
# The future's bright, the future's orange….

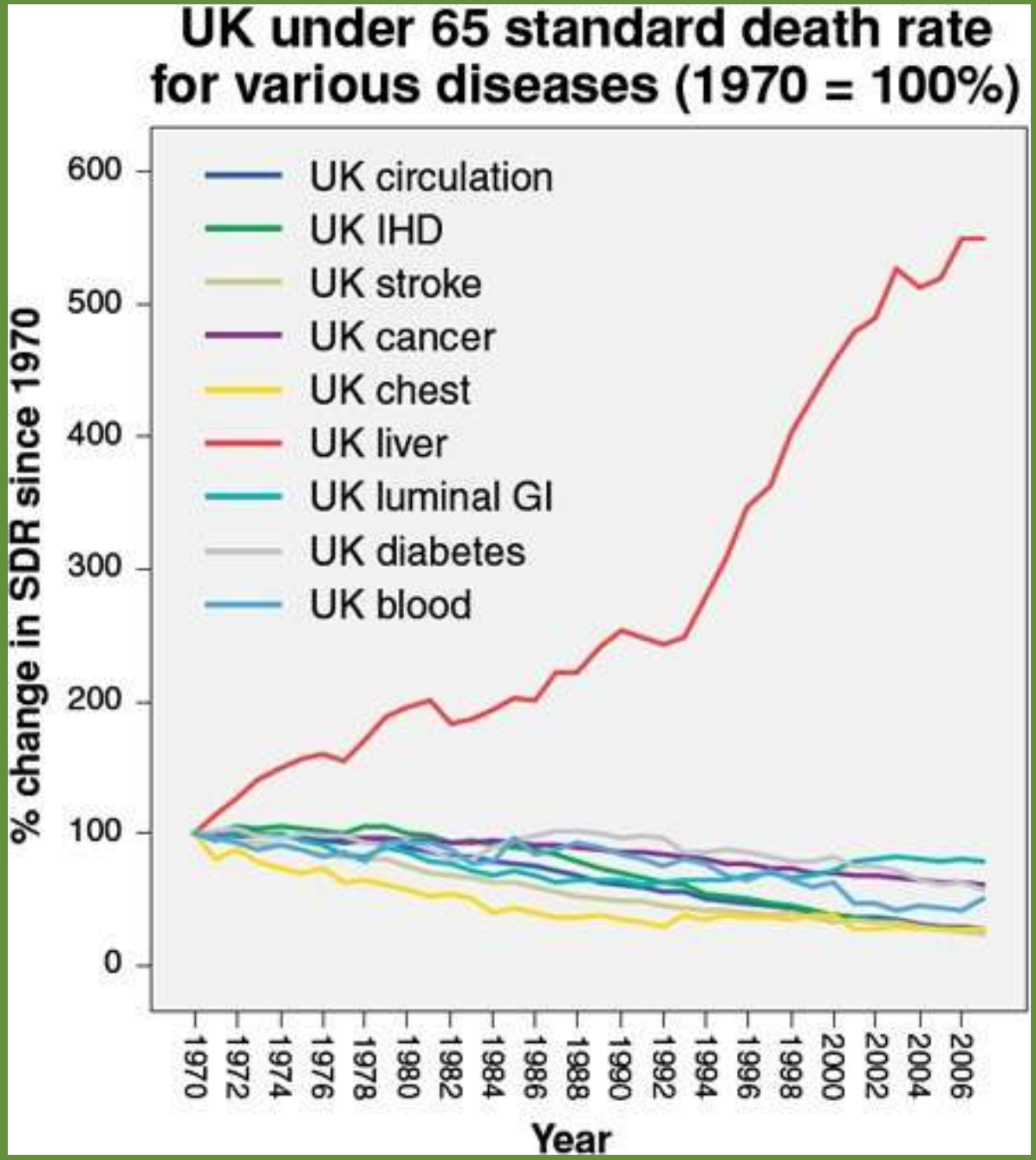
## the challenges of liver disease now and in the next 50 years

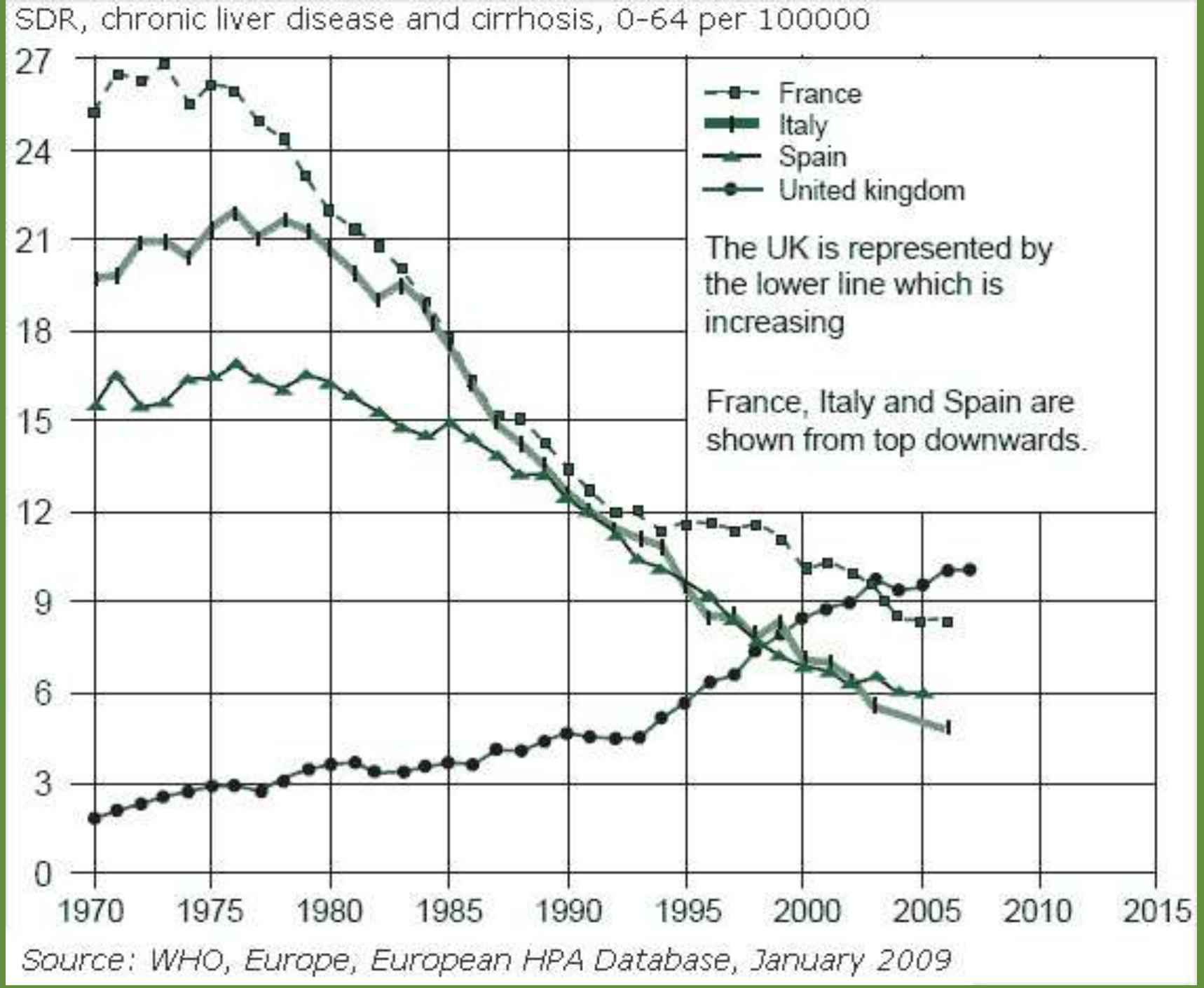
Peter Collins
Consultant Hepatologist
Bristol Royal Infirmary

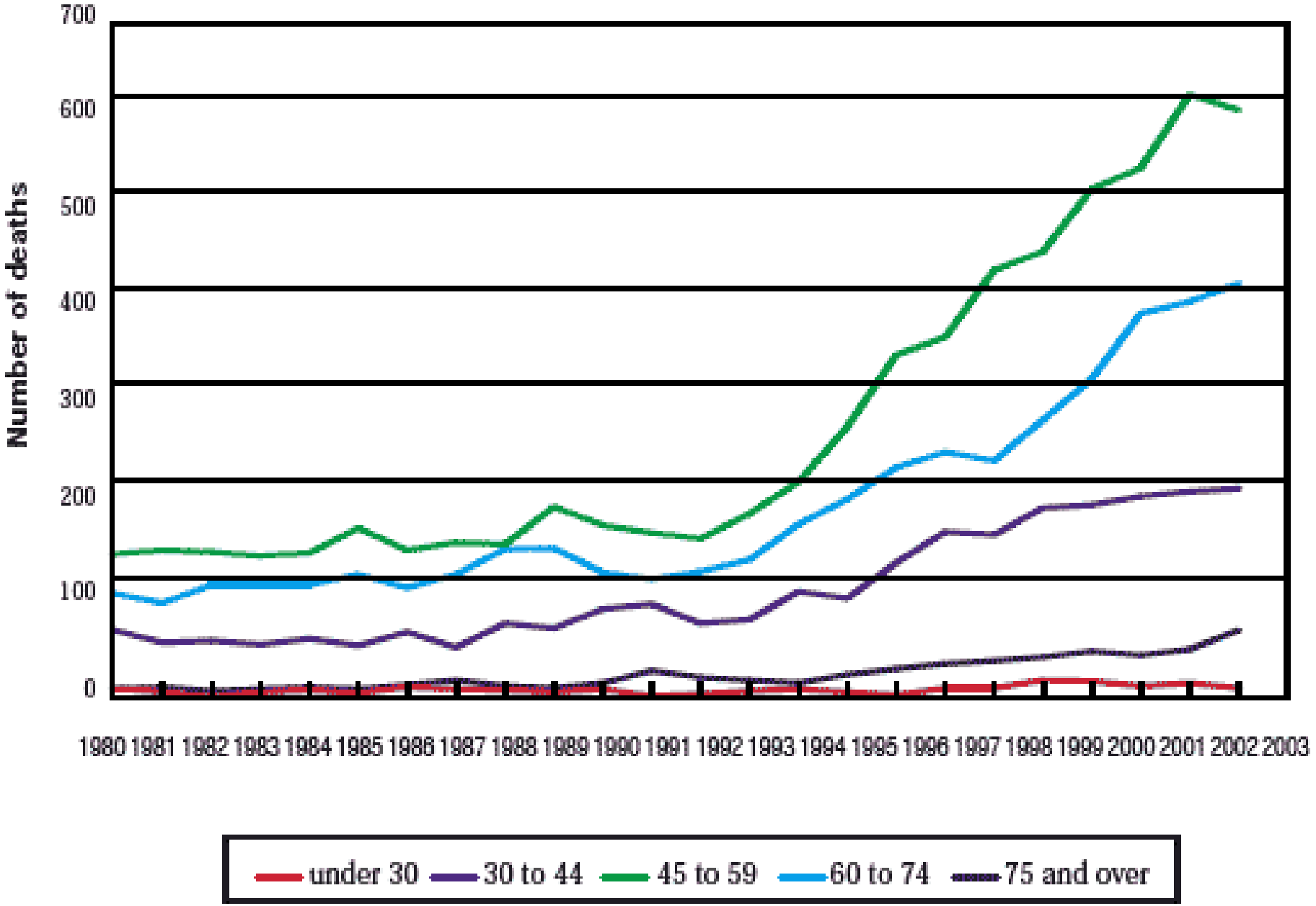
UHBristol liver unit

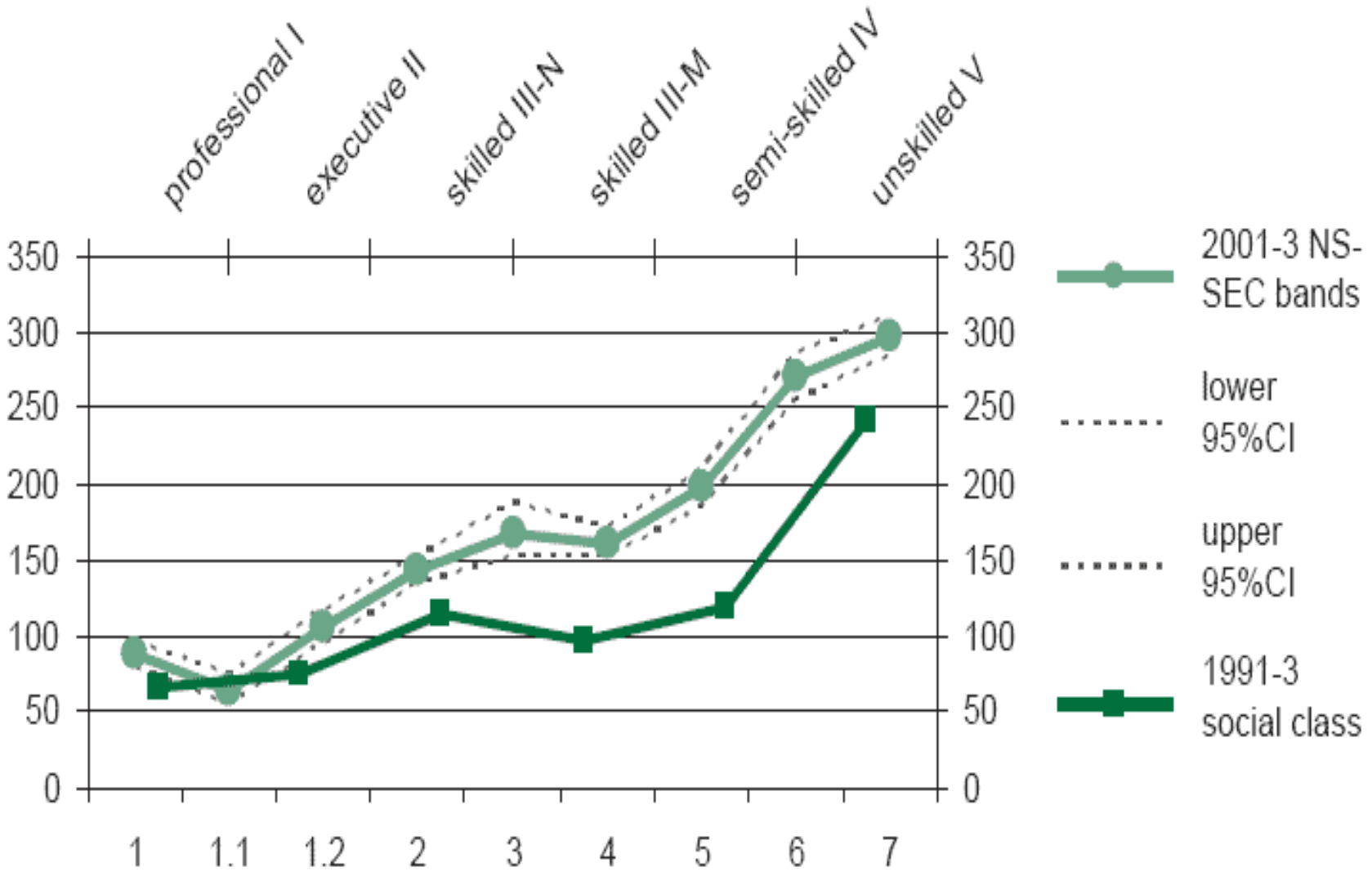

# the challenges of liver disease now and in the next 50 years

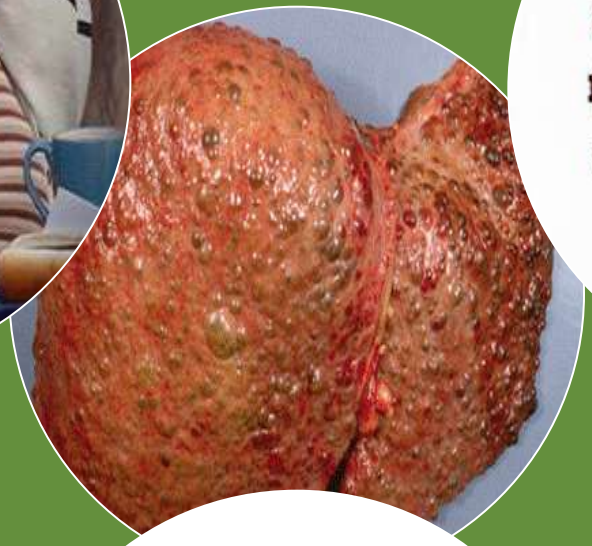

- The scale of the problem
- The main culprits
- What are we trying to look out for?
- How good are our tests?
- Is there anything better to use?

