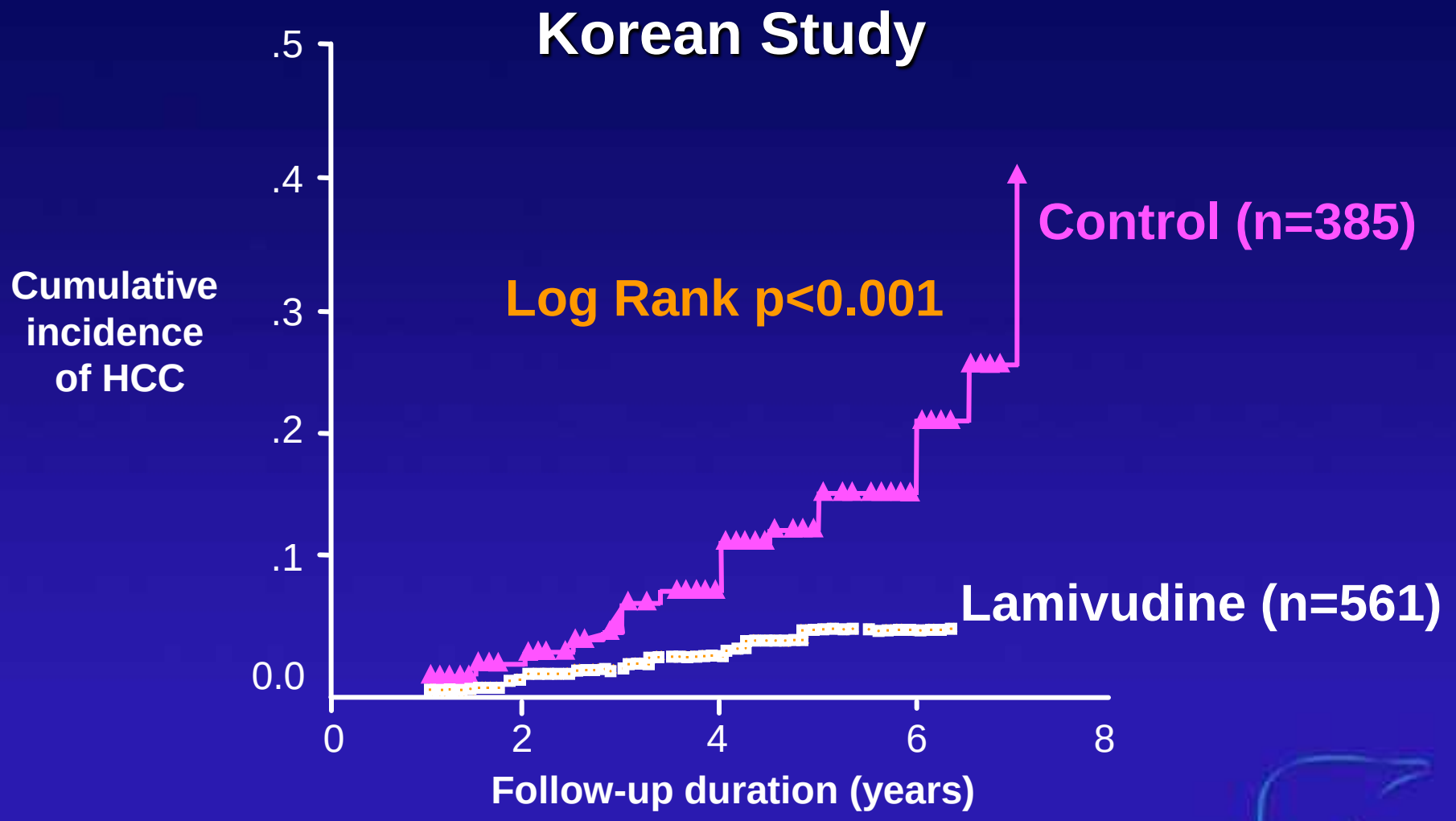
Pre-treatment
Fibrosis Score = 4



Month 36
Fibrosis Score = 2



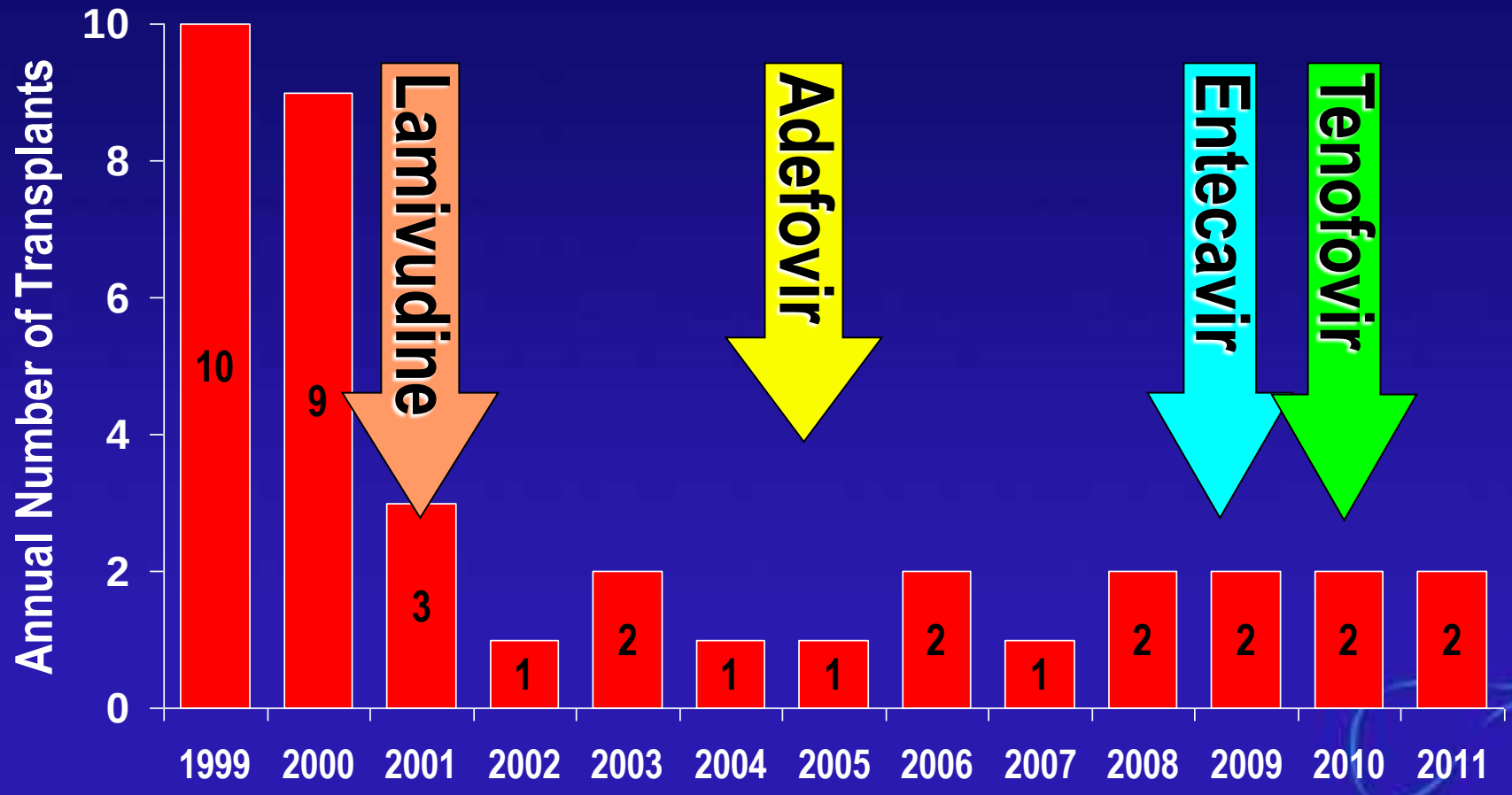
Viral Suppression with Lamivudine may prevent Hepatocellular Carcinoma