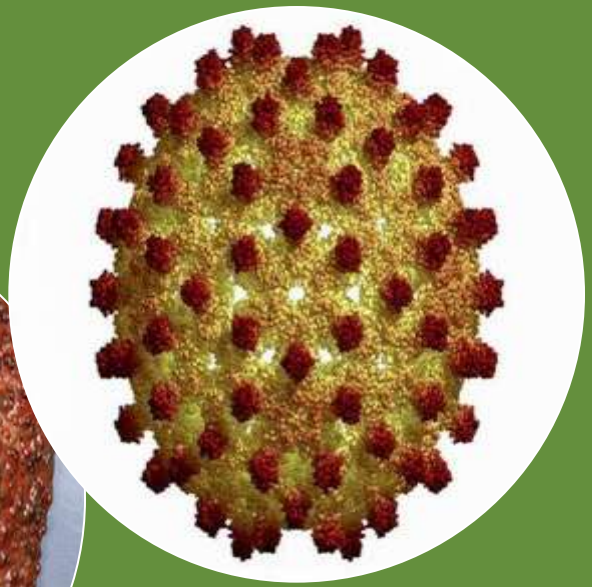

UK under 65 standard death rate for various diseases (1970 = 100%)
% change in SDR since 1970
600
500
400
300
200
100
0
UK circulation
UK IHD
UK stroke
UK cancer
UK chest
UK liver
UK luminal GI
UK diabetes
UK blood
1970
1972
1974
1976
1978
1980
1982
1984
1986
1988
1990
1992
1994
1996
1998
2000
2002
2004
2006
Year

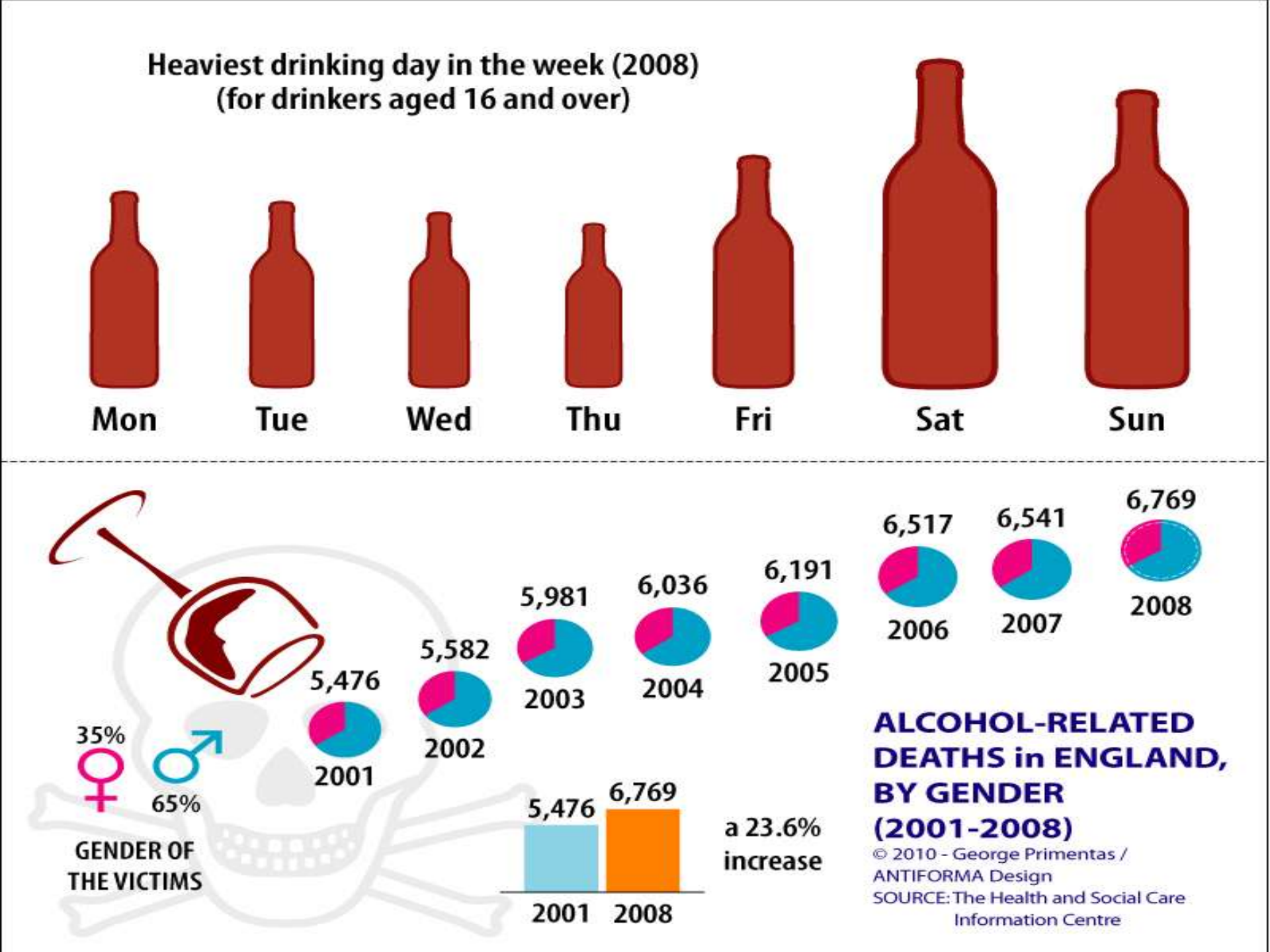

SDR, chronic liver disease and cirrhosis, 0-64 per 100000
27
24
21
18
15
12
9
6
3
0
1970
1975
1980
1985
1990
1995
2000
2005
2010
2015
France
Italy
Spain
United kingdom
The UK is represented by the lower line which is increasing
France, Italy and Spain are shown from top downwards.
Source: WHO, Europe, European HPA Database, January 2009


Number of deaths
700
600
500
400
300
200
100
0
1980 1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003
under 30
30 to 44
45 to 59
60 to 74
75 and over

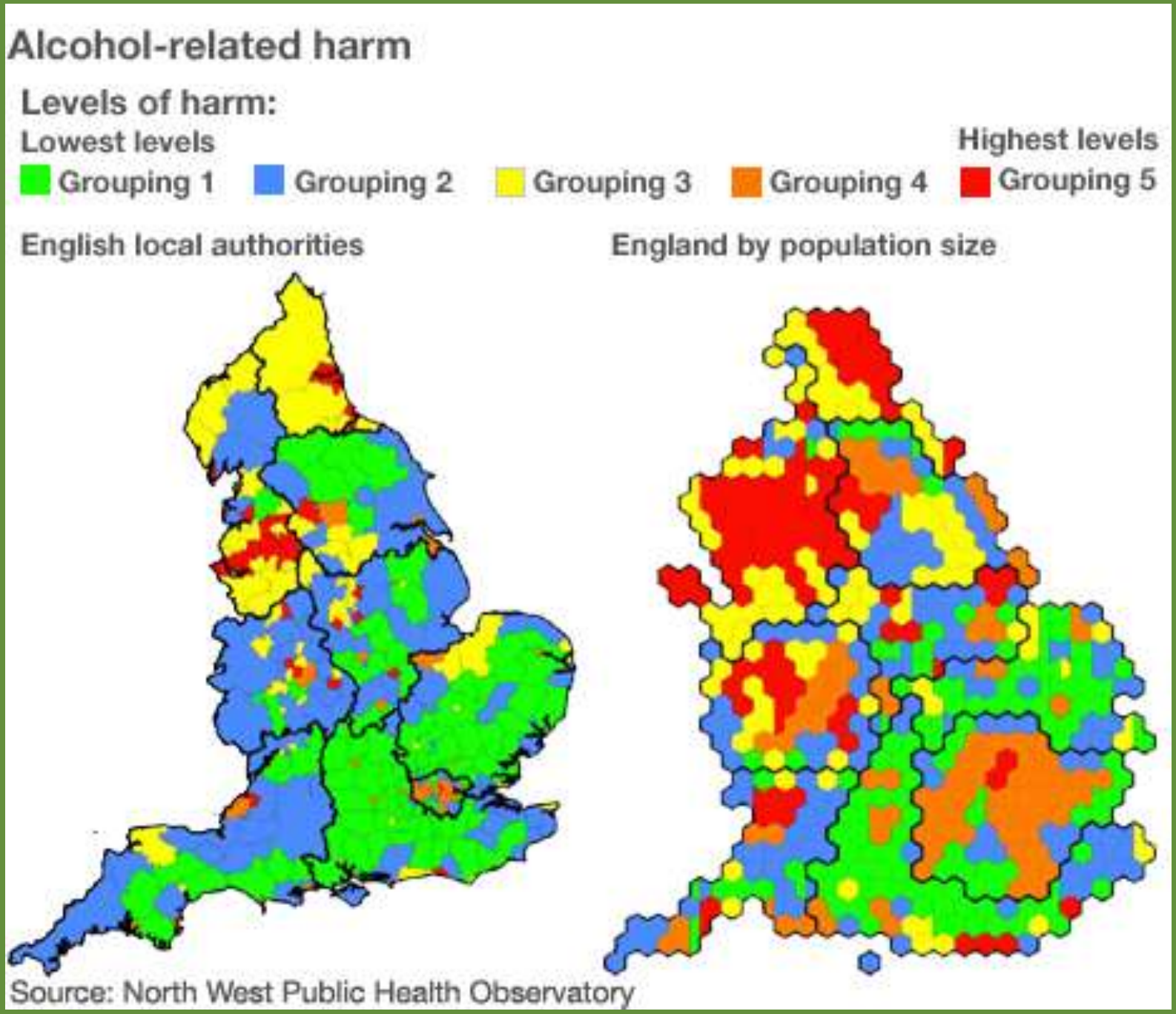

professional I
executive II
skilled III-N
skilled III-M
semi-skilled IV
unskilled V
350
300
250
200
150
100
50
0
1
1.1
1.2
2
3
4
5
6
7
2001-3 NS-SEC bands
lower 95%CI
upper 95%CI
1991-3 social class






Heaviest drinking day in the week (2008)
(for drinkers aged 16 and over)
Mon
Tue
Wed
Thu
Fri
Sat
Sun
35%
65%
GENDER OF THE VICTIMS
5,476
2001
5,582
2002
5,981
2003
6,036
2004
6,191
2005
6,517
2006
6,541
2007
6,769
2008
5,476
6,769
2001
2008
a 23.6% increase
ALCOHOL-RELATED DEATHS in ENGLAND, BY GENDER (2001-2008)
© 2010 - George Primentas / ANTIFORMA Design
SOURCE: The Health and Social Care Information Centre

# Alcohol-related harm



| Region | Deaths[a] | | Years of life lost[a] | | Number of disability-adjusted life-years lost[a] | |
|---|---|---|---|---|---|---|
| | Number of deaths (thousands) | Percentage of all deaths | Number (thousands) | Percentage of all years of life lost | Number (thousands) | Percentage of all disability-adjusted life-years lost |
| **Global** | **2,123** | **3.7** | **38,177** | **4.1** | **64,975** | **4.4** |
| Men | 1,836 | 6.1 | 32,553 | 6.6 | 54,970 | 7.1 |
| Women | 287 | 1.1 | 5,625 | 1.3 | 10,006 | 1.4 |
| **African** | | | | | | |
| Men | 184 | 3.4 | 4,165 | 3.0 | 5,757 | 3.2 |
| Women | 50 | 1.0 | 1,050 | 0.8 | 1,429 | 0.8 |
| **The Americas** | | | | | | |
| Men | 277 | 8.7 | 5,616 | 14.1 | 12,026 | 15.2 |
| Women | 46 | 1.7 | 871 | 3.2 | 2,569 | 3.9 |
| **SE Asia** | | | | | | |
| Men | 285 | 3.7 | 5,314 | 3.8 | 8,088 | 3.8 |
| Women | 28 | 0.4 | 586 | 0.5 | 867 | 0.4 |
| **European** | | | | | | |
| Men | 532 | 10.8 | 9,085 | 17.8 | 14,017 | 16.7 |
| Women | 77 | 1.7 | 1,644 | 5.2 | 2,553 | 3.8 |
| **East Mediterranean** | | | | | | |
| Men | 20 | 0.9 | 394 | 0.9 | 480 | 0.7 |
| Women | 3 | 0.2 | 57 | 0.1 | 77 | 0.1 |
| **Western Pacific** | | | | | | |
| Men | 539 | 8.5 | 7,979 | 10.1 | 14,603 | 10.3 |
| Women | 82 | 1.5 | 1,417 | 2.3 | 2,511 | 2.1 |

**Table 1.** Global and regional burden of disease attributable to alcohol consumption, 2002

[a] Adjusted for beneficial effects attributable to alcohol consumption.

- **The global economic cost of the harmful use of alcohol in 2002**
  **(Cost in US$)**

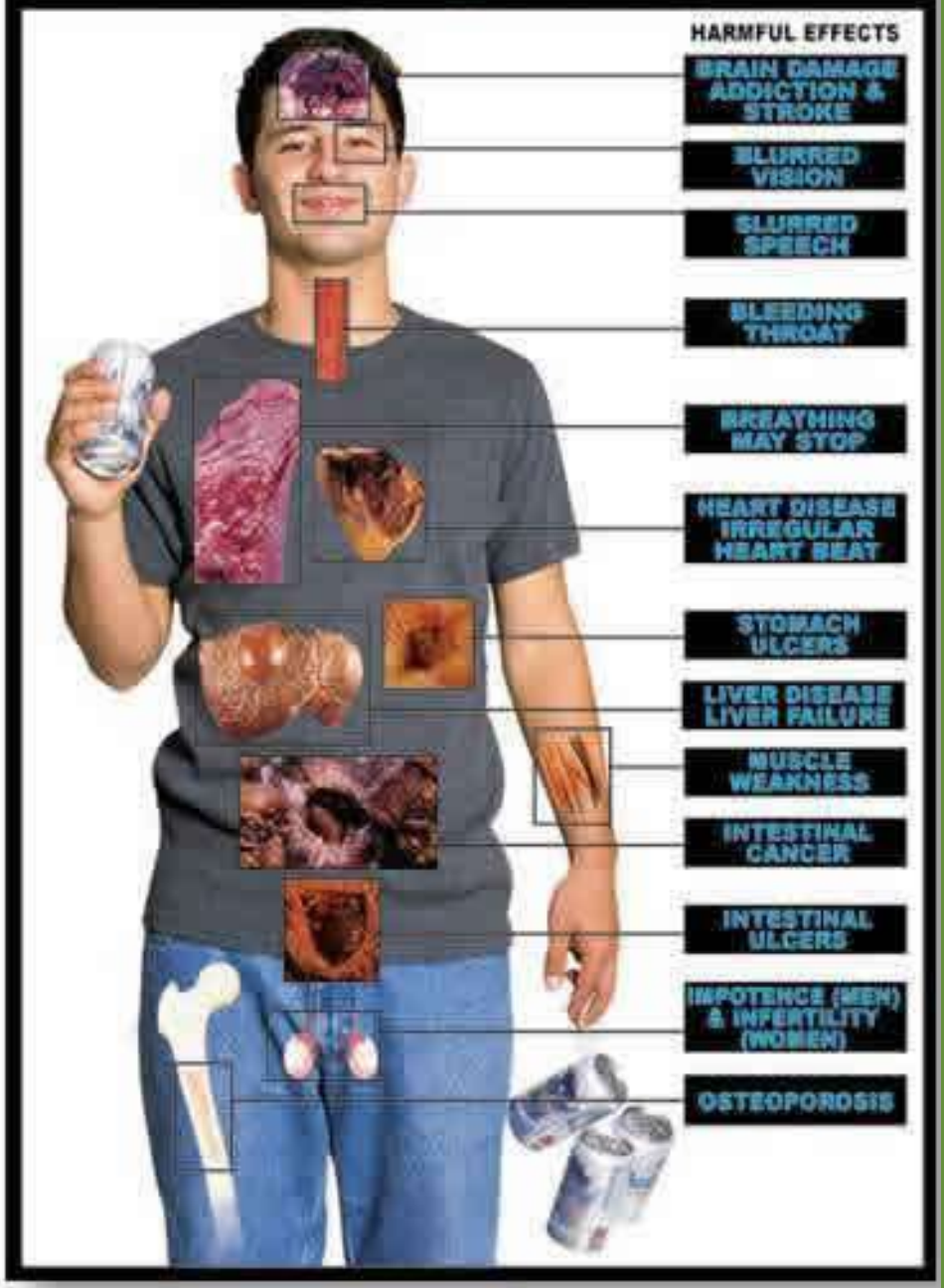
- This has been estimated to be between 210,000 million and 665,000 million:

- Illness 50,000–120,000 million
- Premature mortality 55,000–210,000 million
- Drink-driving 30,000–55,000 million
- Absenteeism 30,000–65,000 millio
- Unemployment 80,000 million
- Criminal justice 30,000–85,000 million
- Criminal damage 15,000–50,000 million
- The total equates to between 0.6% and 2.0% of global gross domestic product.
- The WHO assessment cautions that "due to current trends both in availability of alcohol and increases in alcohol consumption the detrimental impact of alcohol is expected to increase in the future if further interventions are not introduced."