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

Viral Suppression with Lamivudine may prevent Liver Transplantation

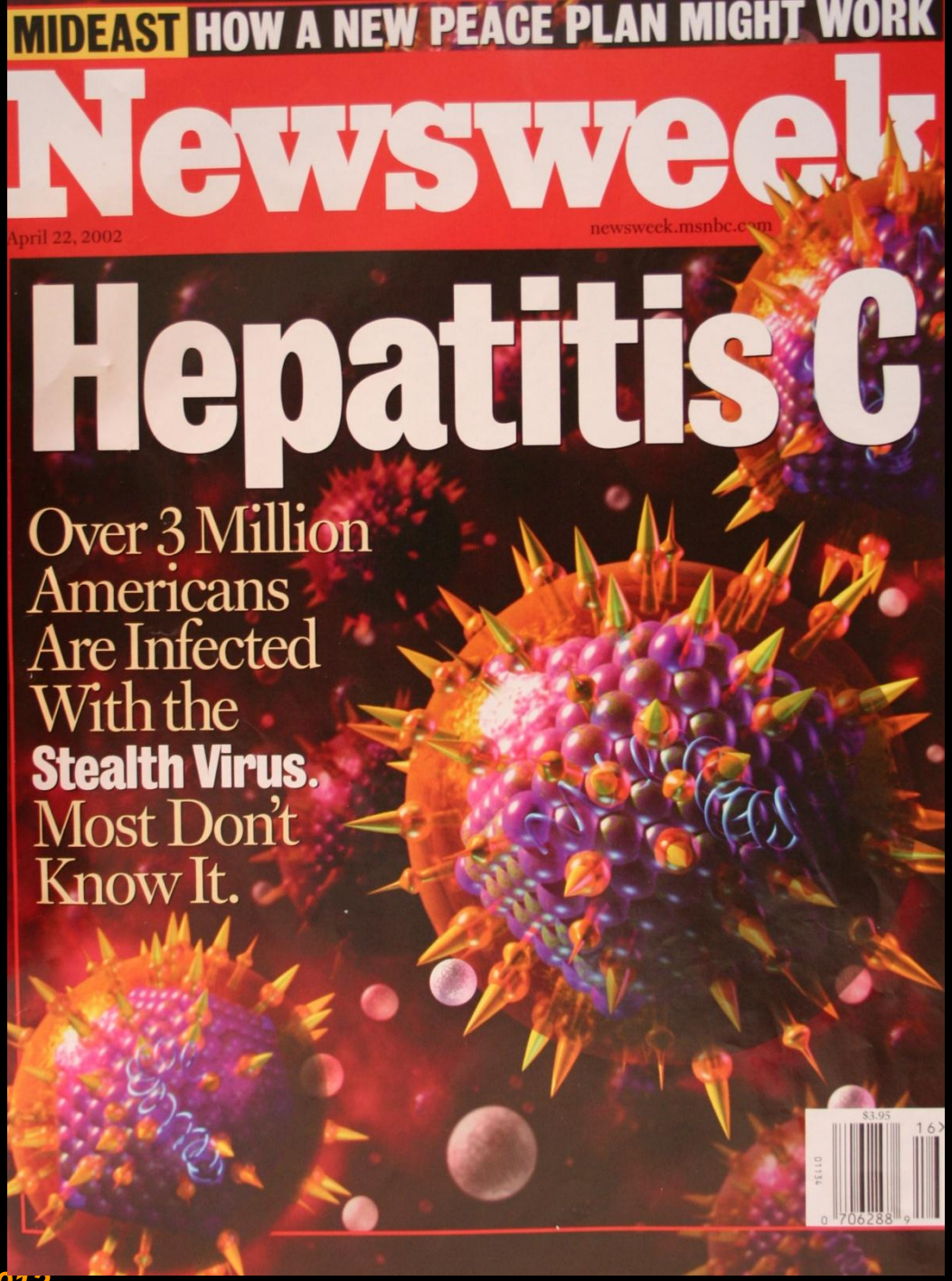
Transplants for Decompensated CHB



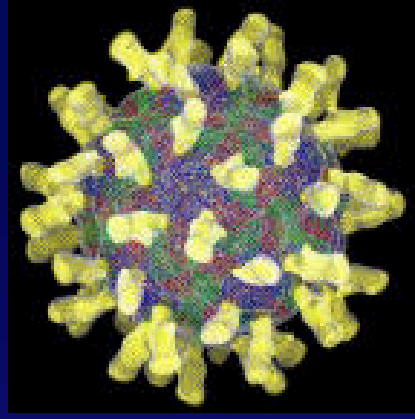
NZLTU data 1999-2011

Management of CHB in NZ Challenges

- >100,000 New Zealanders have chronic HBV
  - »Maori, Pacific Islanders and Asians
  - »Over 20 uyears (< 25% all HBsAg+ are identified
  - »< 5% all active CHB have been treated
  - »25-40% will die due to HBV if untreated
- HBV suppression prevents disease progression
- Earlier diagnosis and treatment of CHB will prevent liver cancer, liver failure, and death
- Effective vaccination available and cheap


MIDEAST HOW A NEW PEACE PLAN MIGHT WORK
Newsweek
April 22, 2002
newsweek.msnbc.com
Hepatitis C
Over 3 Million Americans Are Infected With the Stealth Virus. Most Don't Know It.
$3.95

Hepatitis C



- Single stranded RNA virus
- 10^{12} viruses made each day
- High mutation rate
  - »No Vaccine likely
- 10^{5} viruses per ml blood (c.f. 10^{12} for HBV)
  - »Transmitted only via blood
  - »No risk of sexual transmission
  - »Low risk of vertical transmission

Hepatitis C – Facts

- 180 million HCV+ worldwide
  - »>50,000 HCV+ New Zealanders
- **NO VACCINE AVAILABLE**
- Since 1992, HCV screening of blood donors
  - »Eradicated post-transfusional hepatitis C
  - »Now most infections from injecting drug use
- Strategies to reduce risk of injecting drug use
  - »Education of at-risk youth
  - »Safe injecting practices
  - »Needle exchange

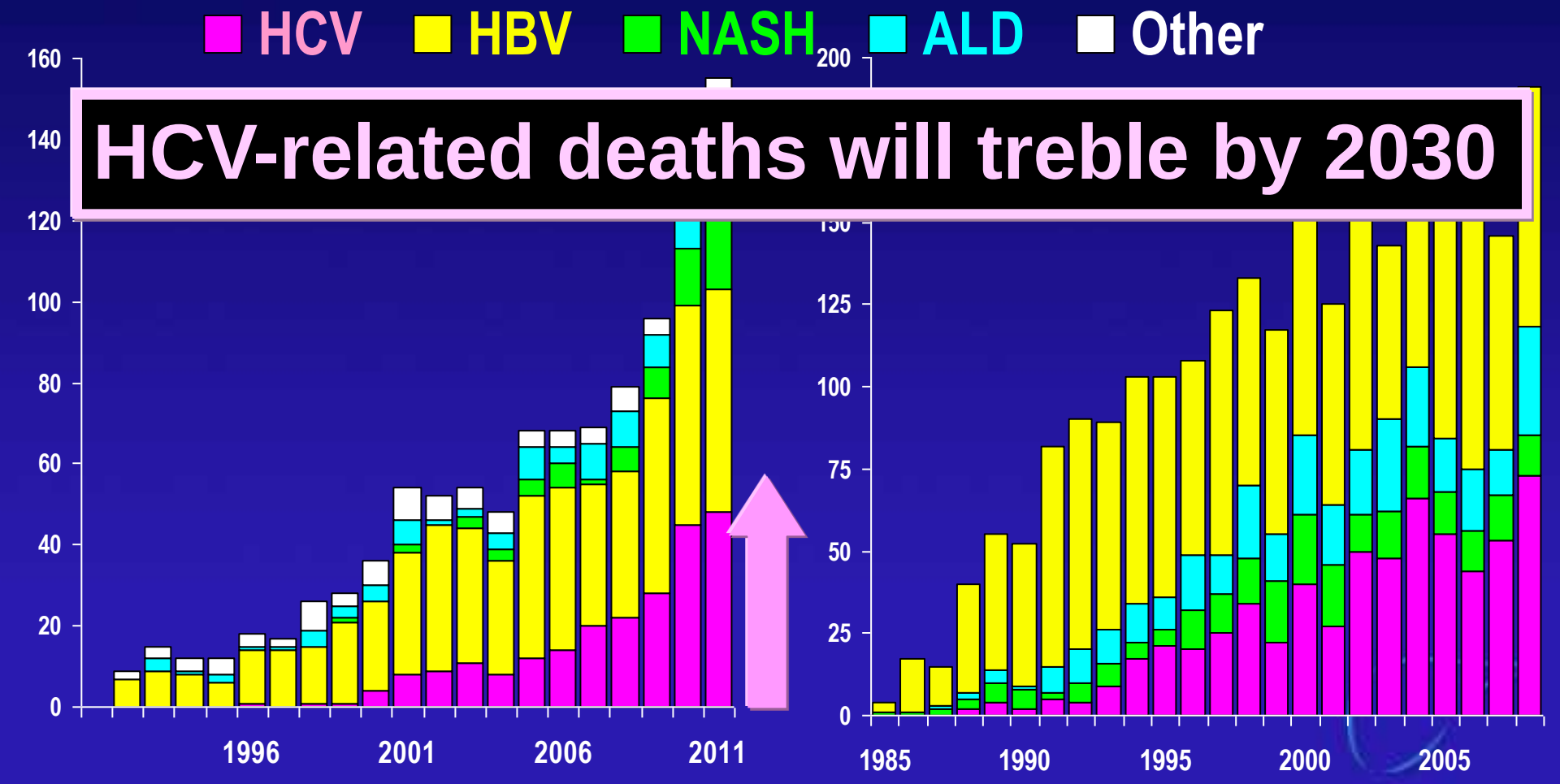
➡**Incidence of HCV has halved since 2000**

Chronic Hepatitis C - the Problem

3. Increasing liver-related complications

(2) Liver Cancer at ACH

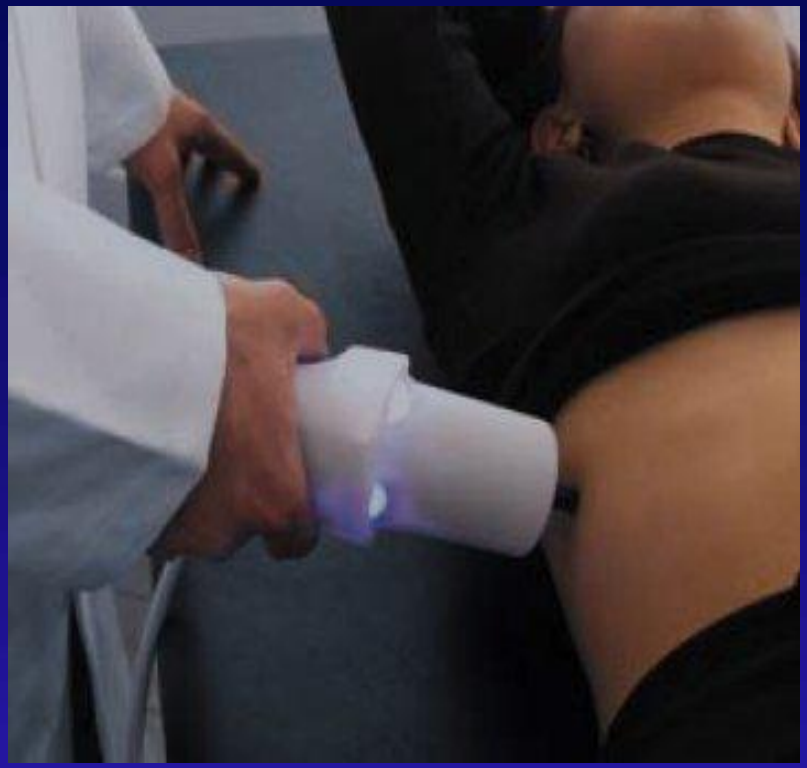
(2) Liver Transplants in ANZ



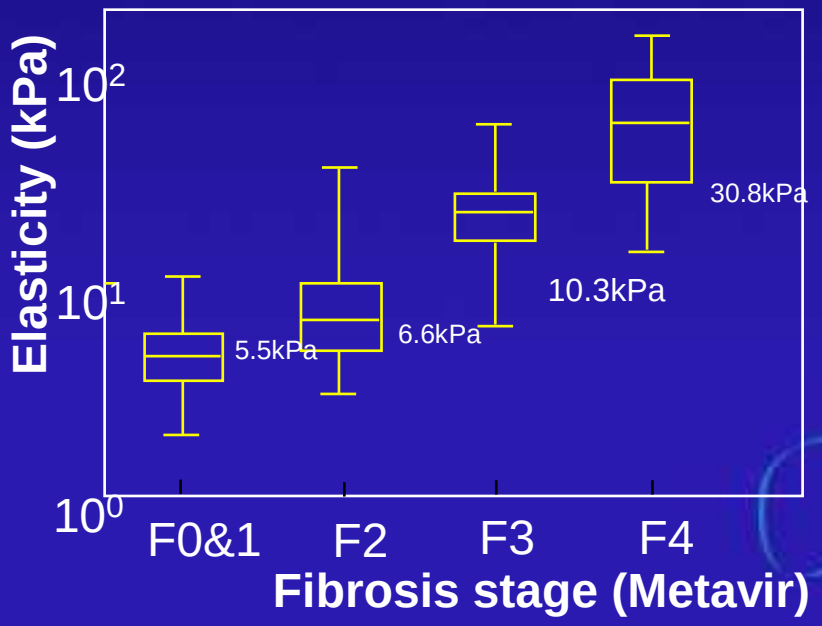
HCV diagnosis and staging

- **Symptoms and Signs**
  - Unhelpful as nonspecific until advanced cirrhosis
- **Anti-HCV ELISA screening assay**
  - Inexpensive ($15), performed daily at all labs
  - Reflects HCV exposure, not active infection
    - may persist after viral clearance
- **Serum HCV RNA PCR assay**
  - Expensive ($250), performed weekly only at reference laboratories
  - Confirms active infection
- **Liver Function Test**
  - POOR marker of liver injury in HCV
  - Need liver biopsy or Fibroscan