# Occupations with highest alcohol-related mortality, 2001-5

| Men aged 20 – 64 | Proportional mortality ratio* |
|---|---|
| Bar staff | 223 |
| Seafarers (merchant navy), barge, lighter & boat operatives | 216 |
| Publicans and managers of licensed premises | 202 |
| Civil service executive officers | 189 |
| Musicians | 156 |
| NCOs and other ranks | 136 |
| Coal mine operatives | 121 |
| **Women aged 20 – 64** | |
| Bar staff | 203 |
| Publicans and managers of licensed premises | 193 |
| Actors, entertainers | 185 |
| Hairdressers, barbers | 146 |

# ALCOHOL


HARMFUL EFFECTS
BRAIN DAMAGE ADDICTION & STROKE
BLURRED VISION
SLURRED SPEECH
BLEEDING THROAT
BREATHING MAY STOP
HEART DISEASE IRREGULAR HEART BEAT
STOMACH ULCERS
LIVER DISEASE LIVER FAILURE
MUSCLE WEAKNESS
INTESTINAL CANCER
INTESTINAL ULCERS
IMPOTENCE (MEN) & INFERTILITY (WOMEN)
OSTEOPOROSIS


Women should drink no more than 2 to 3 units in a day

Men should drink no more than 3 to 4 units in a day

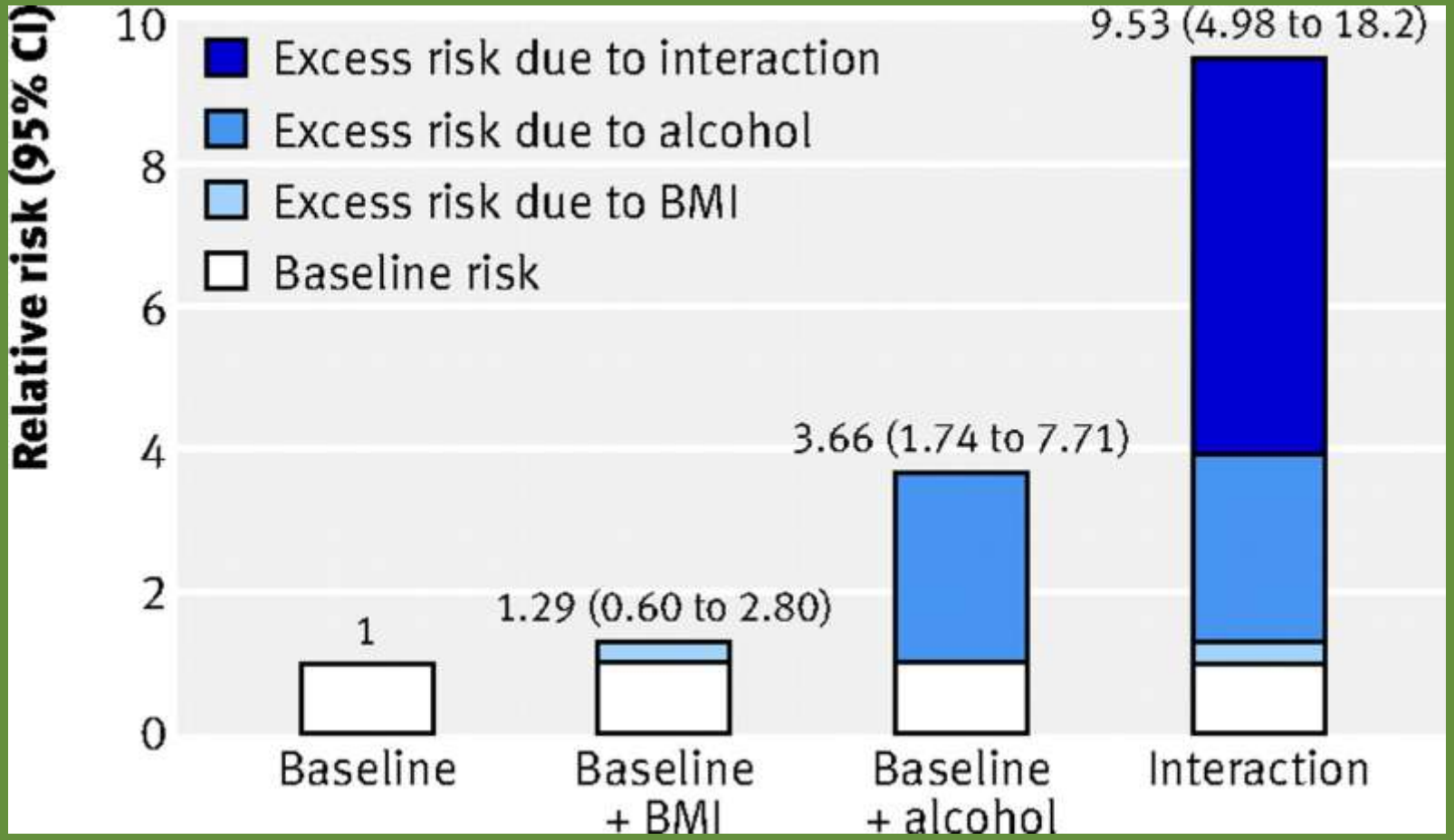
Don't save up several days 'allowance' and drink it all at once

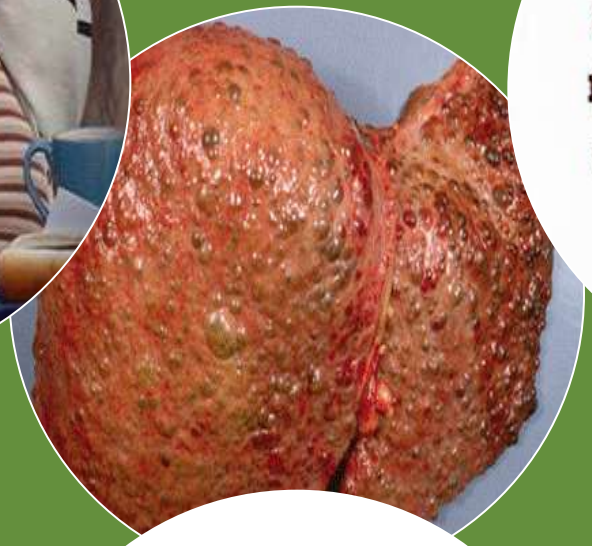
Give your liver two days in a row without alcohol every week to reduce the impact that alcohol can have on your liver and break the habit of drinking every day.

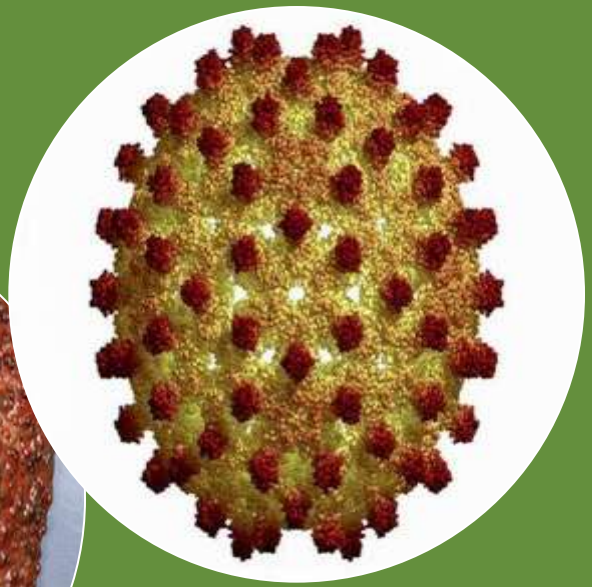
BMJ

**Effect of body mass index and alcohol consumption on liver disease: analysis of data from two prospective cohort studies**

*BMJ 2010; 340 doi: 10.1136/bmj.c1240 (Published 11 March 2010)*

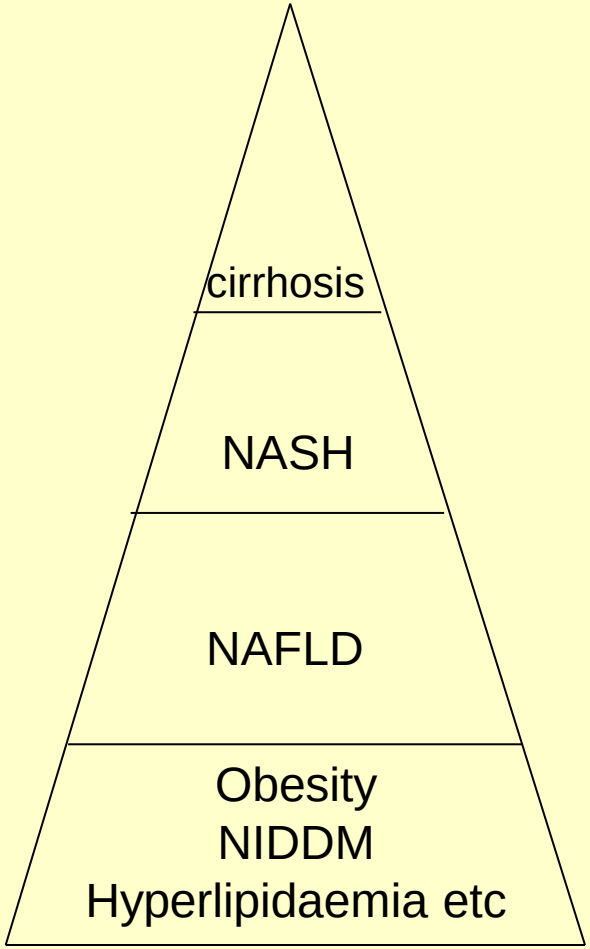




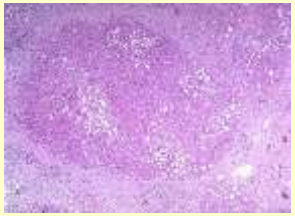
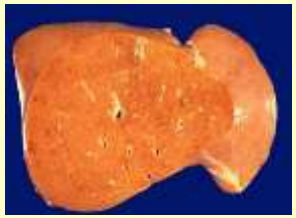
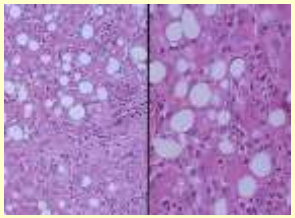
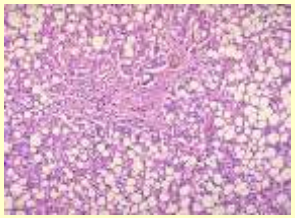


# Metabolic

- NAFLD
- NASH






# THE METABOLIC SYNDROME

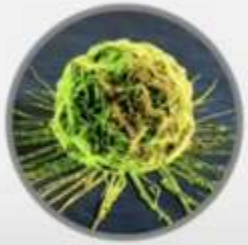
HEART DISEASE

LIPID PROBLEMS

HYPERTENSION

TYPE 2 DIABETES

DEMENTIA



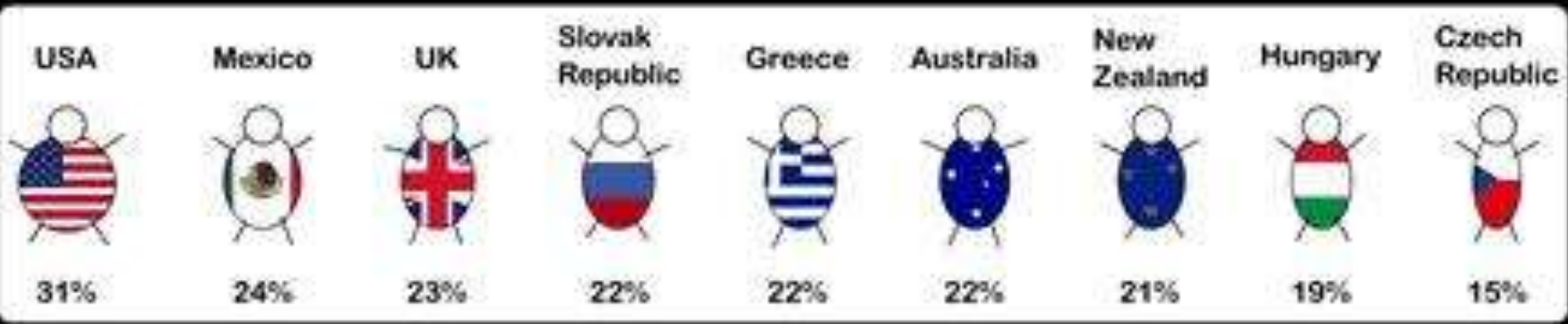
CANCER

POLYSYSTIC OVARIAN SYNDROME

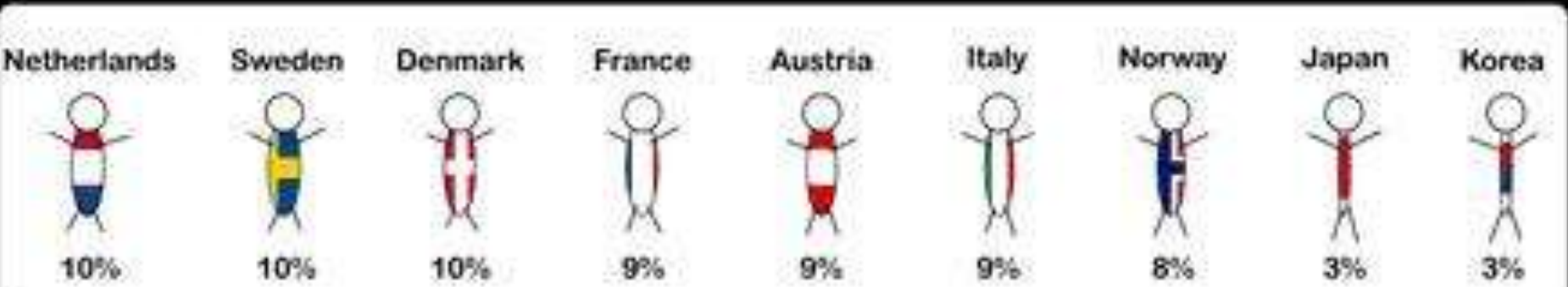
NON-ALCOHOLIC FATTY LIVER DISEASE

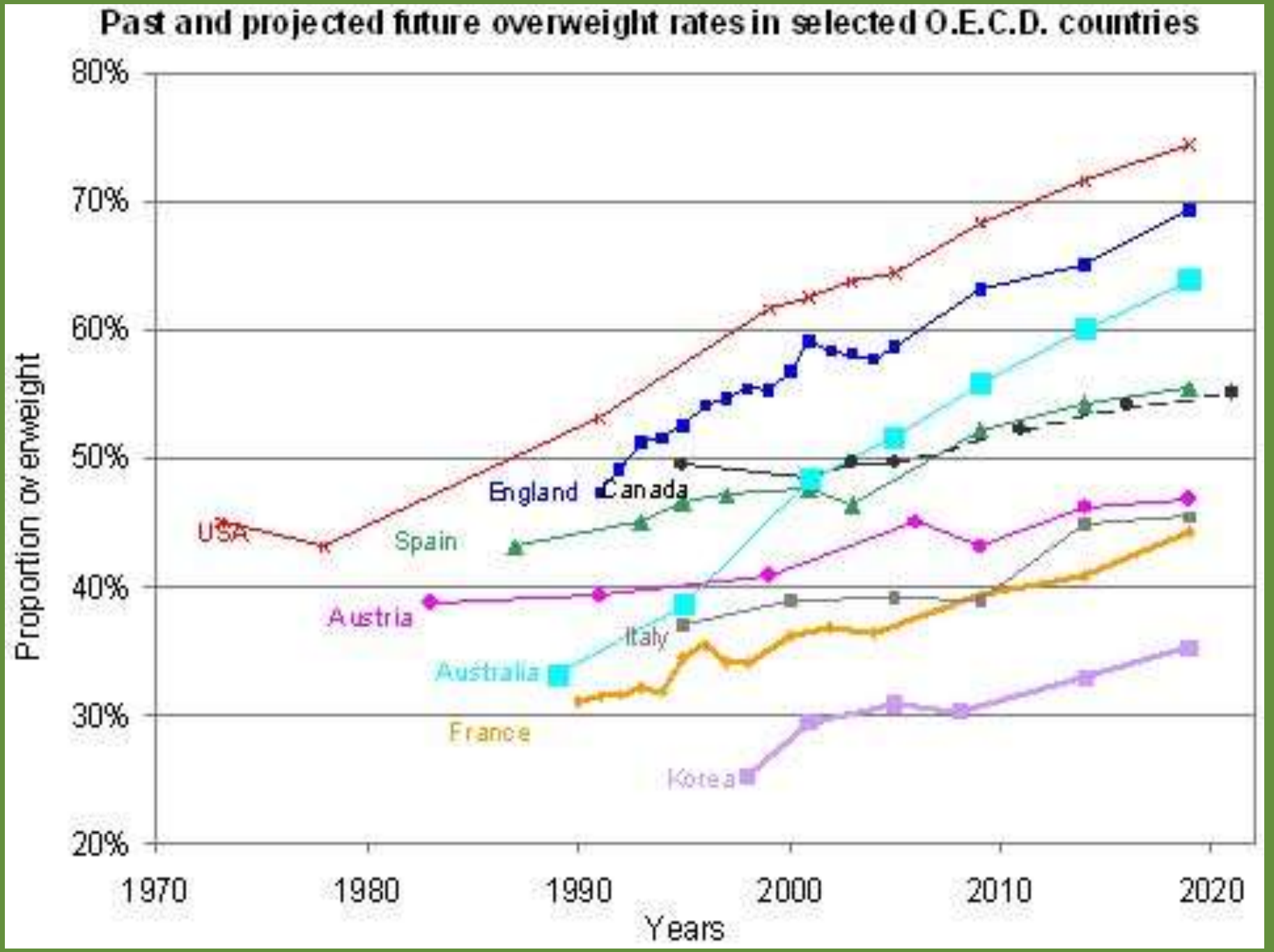
# OBESITY:

The percentage of the population older than 15 with a body-mass index greater than 30.