Fibroscan



- Painless, noninvasive
- Takes 2-3 minutes
- Performed in clinic
- No sedation
- No complications



Hep C – what Factors are associated with rapid progression to Cirrhosis

- **Alcohol > 5 drinks/day**
  - »Paralyses immune response to HCV
    - Increases HCV replication + injury
  - »Recommended limit
    - Keep below ALAC guidelines
    - Nil if cirrhosis or on IFN
- **Cannabis >2 joints per day**
  - »Cannabinoid receptors in liver cause fibrosis
- **Obesity**

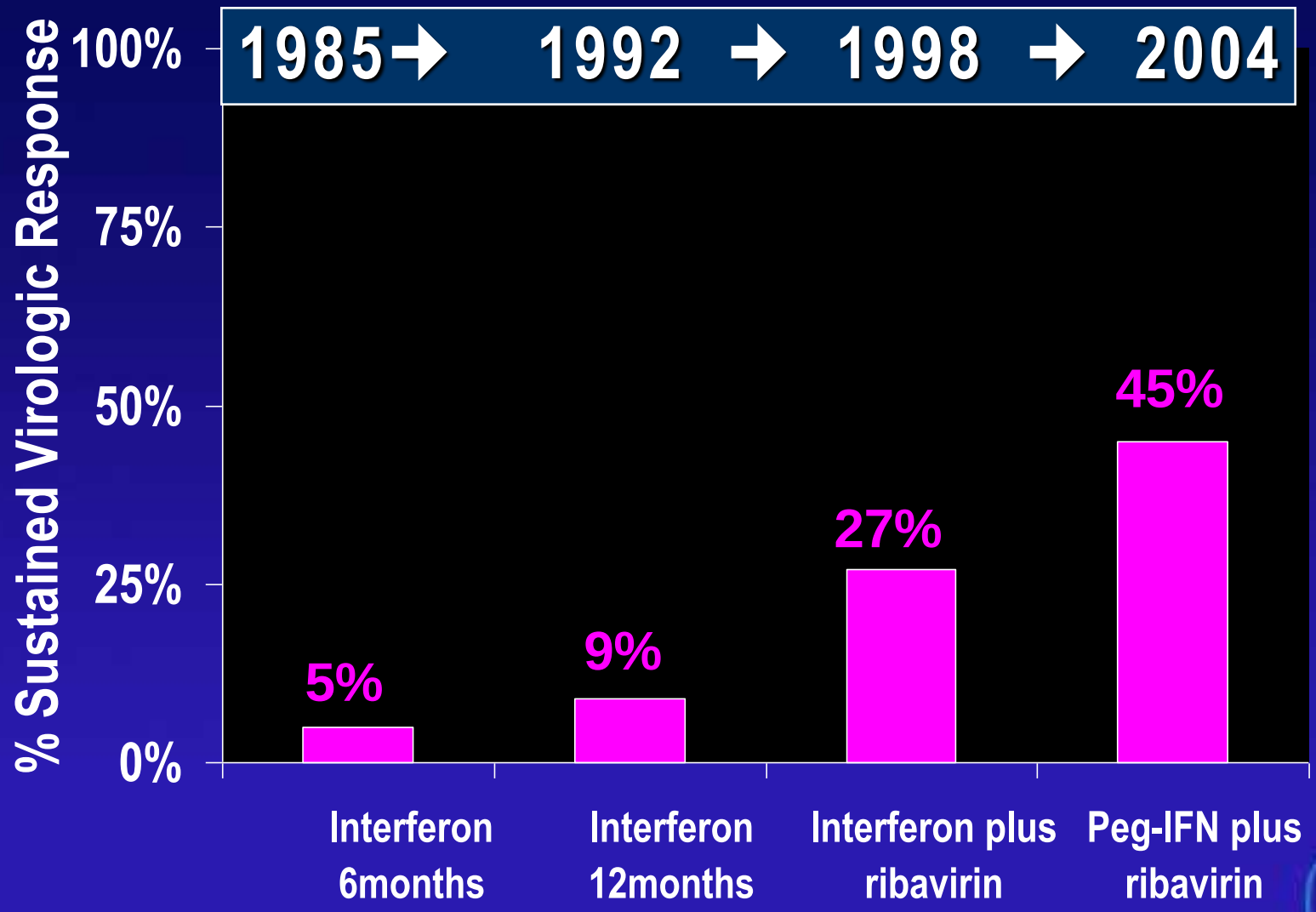
Hep C – what Factors are associated with slow progression to Cirrhosis

1. **Young age**
2. **Female gender**
3. **Coffee!**
   - » Dose-related ↓ risk of cirrhosis
     - 1 cup/day ⇨ reduce risk by 30%
     - 2 cups/day ⇨ reduce risk by 40%
     - >4 cups/day ⇨ reduce risk by 80%

Klatsky,2006

4. **Antiviral therapy**

Improving results of antiviral therapy in HCV Genotype 1 infection

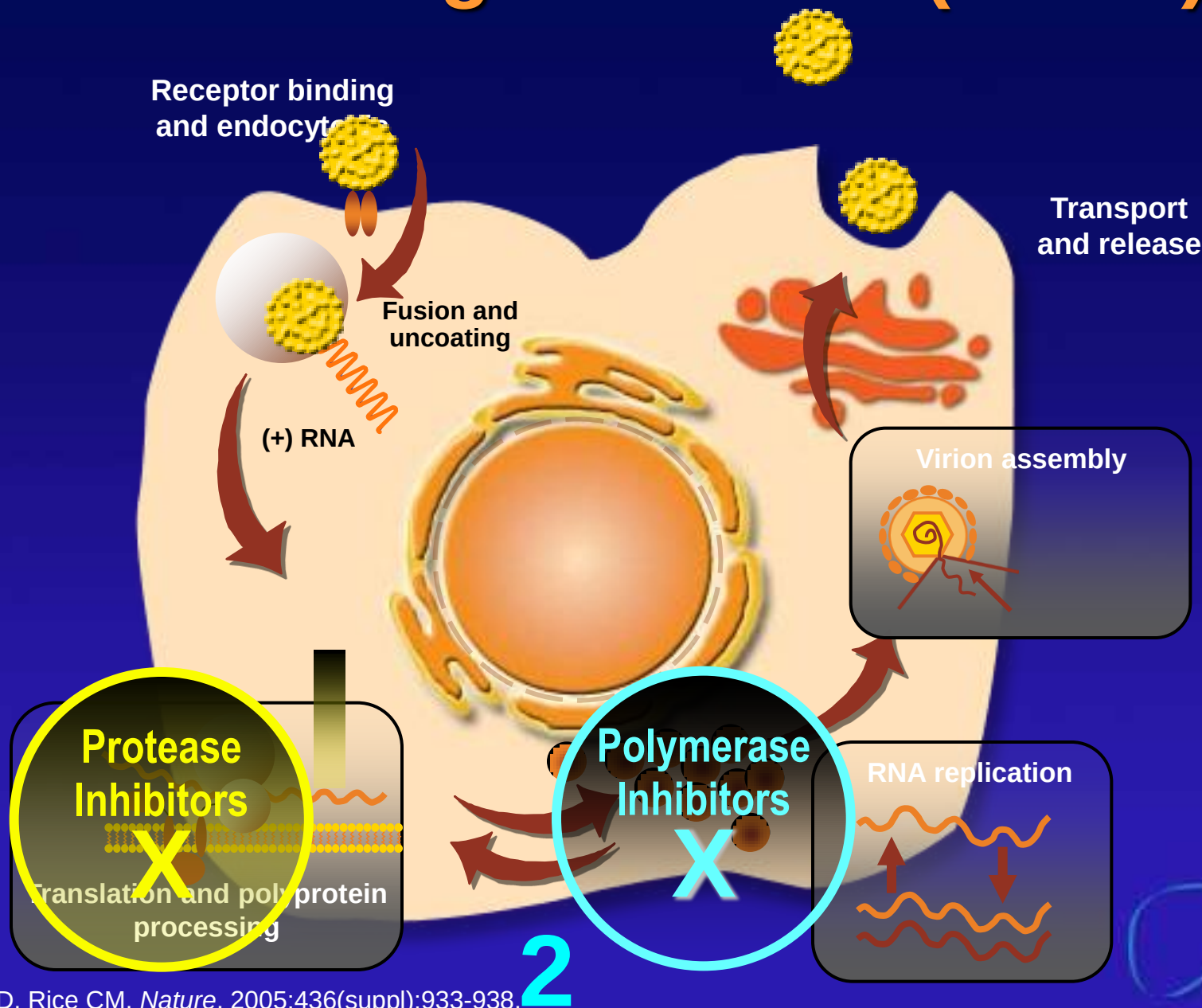


Treatment is POORLY tolerated

1. **Side effects of Interferon**
   1. Flue-like syndrome in 100%
   2. Anorexia, weight loss in 100%
   3. Insomnia in >90%
   4. Bone marrow suppression in >50%
   5. Depression in 40%
2. **Contraindications to Peg or RBV**
   1.
   2.
   3.
   4.
   5.
   6. Elderly

NEW THERAPUTIC APPROACHES

Direct Acting Antivirals (DAAs)



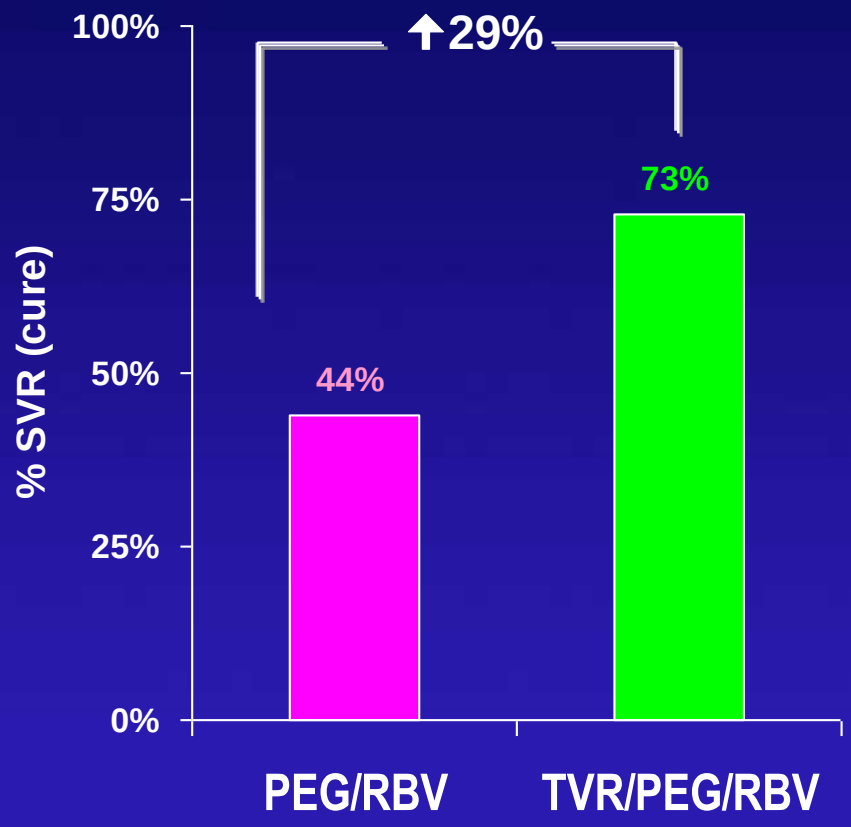
Lindenbach BD, Rice CM. *Nature*. 2005;436(suppl):933-938.

Protease Inhibitors

Target	Agent	Company	Phase
NS3/4a Serine Protease	Boceprevir	Merck	Phase III
	Telaprevir	Vertex	Phase III
	Danoprevir	Roche	Phase III
	TMC435	Tibotec	Phase III
	MK-7009	Merk	Phase III
	BI201335	Boehringer	Phase III
	MK-5172	Merck	Phase II
	SCH900518	Merck	Phase II
	ABT450	Abbott	Phase II
	BMS-650032	BMS	Phase II
	GS 9256	Gilead	Phase II
	GS 9451	Gilead	Phase II
	VX-985	Vertex	Phase I
	ACH1625	Achillon	Phase I
	IDX-320	Idenix	Phase I
	ACH1284	Achillon	Phase I
	BMS-791325	BMS	Phase I
	VX-500	Vertex	Phase I
	PHX1766	Pfizer	Phase I

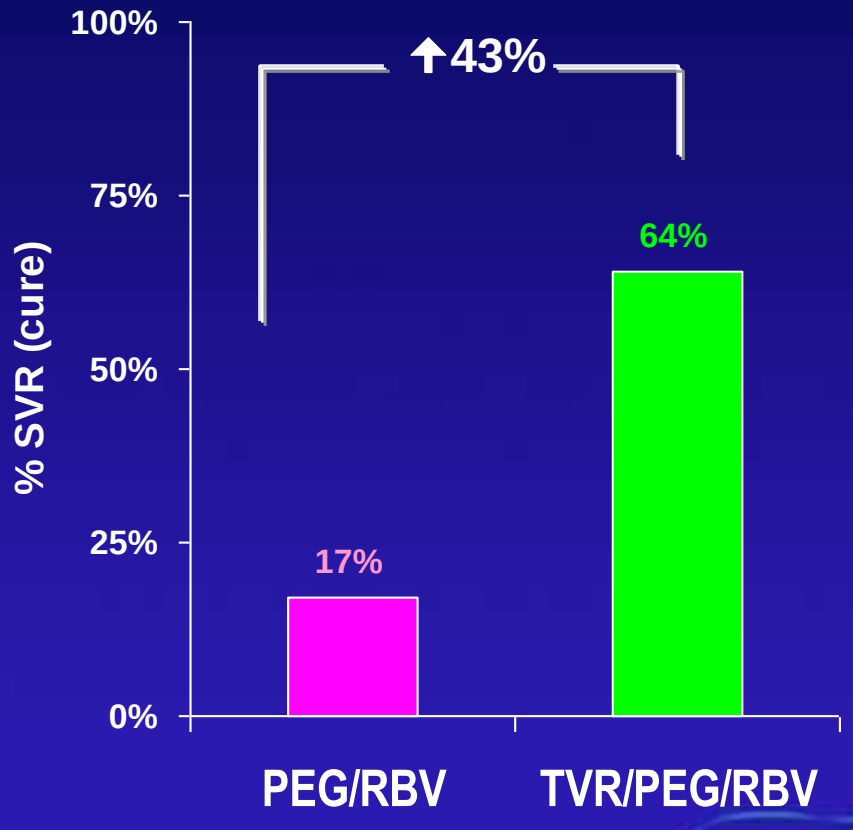
Adding Protease inhibitors to Interferon

Treatment-naïve



Jacobson I, et al. *N Engl J Med* 2011; 364: 2405-16

Previous Interferon



Zeuzem S, et al. *N Engl J Med* 2011; 364: 2417-28

Will Telaprevir and Boceprevir fill the current unmet medical need?