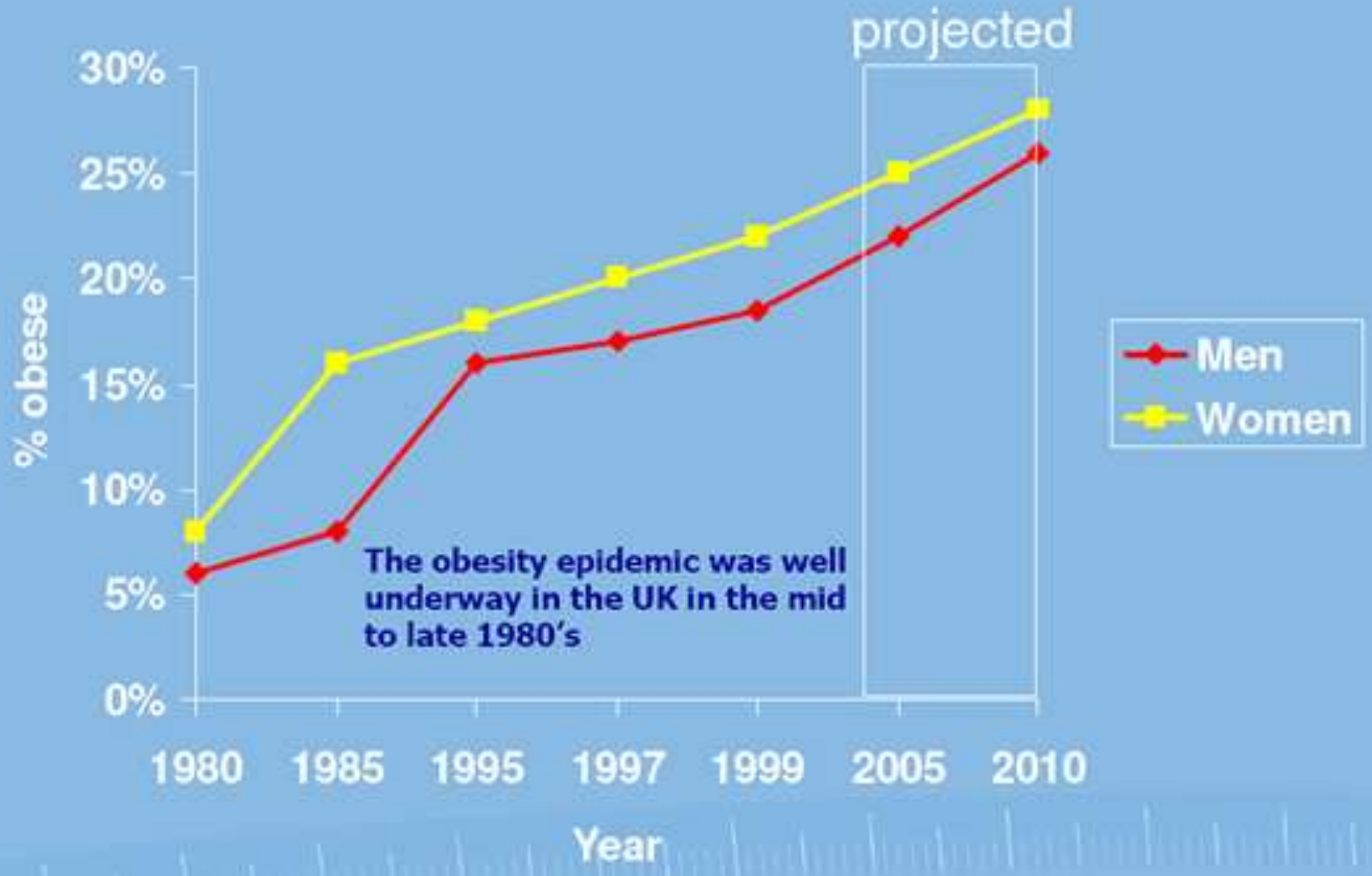






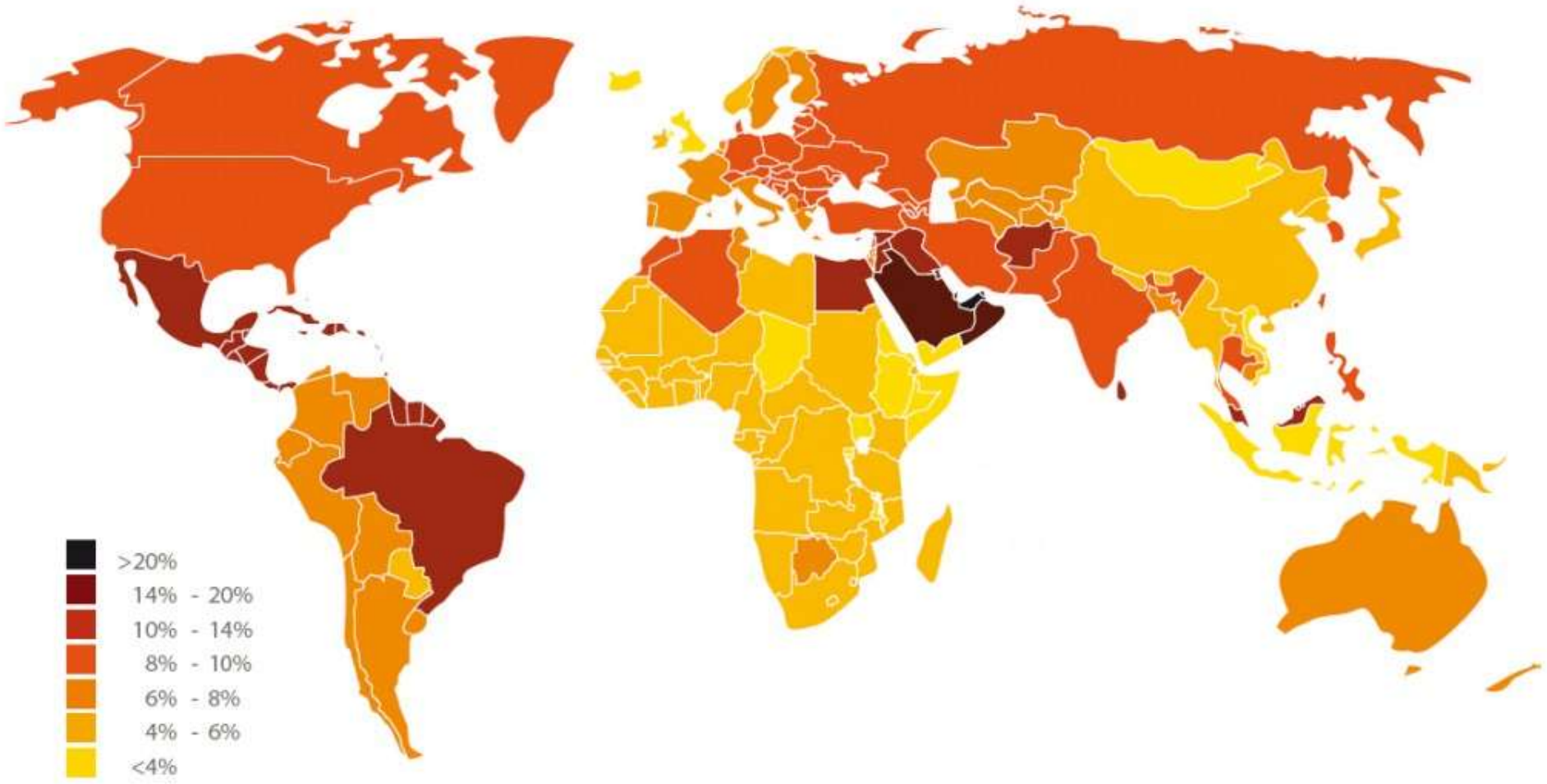

Past and projected future overweight rates in selected O.E.C.D. countries
80%
70%
60%
50%
40%
30%
20%
Proportion overweight
1970
1980
1990
2000
2010
2020
Years
USA
England
Canada
Spain
Austria
Italy
Australia
France
Korea

# Prevalence of obesity - UK



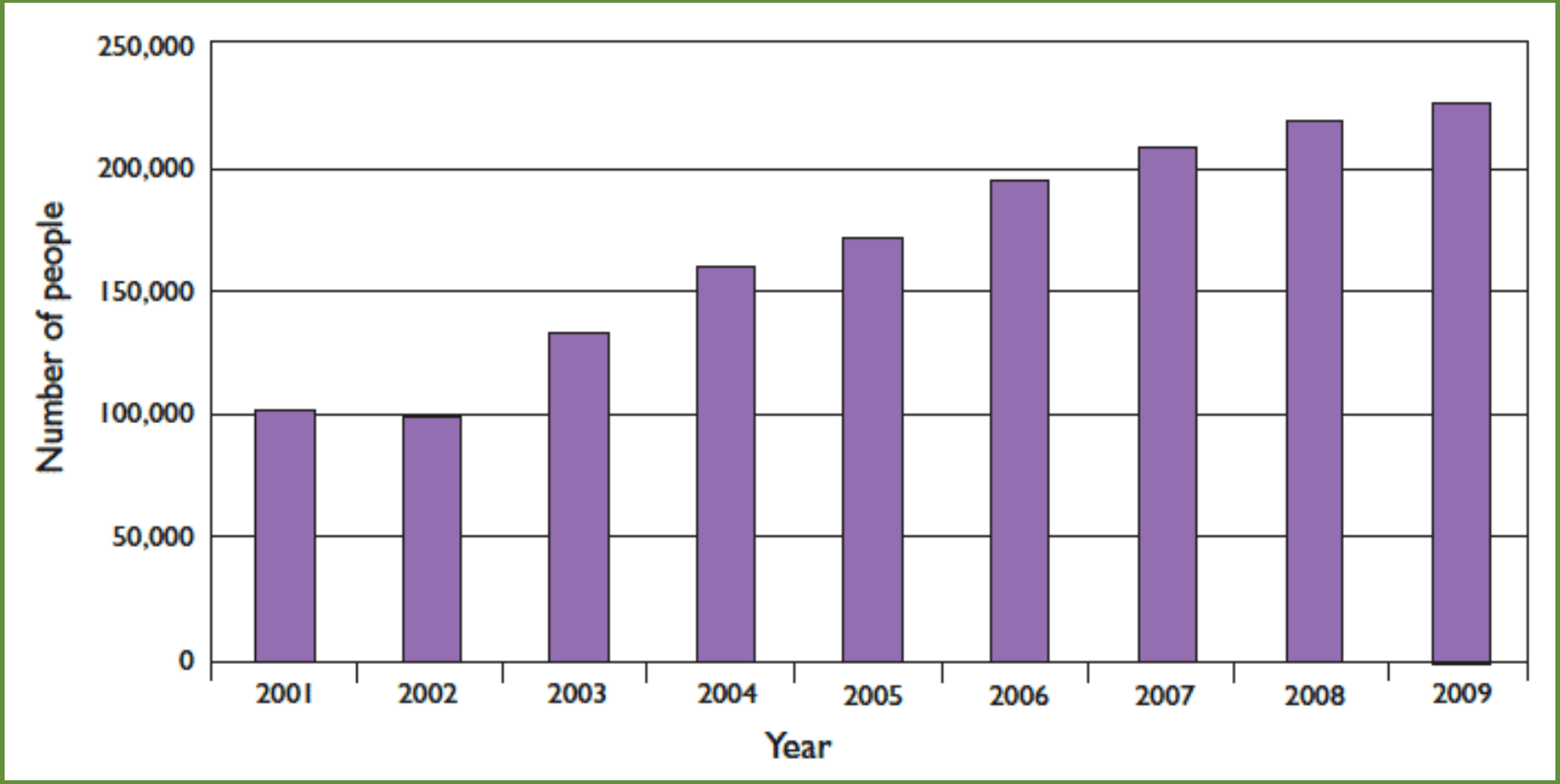

Adapted from Health Survey for England 2003

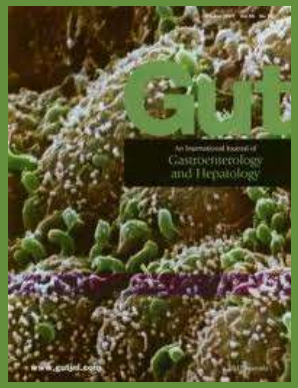
Prevalence estimates of diabetes, 2025




SOURCE: *DIABETES ATLAS THIRD EDITION*, © INTERNATIONAL DIABETES FEDERATION, 2006

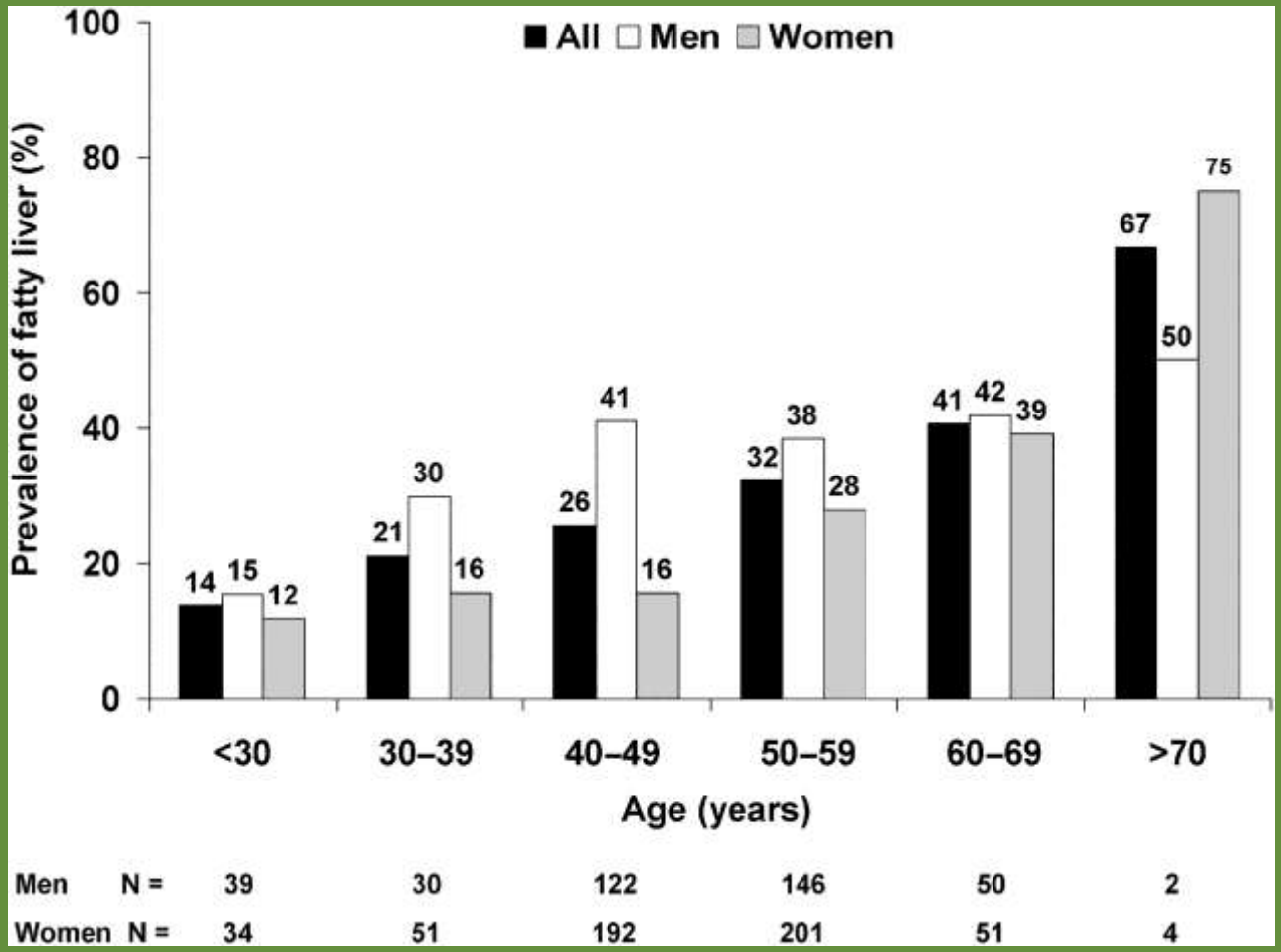
# Increasing prevalence of diabetes in Scotland






# Prevalence of non-alcoholic fatty liver disease and advanced fibrosis in Hong Kong Chinese: a population study using proton-magnetic resonance spectroscopy and transient elastography

Gut 2012 61 p409-415




# The natural history of nonalcoholic fatty liver disease: a population-based cohort study.

Adams LA, Lymp JF, St Sauver J, Sanderson SO, Lindor KD, Feldstein A, Angulo P.

- Rochester Epidemiology Project
  - Olmsted county Minnesota
    - 95% residents have at least 1 health encounter in a 4 year period
    - 124,000 (81% urban 90.35 Caucasian)
  - Study Period 1980-2000

Gastroenterology. 2005 Jul;129(1):113-21.


**The natural history of nonalcoholic fatty liver disease: a population-based cohort study.**

Adams LA, Lymp JF, St Sauver J, Sanderson SO, Lindor KD, Feldstein A, Angulo P.

- 435 patients diagnosed with NAFLD
  - Age 49 ±15
  - BMI 33.5 ±6.5
  - Diabetes 26%
  - Abnormal ALT 66%

  - Incidence 4.2/100,000 (1980-85)
  - Incidence 38/100,000 (1995-00)

Gastroenterology. 2005 Jul;129(1):113-21.


**The natural history of nonalcoholic fatty liver disease: a population-based cohort study.**

Adams LA, Lymp JF, St Sauver J, Sanderson SO, Lindor KD, Feldstein A, Angulo P.

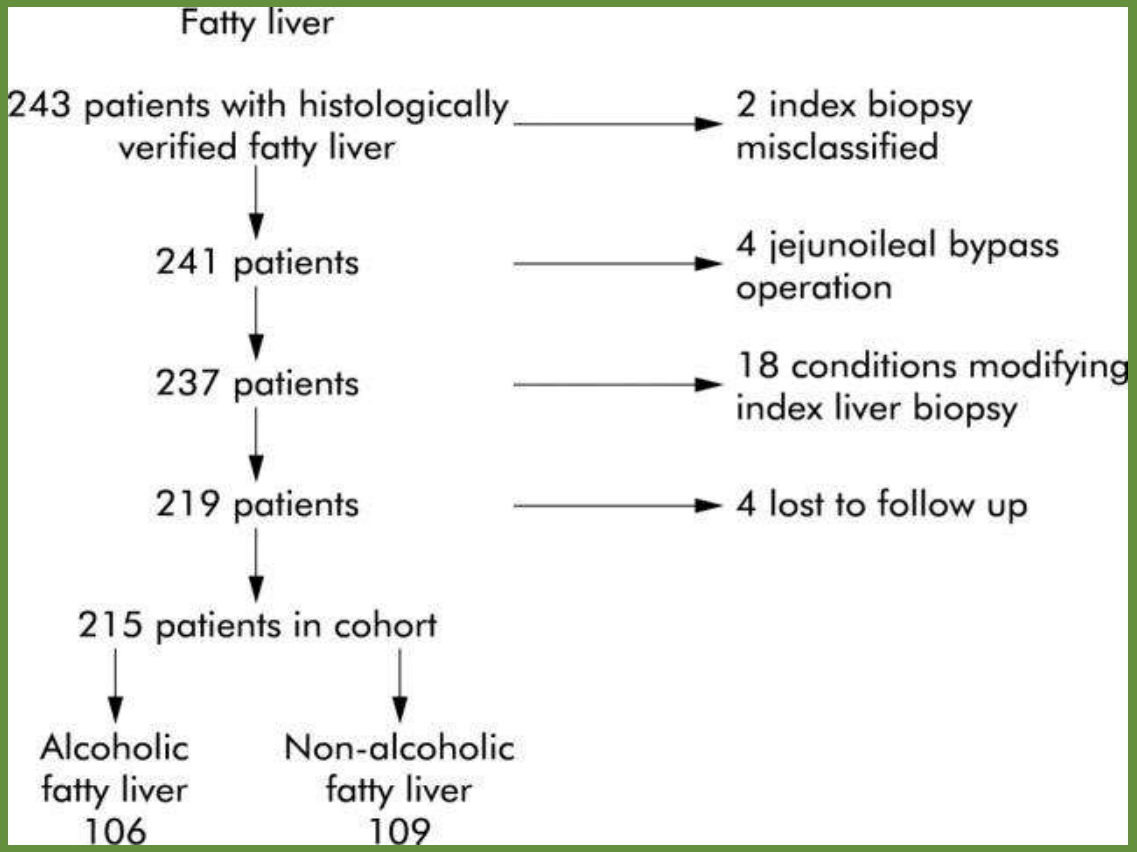
- 435 patients diagnosed with NAFLD
  - Follow up for 7.6 years ±4
  - 12.6% died by end of follow up period
    - Malignancy 28%
    - Heart disease 25%
    - Liver disease 13% (<1% in general population)