1. Limited efficacy

- Nil in HCV Gt 3 (⇨ 40% of HCV in NZ)

2. Limited tolerability

- Inconvenient, q8hrly dosing
- Need to take with high fat meal
- STILL NEED INTERFERON⇨S/E
- Protease inhibitor S/E: rash, anaemia
- multiple direct drug interactions

Inhibitors of the HCV Polymerase Complex

Target	Agent	Phase
NS5b Non-nucleoside analogue (NNA)	Filibuvir	Phase II
	Tegobuvir	Phase II
	JTK-003	Phase II
	BI207127	Phase II
	BMS-824393	Phase II
	VX-222	Phase II
	ABT-072	Phase II
	ABT-333	Phase II
	MK3281	Phase II
	ANA598	Phase II
	HCV-796	Phase I
	IDX375	Phase I
	VX759	Phase II
	PF4878691	Phase I
	RO5471354	Phase I
	GS-9669	Phase I

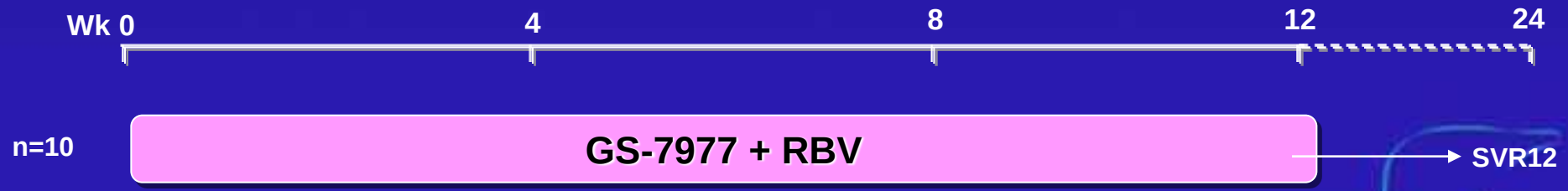
Target	Agent	Phase
Cyclophyllin B inhibitors	Alisporivir	Phase III
	NIM811	Phase I
	SYC-635	Phase I

Target	Agent	Phase
NS5a Non-nucleoside analogue	BMS790052	Phase III
	ABT-267	Phase II
	AZD7295	Phase II
	GS-5885	Phase II
	PPI-461	Phase II
	PPI-668	Phase I
	PPI-1833	Phase I
	ACH-2928	Preclin
	ACH-3102	Preclin
	BMS-824393	Preclin
	PPI-437	Preclin

Target	Agent	Phase
NS5b Nucleoside Analogue (NA)	RG7128	Phase III
	GS-7977	Phase III
	NM283	Phase II
	INX-189	Phase II
	PSI-938	Phase I
	ALS-002158	Phase I
	ALS-002200	Phase I
	GS-6620	Phase I
	IDX184	Phase I
	RG7348	Phase I
	MK-0608	Phase I

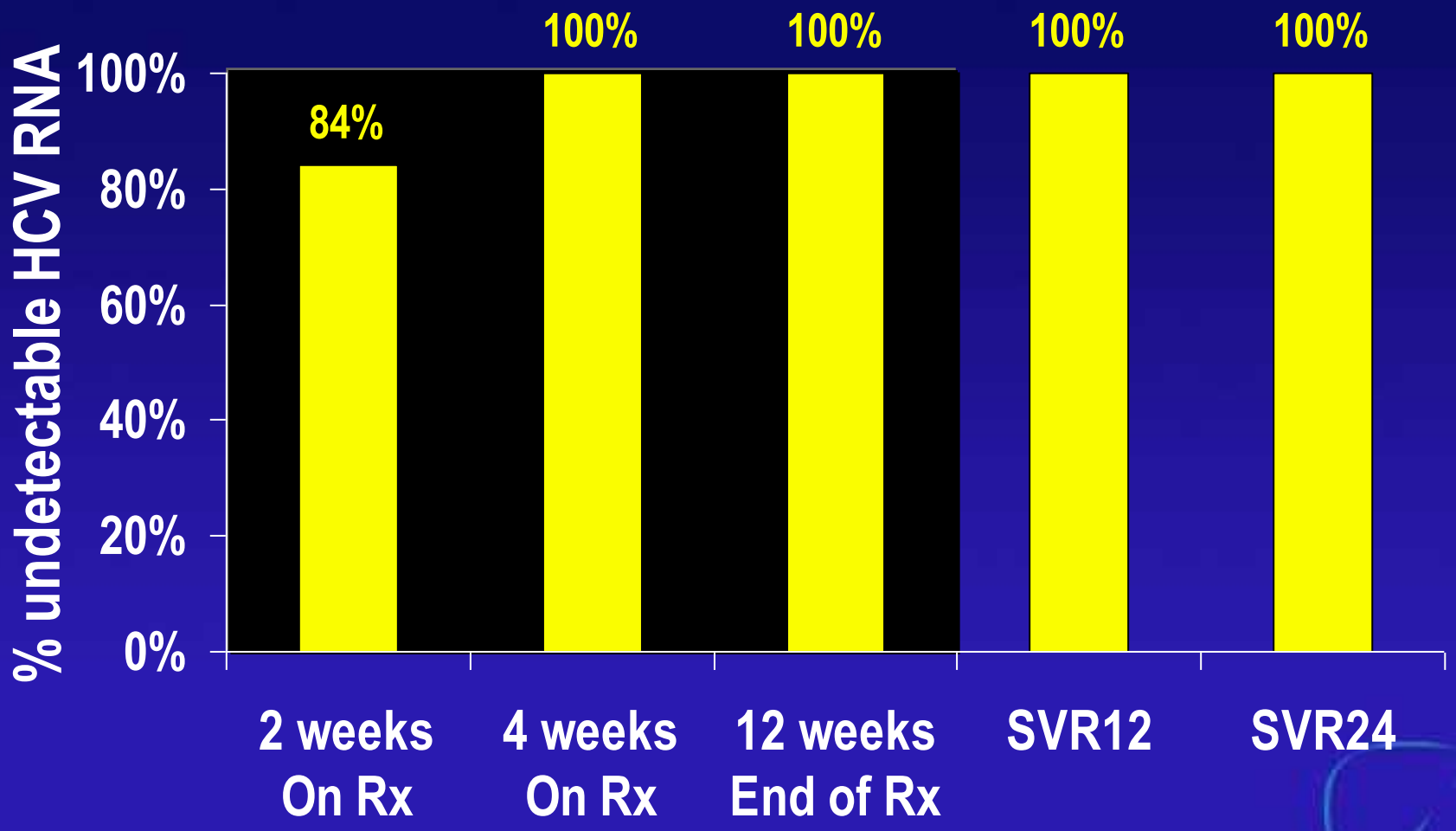
GS-7977 ELECTRON
Study Design for HCV GT2/3