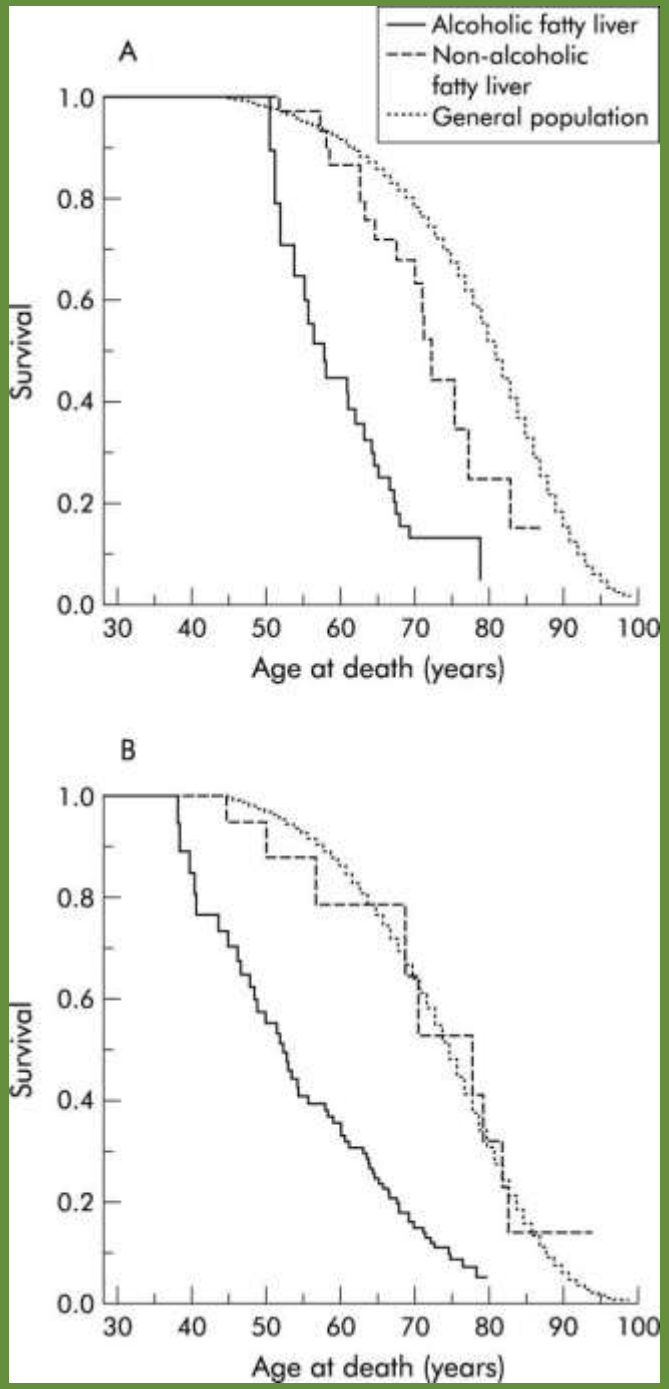
Gastroenterology. 2005 Jul;129(1):113-21.

# Long term prognosis of fatty liver: risk of chronic liver disease and death

S Dam-Larsen, M Franzmann, I B Andersen, P Christoffersen, L B Jensen, T I A Sørensen, U Becker, F Bendtsen

*Gut* 2004;**53**:750–755. doi: 10.1136/gut.2003.019984



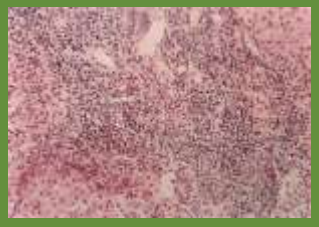

Median follow up 17 years

Only 1 patient developed cirrhosis

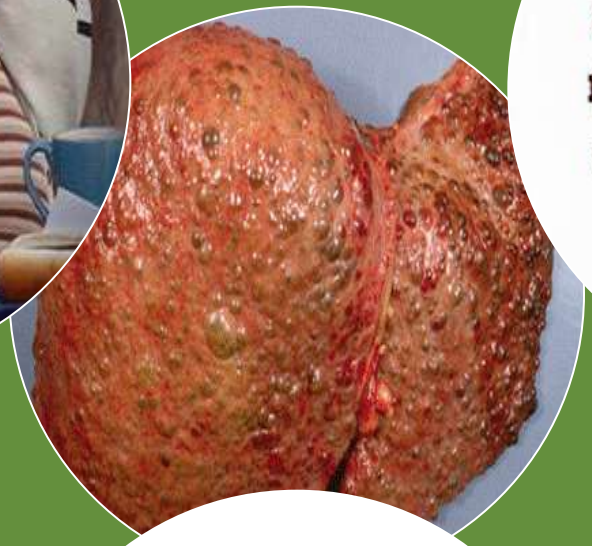

# Clinical and histologic spectrum of nonalcoholic fatty liver disease associated with normal ALT values.

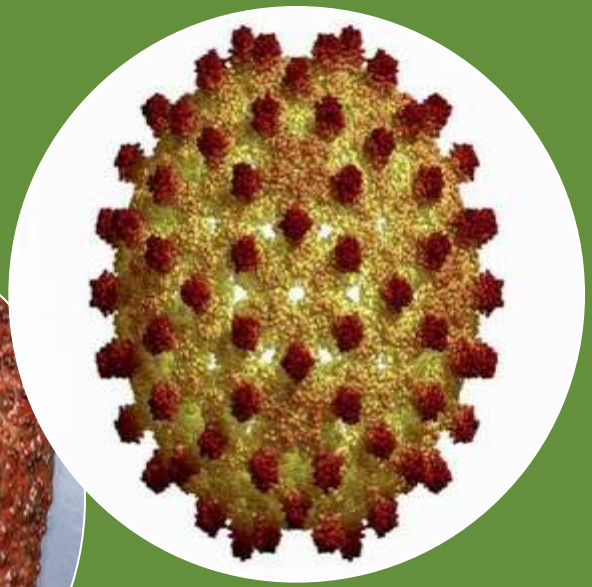
Mofrad P, Contos MJ, Haque M, Sargeant C, Fisher RA, Luketic VA, Sterling RK, Shiffman ML, Stravitz RT, Sanyal AJ.

- 51 subjects with liver biopsies confirming NAFLD with normal ALT
- Compared with 50 biopsies of patients with abnormal ALT
- No difference in the spectrum of liver disease (including cirrhosis) between groups

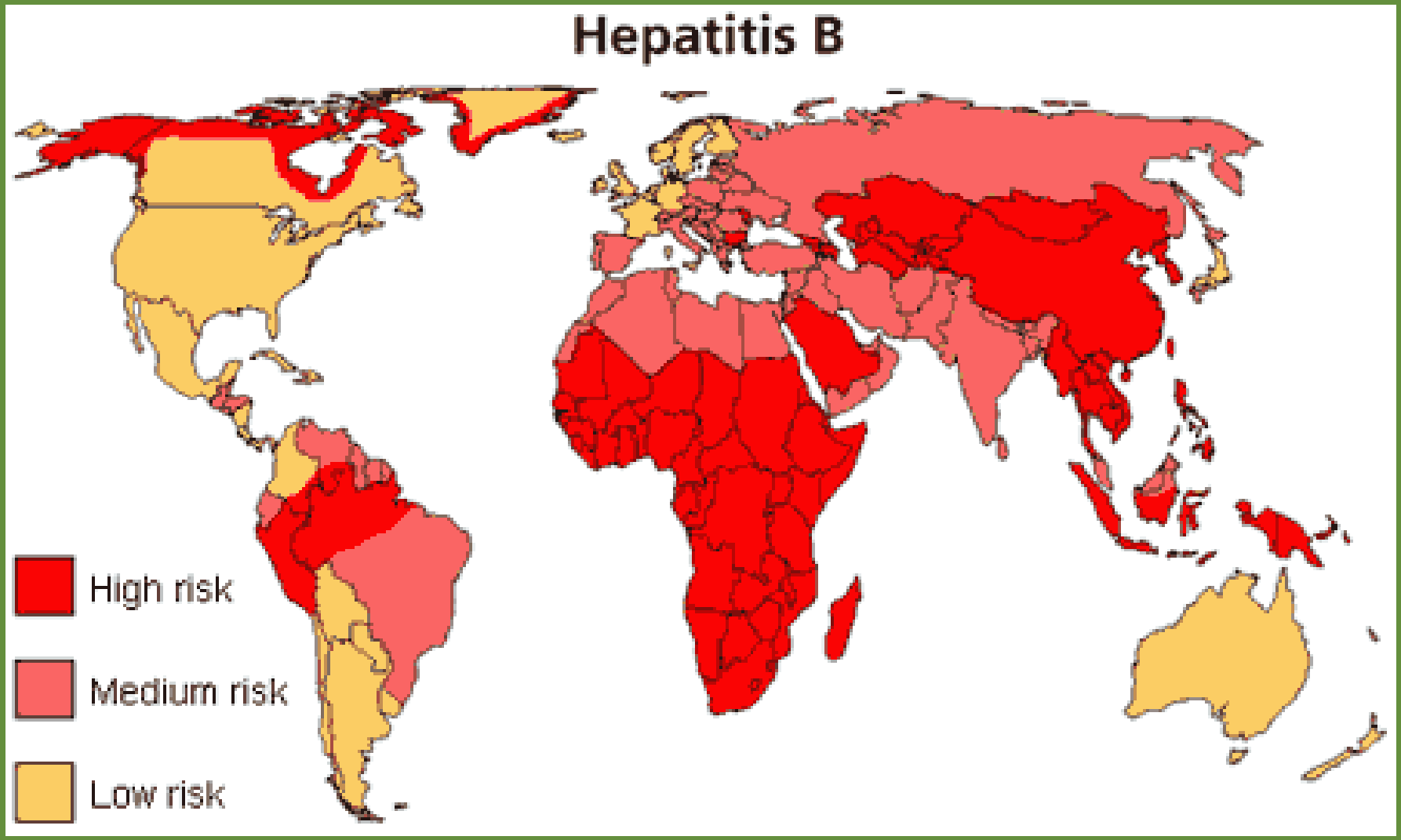


Hepatology. 2003 Jun;37(6):1286-92.





# Countries with Moderate-High Risk of Chronic Hepatitis B



# Immune tolerance

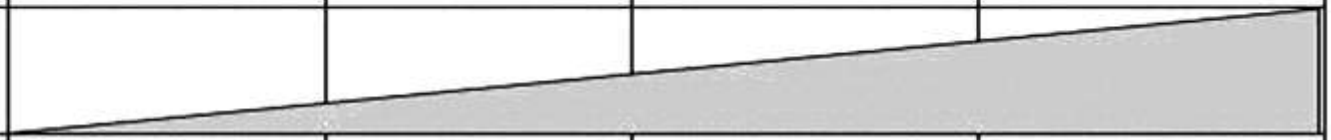
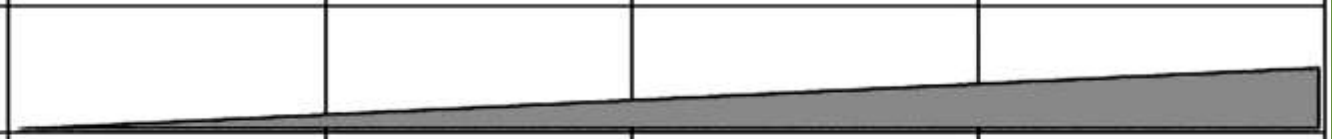
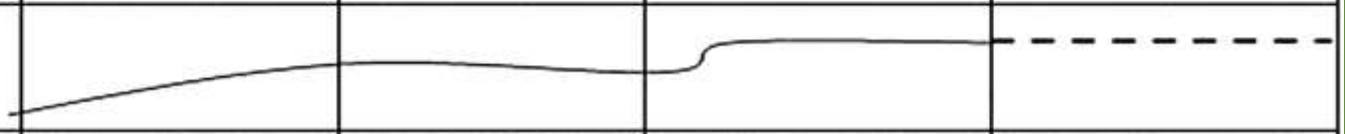
High levels of virus replication
Little cell damage and inflammation

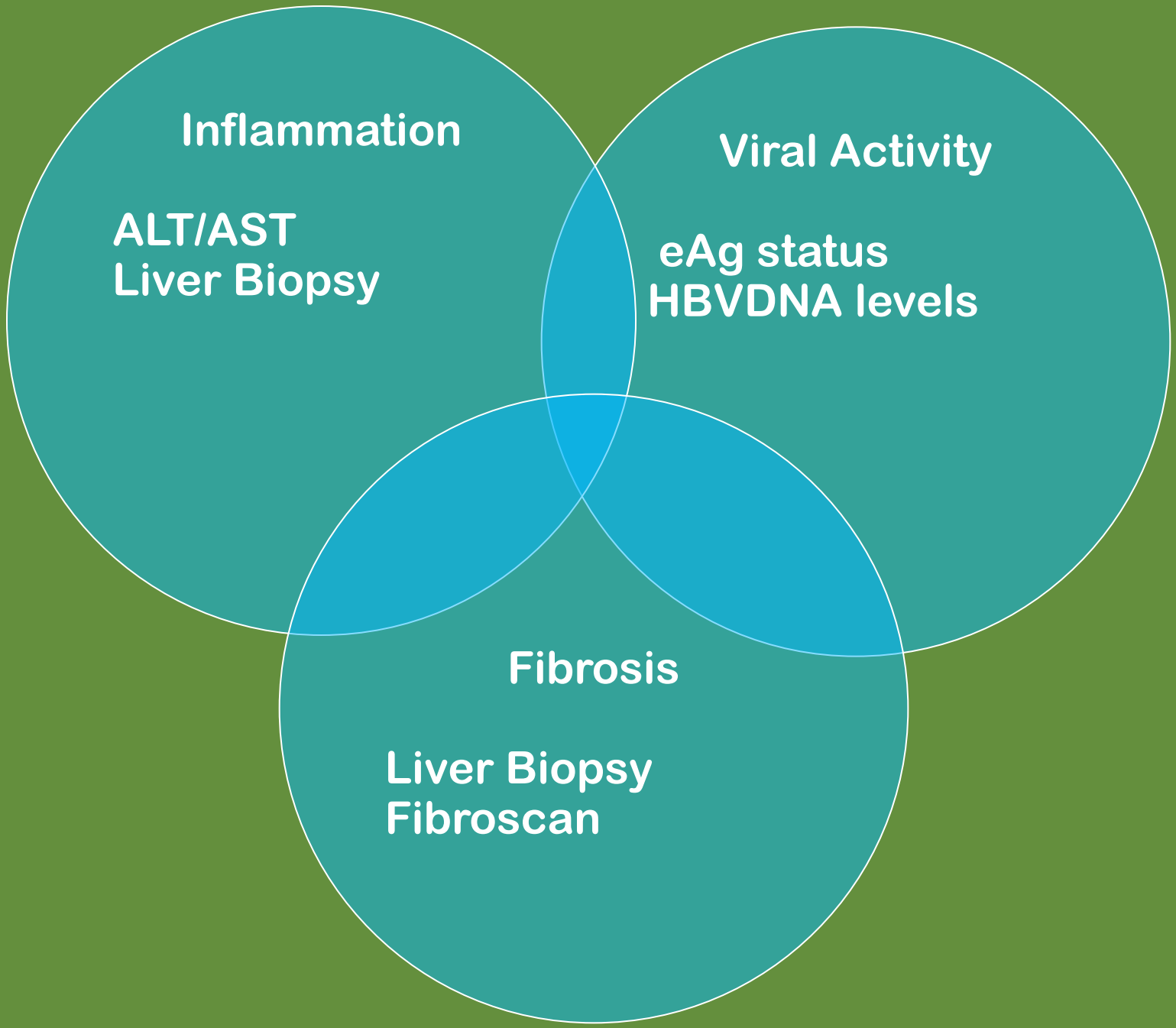
# Immune clearance

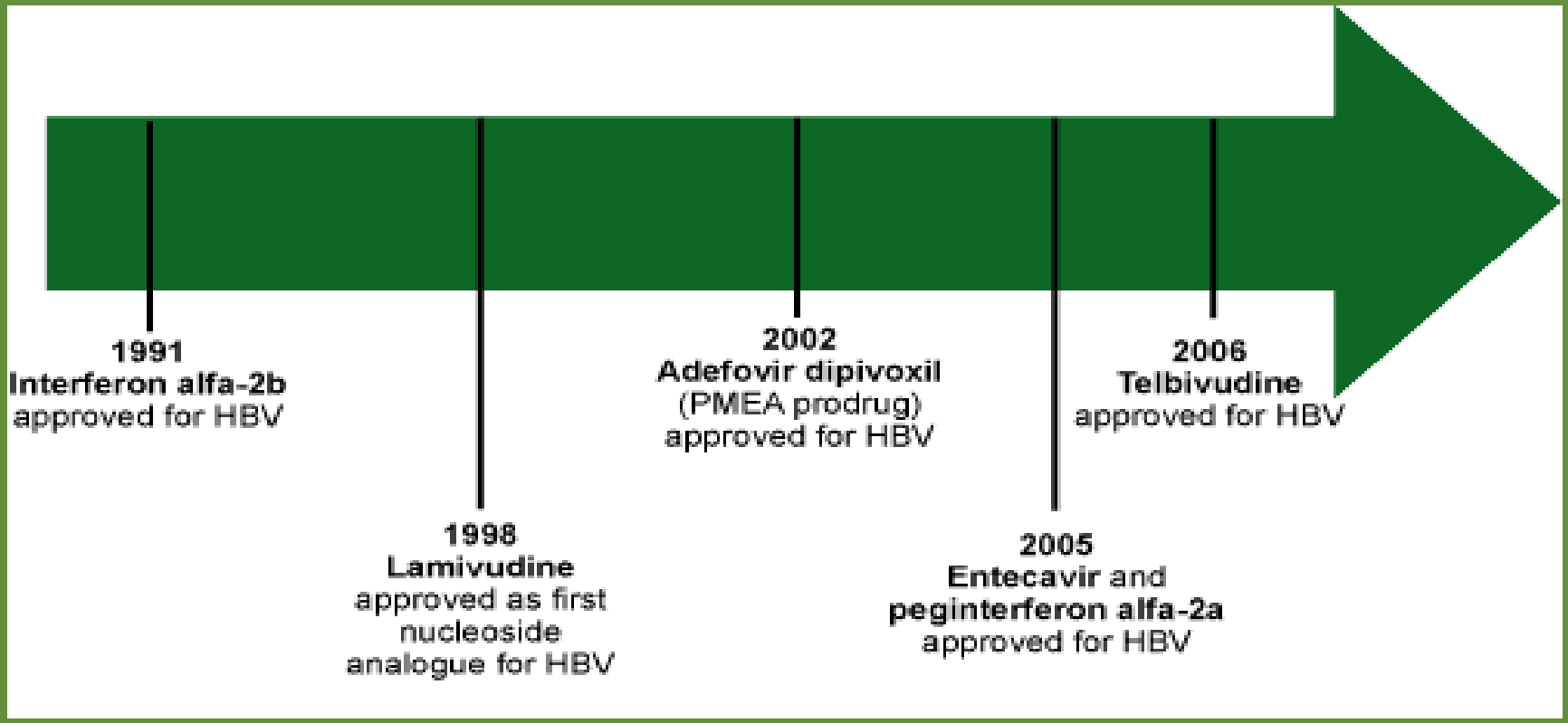
High levels of inflammation
Cell destruction
Viral clearance in short term
Chronic hepatitis and scarring in long term

# Immune control

Low levels of inflammation
Low level of viral replication
Little liver damage or scarring

| | Immune tolerant | HBeAg-positive CHB [immune clearance] | Immune control [low or non-replicative] | HBeAg-negative CHB [immune escape] |
|---|---|---|---|---|
| HBeAg | Positive (2000–5000 PEIU/ml) | Positive (100–1000 PEIU/ml) | Negative | Negative |
| Anti-HBe |  | | | |
| HBsAg (log IU/ml) | 4.5–5 | 4.0–4.5 | 2.9–3.0 | 3.3–3.9 |
| Anti-HBs |  | | | |
| HBV DNA (IU/ml) | >20 000 | >20 000 | <2000 | >2000 |
| Viral diversity (PC/C ORF) |  | | | |
| Serum ALT level (U/l) | Persistently normal | Elevated (1–2X) and fluctuating | Normal | Elevated and fluctuating |
| Liver histology | Normal or mild hepatitis | Moderate to severe hepatitis | Normal to mild hepatitis. May have cirrhosis | Moderate to severe hepatitis. May have cirrhosis |
| Intra-hepatic HBV replicative, intermediates | rcDNA/cccDNA (100–1000) >1 cccDNA/cell | rcDNA/cccDNA (10–1000) 1 cccDNA/cell (0.1–10/cell) | rcDNA/cccDNA (10–100) 0.1 cccDNA/cell (0.001–1/cell) | rcDNA/cccDNA (100–1000) 1 cccDNA/cell (0.1–10/cell) |


Inflammation
ALT/AST
Liver Biopsy
Viral Activity
eAg status
HBVDNA levels
Fibrosis
Liver Biopsy
Fibroscan




## Aims of treatment:

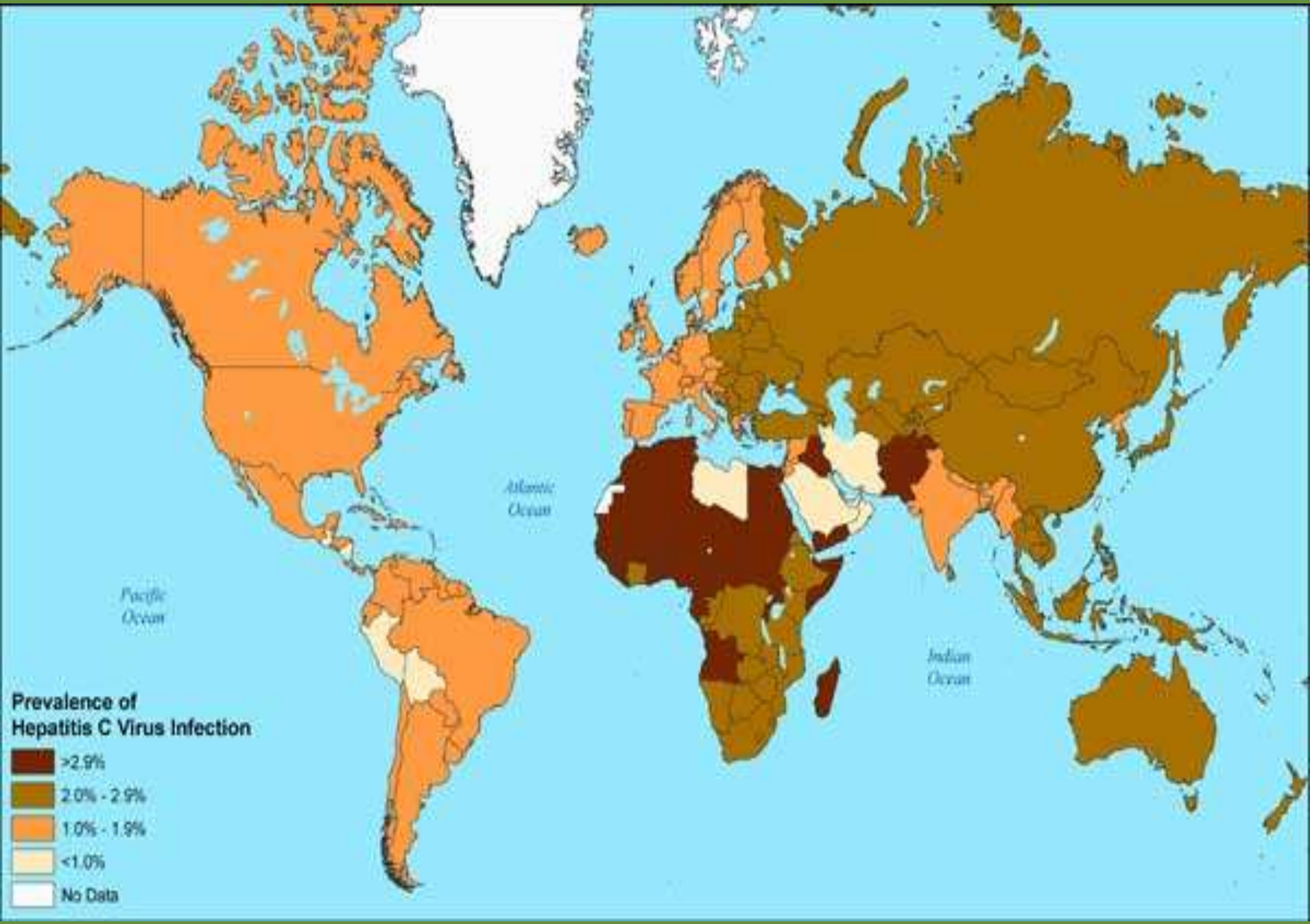
***Not cure*** but control of viral damage (and therefore risk of cirrhosis and cancer) either by boosting immune system (interferon) or suppressing viral replication

Real cure (loss of HBsAg) occurs spontaneously in about 1-2% of people and only a few more on long term treatment

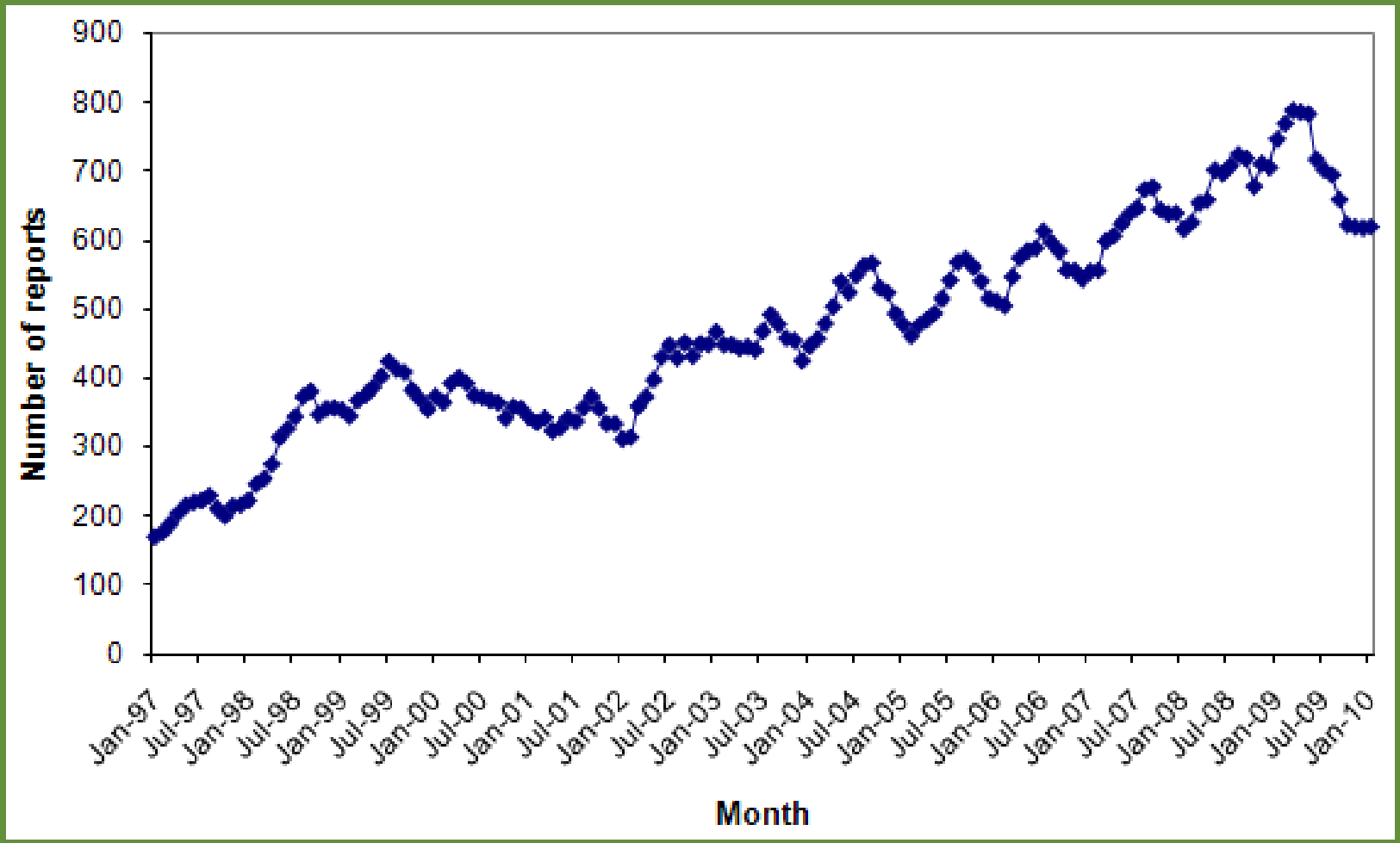

SOLIDARNOŚĆ

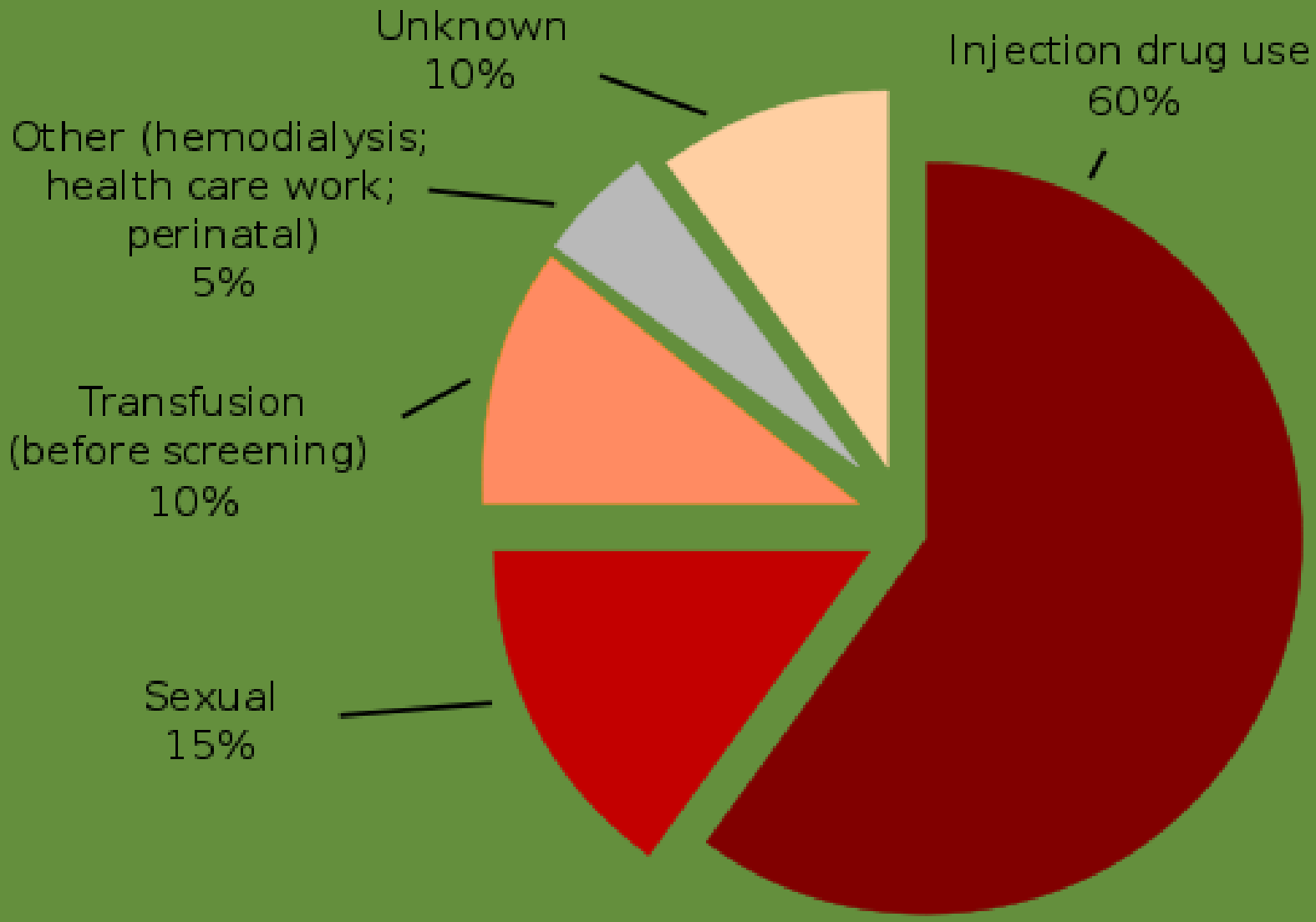

EVIN·COSTNER
All his life, Ray Kinsella was searching for his dreams.
Then one day, his dreams came looking for him.
FIELD OF DREAMS


1989
SOLIDARNOŚĆ
EVIN·COSTNER
All his life, Ray Kinsella was searching for his dreams.
Then one day, his dreams came looking for him.
FIELD OF DREAMS

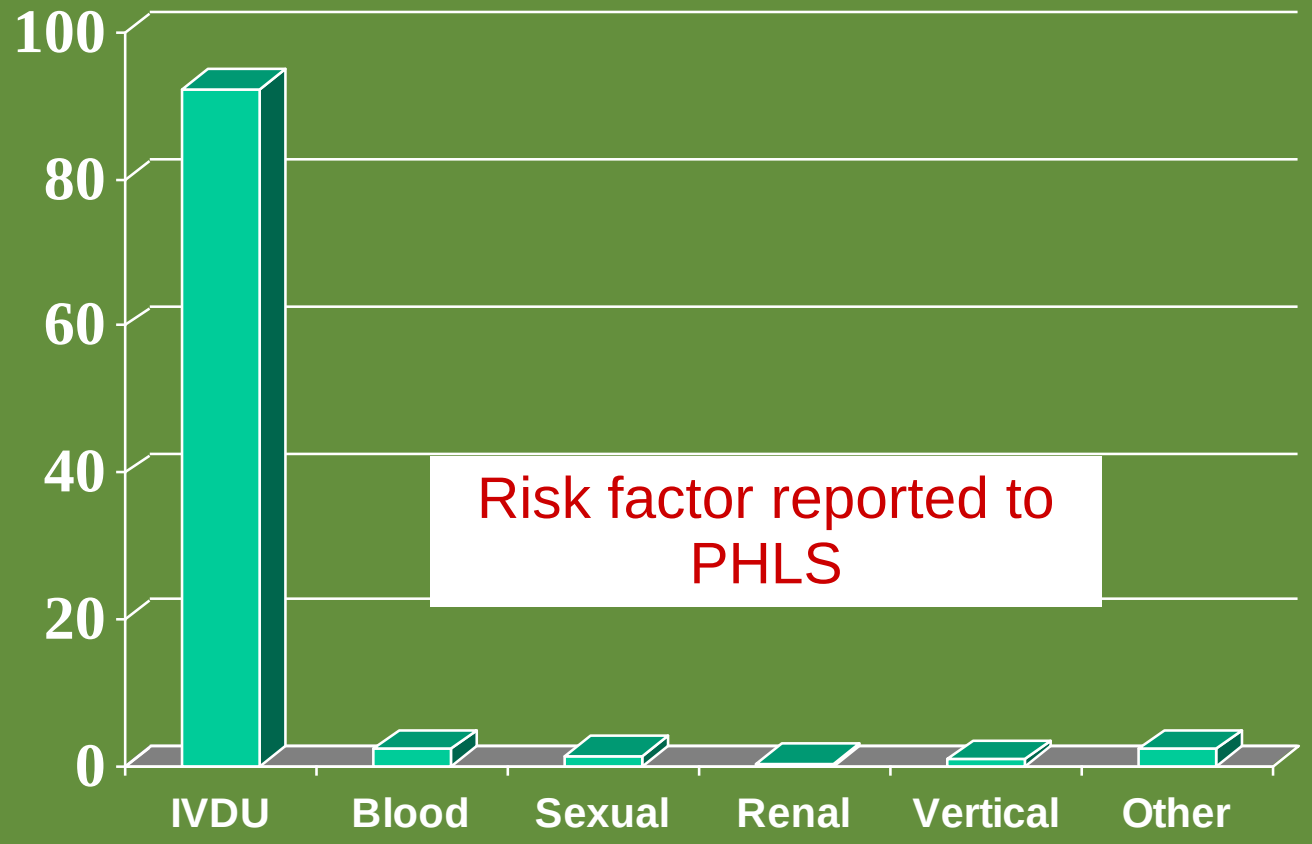

Atlantic Ocean
Pacific Ocean
Indian Ocean
Prevalence of Hepatitis C Virus Infection
>2.9%
2.0% - 2.9%
1.0% - 1.9%
<1.0%
No Data