- GS-7977 is HCV nucleotide polymerase inhibitor
  - »Once daily tablet, no food effect
  - »Very potent (5 log reduction in 1 week)
  - »Works against ALL HCV genotypes
  - »No specific side effects
  - »No drug interactions (give with methadone)
- Phase II trials conducted here in New Zealand
  - »All oral, no interferon
  - »Only 12 weeks duration



Gane E, et al. *Hepatology* 2011; 54: 377A

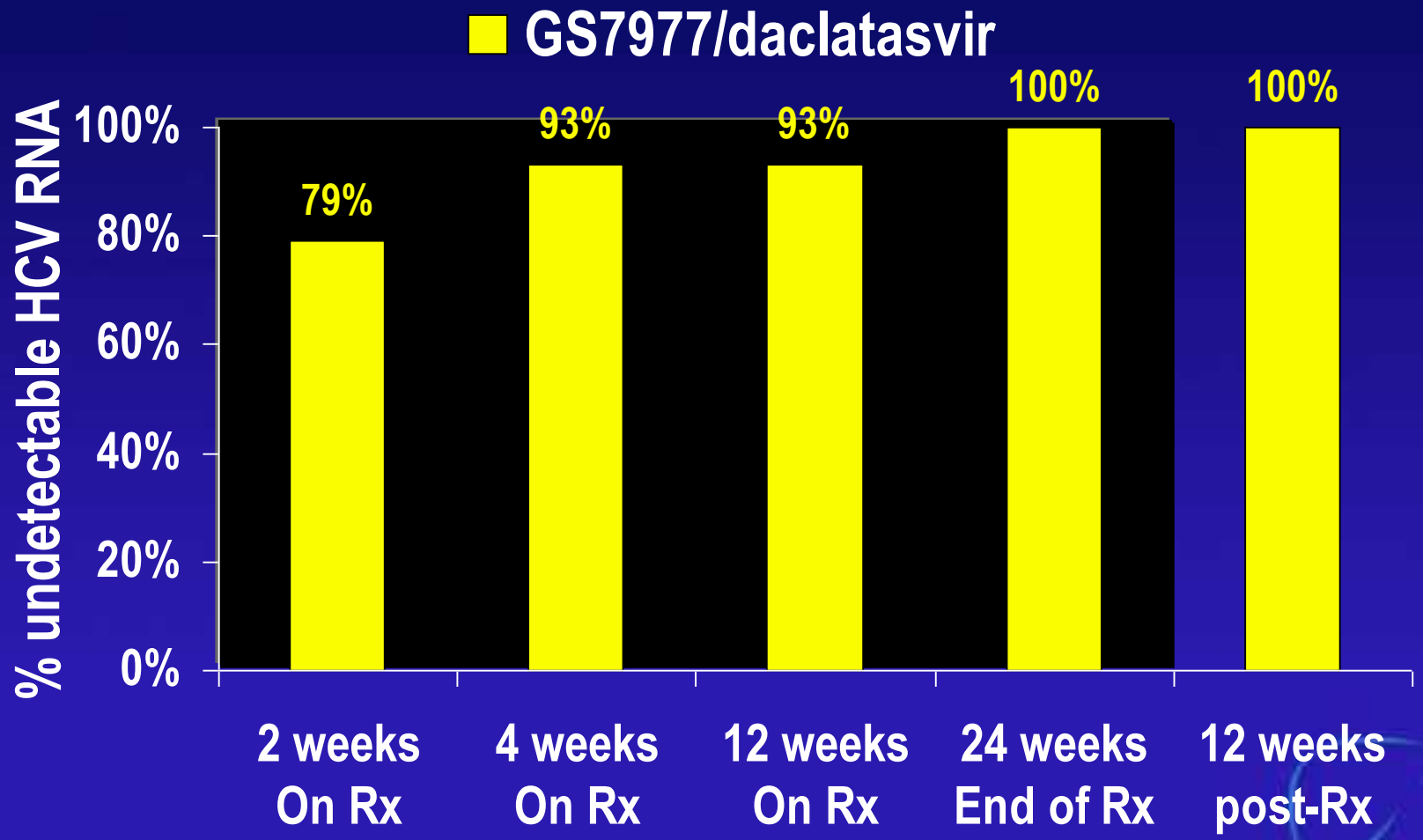
Nucleoside polymerase inhibitor in HCV Genotype 2/3 infection



Gane E, et al. *J Hepatol* 2012; 56: S438

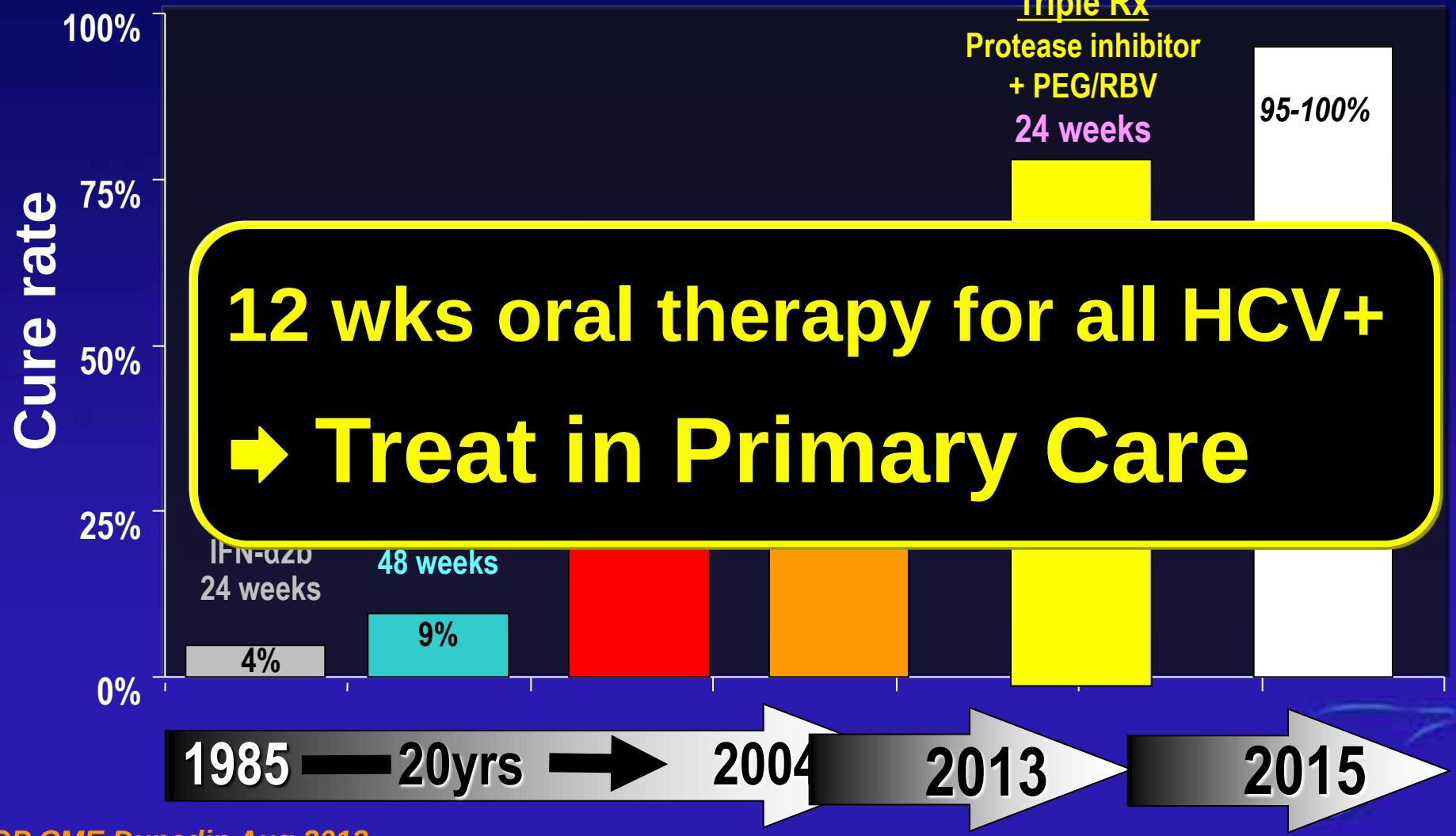
Nucleoside polymerase inhibitor PLUS NS5A inhibitor in HCV Genotype 1