It is estimated that around 185,000 individuals in the UK are chronically infected with hepatitis C (HCV) and at least 130,000 of these are living in England



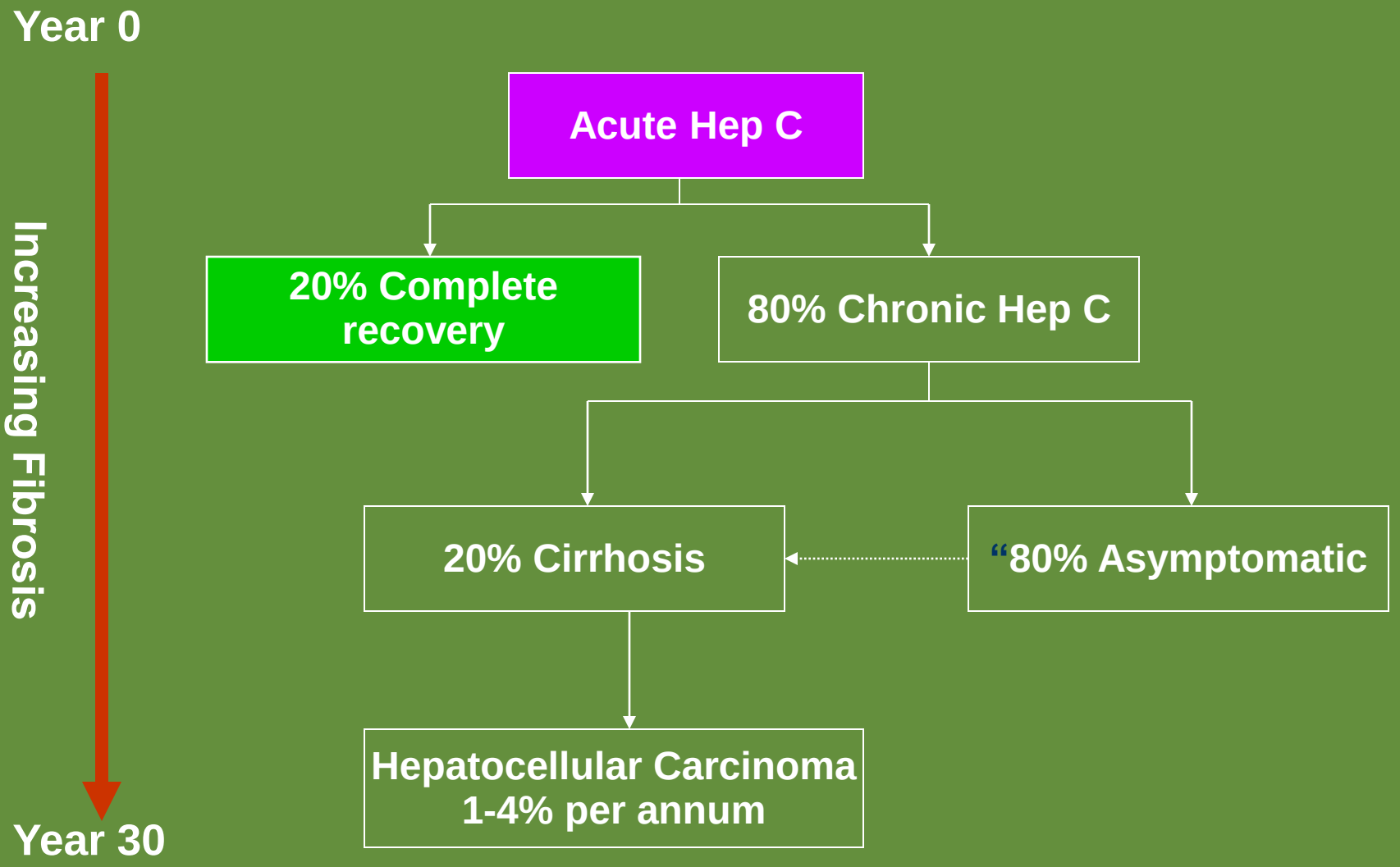

Unknown
10%
Injection drug use
60%
Other (hemodialysis;
health care work;
perinatal)
5%
Transfusion
(before screening)
10%
Sexual
15%

# Transmission




- Mother-baby 6%
- Sexual transmission 5%

# Clinical Outcomes



# Specific Tests for Hepatitis C

Serological tests: a measure of exposure now or in the past

anti-HCV antibody 

Virological tests: these are direct measures of viral activity

 Hepatitis C RNA (HCVRNA): marker of viral replication

Active Hepatitis C

# Aims of treatment:

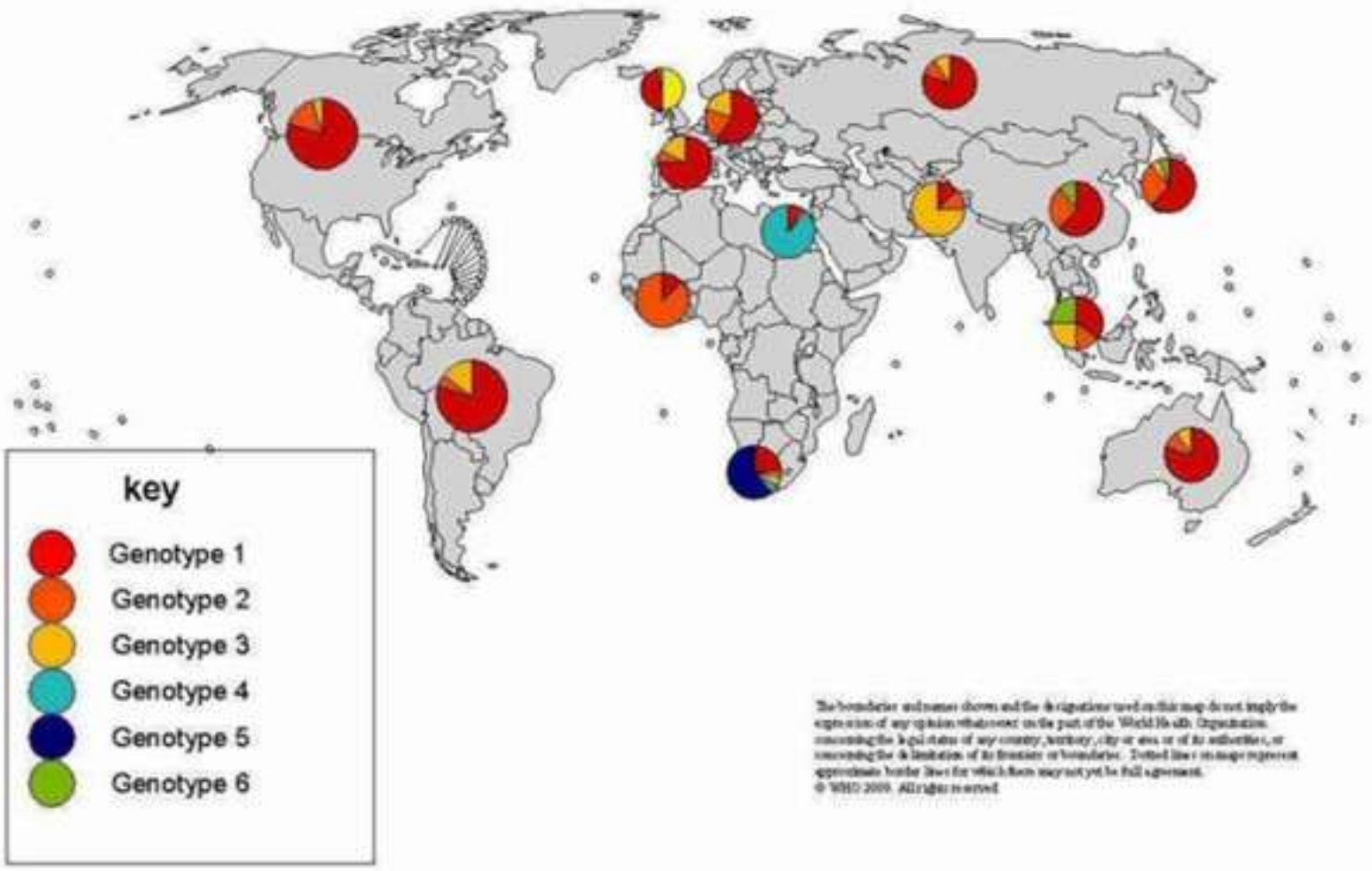
***Sustained virological response (SVR)***

**no evidence of virus 6 months after end of treatment**

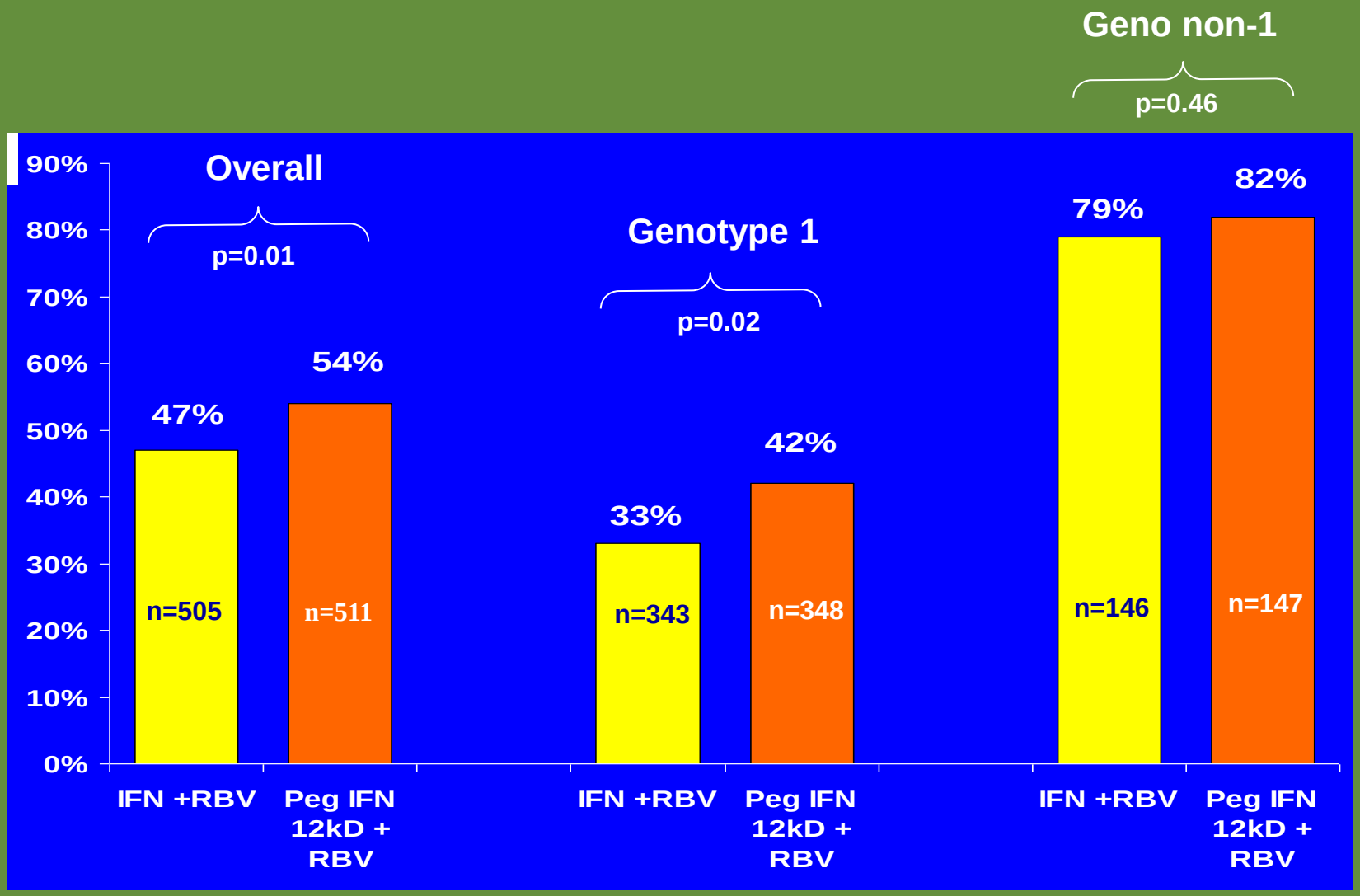
**this is considered a cure and means no further progression (and possible regression) of liver disease**