(a) In HCV Genotype 1 (n=45)



Sulkowski M, et al. *J Hepatol* 2012; 56: S1422

Future Trends in HCV Therapy



Chronic Hepatitis C in NZ

- 50,000+ infected here in NZ
  - »Only 1/3 are aware of their status
- Prevention is always the best strategy
  - »No vaccine for HCV
  - »↓HCV transmission in “at-risk” IDU
- 200 deaths/yr ➡ 600/yr by 2030
  - »All preventable by earlier detection and treatment
  - »<1% are treated each year
- Treatments are getting much better
  - » No need for biopsy
  - » New treatments suitable for primary care

➡ **Need to increase HCV awareness**

A national approach to hepatitis C

2006-9: MoH Hep C Treatment Advisory Group "Strategic Directions for Hepatitis C"

2011: Improvements in Hep C Services Project

2012: National Action Plan, with aims to

- increase awareness of HCV in the community
- improve access to and uptake of HCV testing, assessment and treatment
- improve health outcomes for all New Zealanders who are living with HCV

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THEHEPATITISFOUNDATION

A national approach to hepatitis C

2012: National Action Plan implementation contracted to the Hepatitis Foundation

Pilots of an integrated HCV programme

1. **Wellington regional joint DHB pilot:**
   - Capital & Coast, Hutt Valley, Wairarapa DHBs
2. **Single DHB pilot**
   - Bay of Plenty DHB

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Goals of the Pilots

1. Increasing public awareness
2. Targeted Testing Programme
3. Community assessment and support
4. Integrated service delivery
5. Education, resources, and training

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1. Increasing Awareness

Increase awareness of risk factors for HCV and of pathways to access testing and care

1. Media campaign
2. Provider education and training
3. Educational Resources
4. Helpline (0800-332010)
5. Client-centred quarterly magazine
6. Website

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2. Targeted Testing

* **6 risk factors**

1. **Ever injected drugs**
2. **Ever transfused pre-1992 or overseas?**
3. **Ever lived in or received health care in SE Asia, Middle East, Eastern Europe?**
4. **Ever jaundiced or had acute hepatitis**
5. **Ever imprisoned**
6. **Mother has HCV**

➡ **easy access to testing in community via GPs, CADS, Needle Exchange, Sexual Health**

3. Community-based Assessment and Support Programme

* **Assessment and Support Program**
  - people diagnosed with hep C referred to community based programme
  - Fibroscan service
* **Community Hepatitis Nurse**
  - Provide community-based specialist clinical care,

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4. Integrated Service Delivery

- **Enable people to access the programme in their community**
  - ⇨Initial assessment and support
  - ⇨Safety net for those awaiting treatment
- **Enable secondary care to focus on treatment, complicated cases**

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5. Education resources and training

MoH e-Learning Module for HCV

http://learnonline.health.nz/course

Designed to meet needs of busy practice

1. On-line
2. Accessible from home
3. Easy to navigate and return to on multiple occasions
4. Brief 30-40 minutes only
5. Quiz at end (20 questions)
6. Printable certificate (if >70%)
7. Qualify for 2 CME points

http://learnonline.health.nz/course

Hepatitis C E-Learning for GPs

LearnHealth ▶ Hep C - Doctors

Welcome

Learn about hepatitis C by working through the five learning modules below.
Gain 1 CME credit by passing the assessment, completing the evaluation and then printing your certificate.

Access a range of resources to support you in your day-to-day work.
Help on using this programme.

Learn About

- 15 min — What Is Hepatitis C — Start
- 15 minutes — Identifying Hepatitis C — Start
- 15 minutes — Diagnosing Hepatitis C — Start
- 25 minutes — Treating Hepatitis C — Start
- 10 minutes — The Future - Hepatitis C — Start

Gain Accreditation

- Assessment
- Your feedback
- Print your certificate

Post-Learning Support

Quick facts

- What Is Hepatitis C
- Identifying Hepatitis C
- Diagnosing Hepatitis C
- Treating Hepatitis C
- The Future - Hepatitis C

Resources

- Patient Information Sheet
- GP Communication Guide
- Testing & Treatment Pathway
- Referral Form
- Programme References & Additional Reading

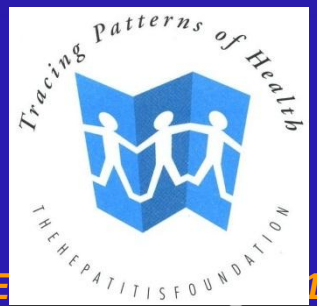
Got a question? Ask the experts
Find out more

Join the conversations
Find out more

Timelines of the Pilots

Pilots of an integrated HCV programme

1. 2012 Aug: Wgtn regional pilot commences
2. 2012 Sept: Single DHB pilot commences
3. 2014 June: both pilots cease
4. 2014 July-Dec: independent evaluation
5. 2015-20: national roll-out across all DHBs



viral HEPATITIS

AUCKLAND 2012

8TH AUSTRALASIAN CONFERENCE

10–12 September 2012

SkyCity Convention Centre – Auckland, New Zealand

ashm

Supporting the HIV, Viral Hepatitis and Sexual Health Workforce

www.hepatitis.org.au


isite
1471
Let's face it.
Hepatitis can't be ignored.
Have you ever lived or received medical treatment in a high-risk country?
Have you ever injected drugs?
Did you have a blood transfusion prior to 1992?
Have you ever been in prison?
... could you be at risk of hepatitis C?
For information and support, call our confidential helpline on 0800 33 20 10 or visit www.hepatitisfoundation.org.nz
In New Zealand, most people with chronic hepatitis C are unaware they have the disease.
Let's open our eyes to hepatitis C on World Hepatitis Day, Saturday 28 July 2012
The Hepatitis Foundation of New Zealand
BSJ164

Special thanks to

- Lucia Bercinskas, Ministry of Health
- Helen Payne, Hepatitis Foundation of NZ
- Kelly Barclay, Project Manager, HFNZ
- John Hornell CEO, HFNZ