**Can be re-infected**

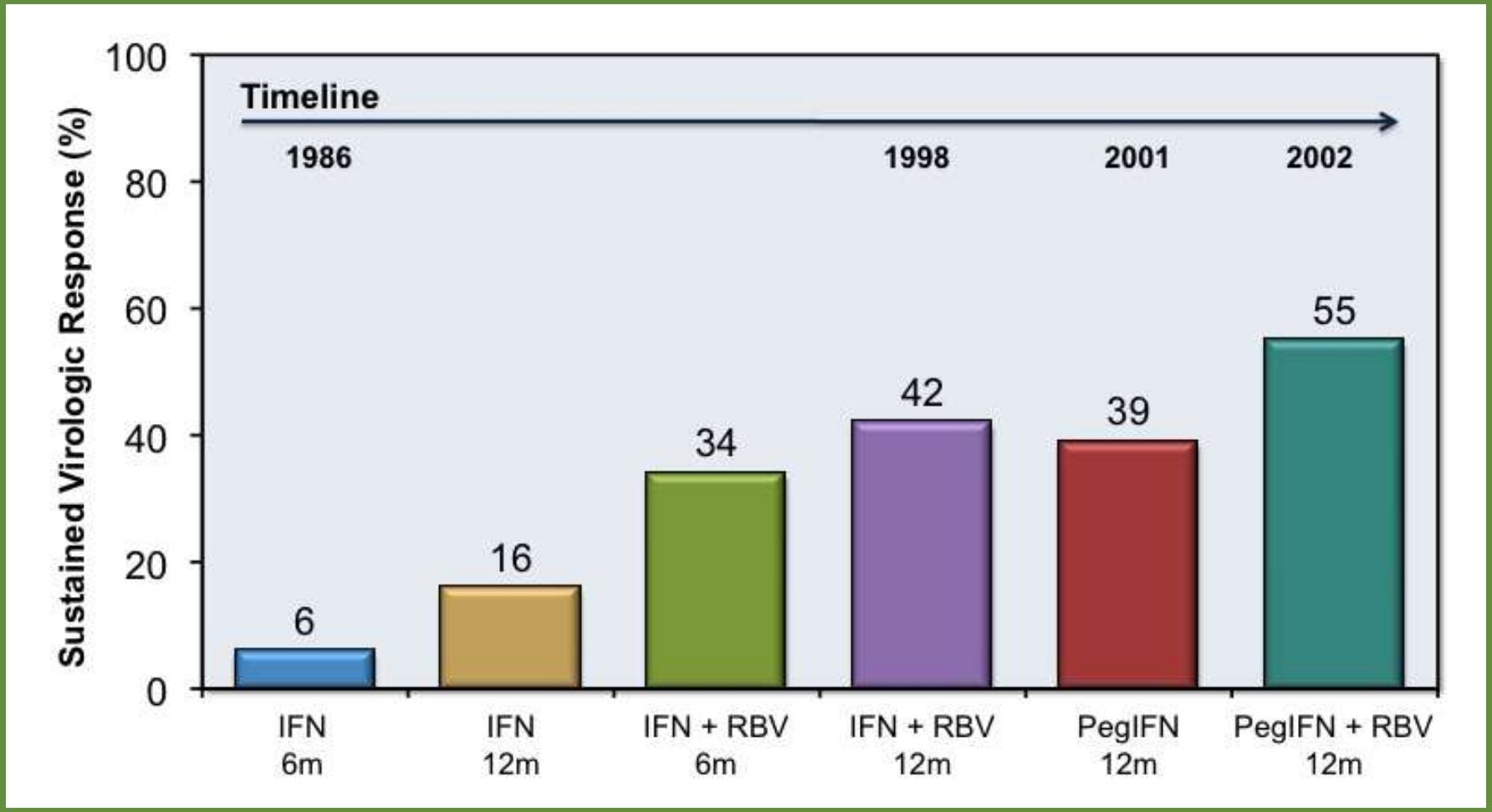
# Global distribution of HCV genotypes



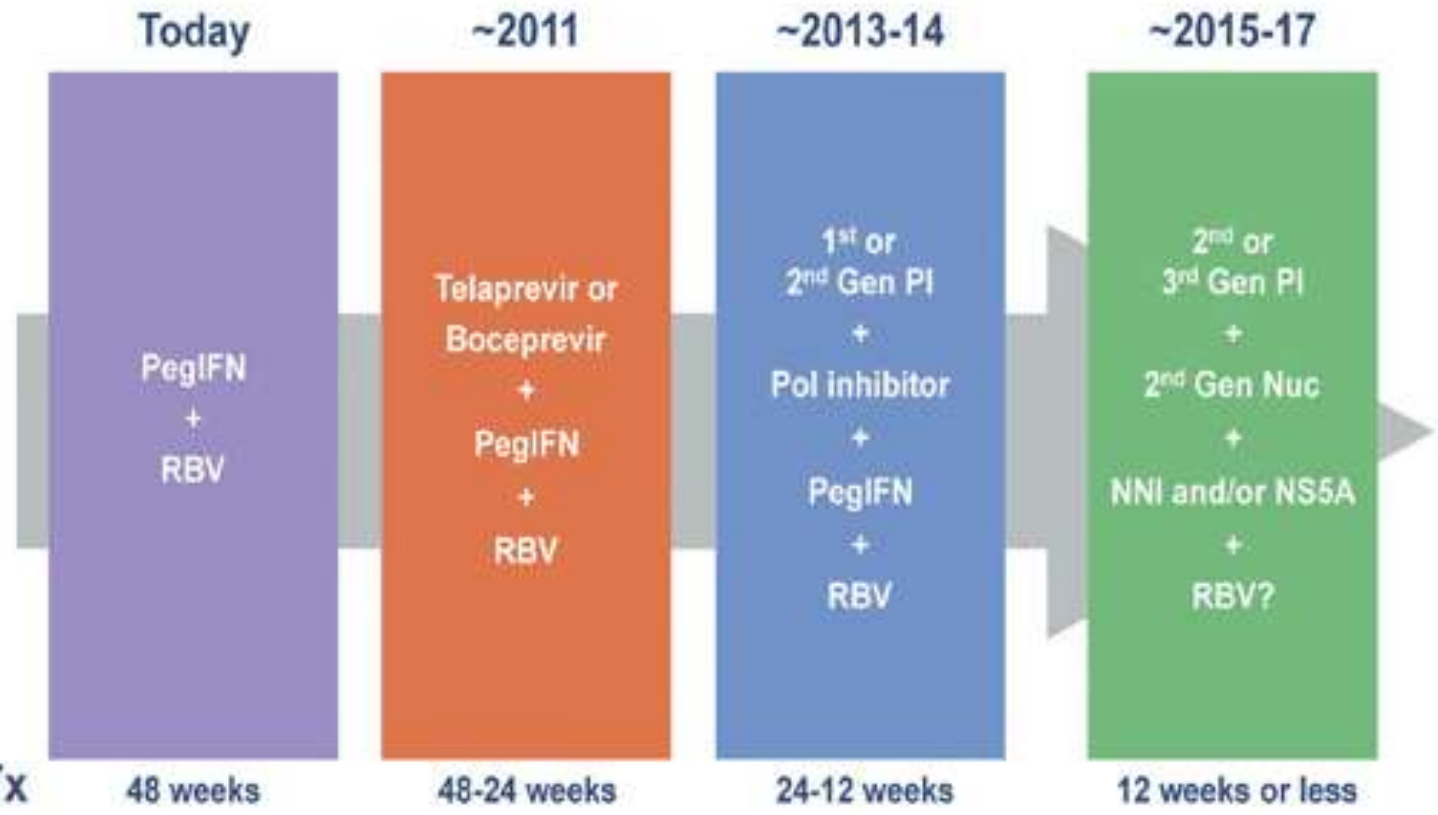
# Peg IFN 12KD 1.5 μg/kg Sustained Viral Responses




Manns et al, Lancet Vol 358.Pg 958 - 965


Sustained Virologic Response (%)
100
80
60
40
20
0
Timeline
1986
1998
2001
2002
6
16
34
42
39
55
IFN 6m
IFN 12m
IFN + RBV 6m
IFN + RBV 12m
PegIFN 12m
PegIFN + RBV 12m

# A RAPIDLY EVOLVING HCV TREATMENT PARADIGM




- Nucleoside/tide and protease inhibitors should be preferred backbone due to distinct modes of action, complementary resistance profiles and broad genotypic activity
- Potent non-nucleosides and NS5A inhibitors as third/fourth components of DAA cocktail may replace interferon.

Source: Market research from MedPanel, LLC

## Who to treat?:

## Everybody with active HCV infection!

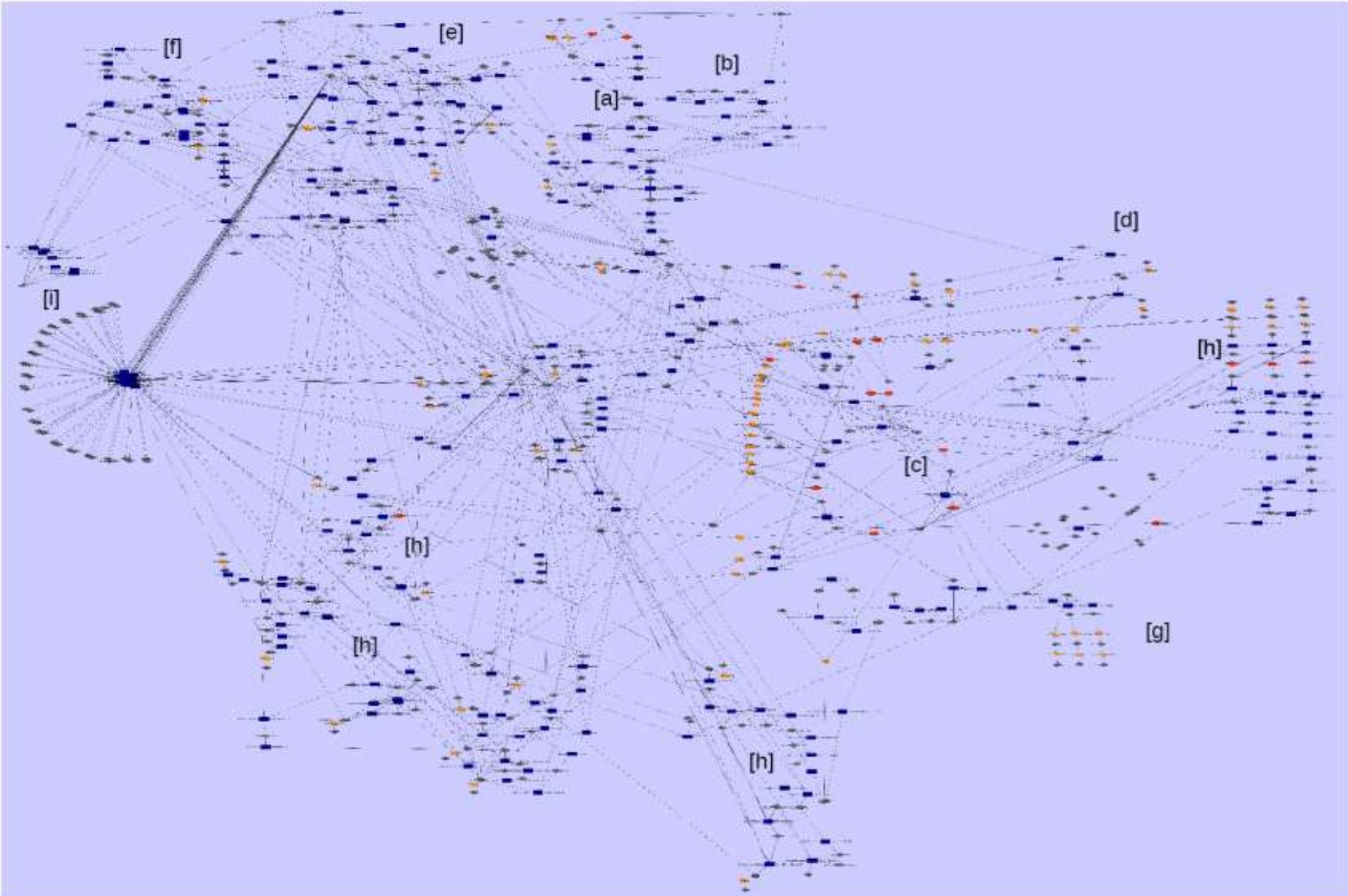
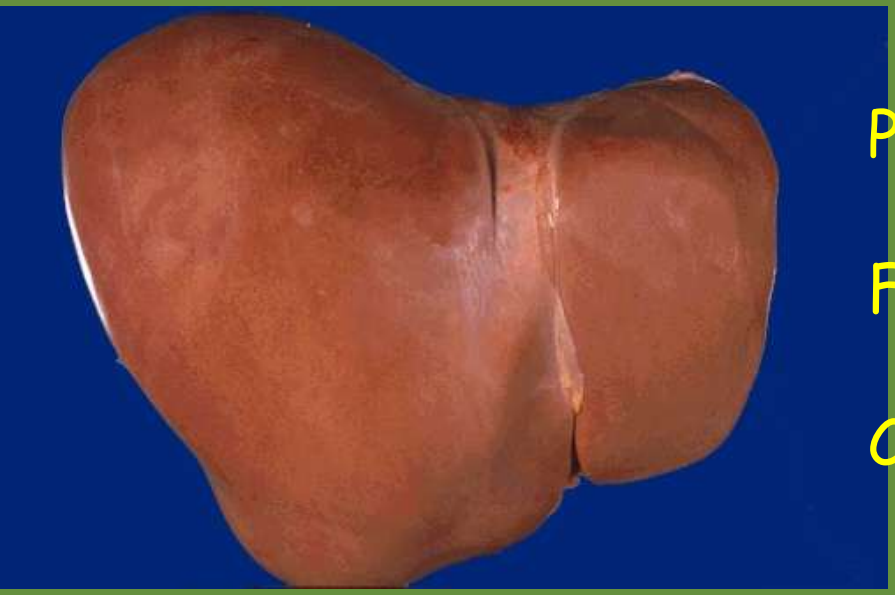



Fig.1: **Reconstructed metabolic network of core Human Hepatocyte metabolism**:
Glycolysis and gluconeogenesis [a], pentose phosphate pathway [b], citrate cycle [c], urea cycle [d], purine metabolism [e], pyrimidine metabolism [f], ketone body synthesis [g], amino acid metabolism [h], protein synthesis [i]
*reactions*: blue rectangle, *processes*: red octagon, *transporter*: orange parallelogram, *compounds*: grey rhombus
*regulations* and *flux objects* not displayed, edges of compounds with highest degree not displayed



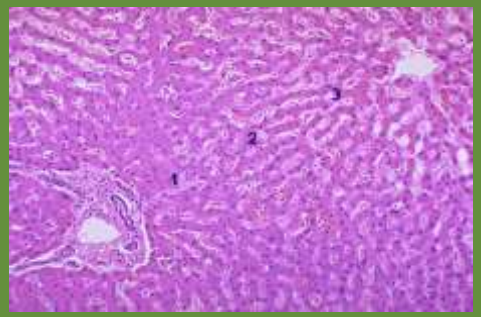
| | |
|---|---|
| Produces | Proteins, clotting factors etc |
| Filters | Drugs, food |
| Changes | Drugs, hormones |

Chronic liver disease

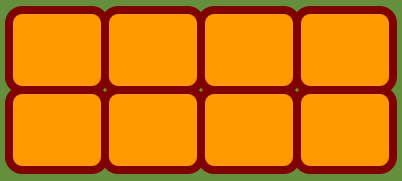
*Less production*

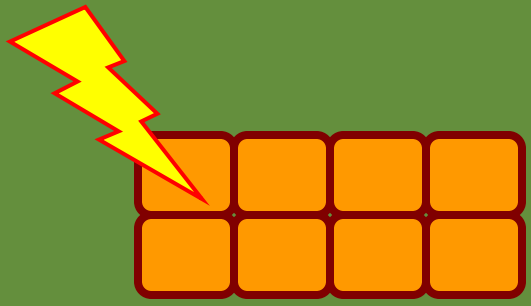
*Filter clogged*

*Substances unchanged*

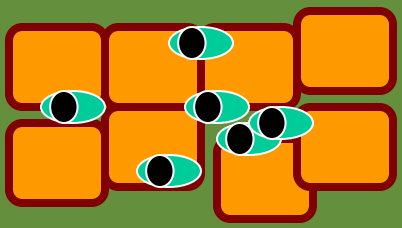


Normal liver

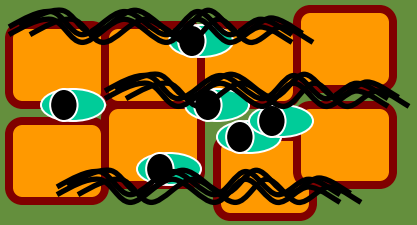




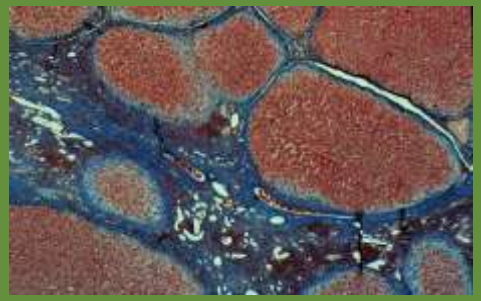
Liver disease



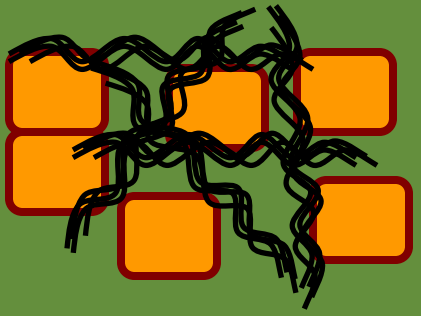
Inflammation



Scarring (fibrosis)



Loss of function (cirrhosis)




PA

# Abnormal Liver Function tests

# Routine liver function tests

- Bilirubin
- Alkaline Phosphatase
- Transaminases (AST and or ALT)
- GGT
- Albumin
- Prothrombin time

# The prevalence and etiology of elevated aminotransferase levels in the United States

Jeanne M Clark MD, MPH[1,2], Frederick L Brancati MD, MHS[1,2] and Anna Mae Diehl MD[1]

*The American Journal of Gastroenterology* (2003) **98**, 960–967

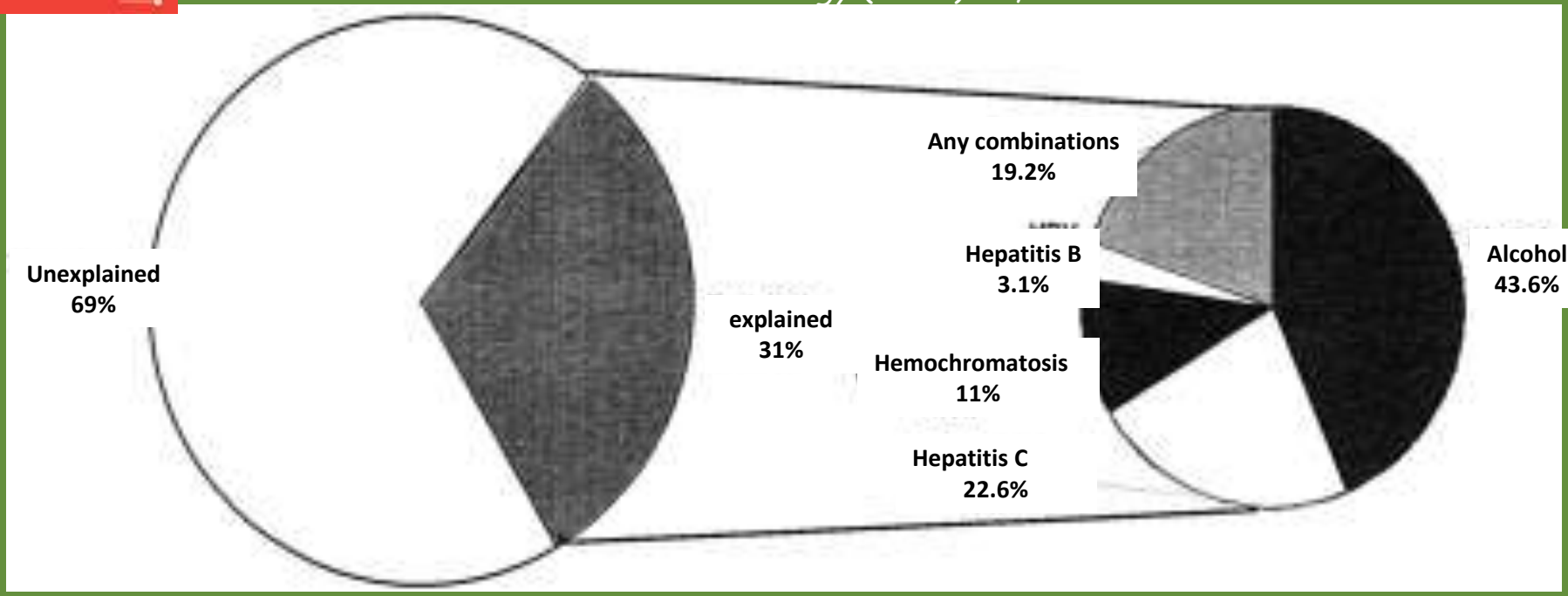
| Characteristic | Population Distribution | Prevalence of Amino- transferase Elevation (%) | SE |
|---|---|---|---|
| Sex | | | |
| Male | (47.9) | 9.3 | 0.7 |
| Female | (52.1) | 6.6 | 0.6 |
| Race/ethnicity | | | |
| Non-Hispanic white | (76.9) | 7.1 | 0.5 |
| Non-Hispanic black | (10.5) | 8.1 | 0.6 |
| Mexican American | (5.2) | 14.9 | 0.9 |
| Others | (7.5) | 10.2 | 1.5 |
| Age (yr) | | | |
| <30 | (26.6) | 6.4 | 0.6 |
| 30–40 | (22.7) | 9.9 | 1.0 |
| 40–50 | (18.4) | 8.8 | 1.1 |
| 50–60 | (12.1) | 9.6 | 1.3 |
| 60–70 | (10.6) | 6.2 | 0.8 |
| >70 | (9.7) | 4.9 | 0.6 |
| Body mass index | | | |
| <18.5 kg/m$^2$ | (2.5) | 6.5 | 1.7 |
| 18.5–24.9 kg/m$^2$ | (43.5) | 5.3 | 0.5 |
| 25–29.9 kg/m$^2$ | (32.2) | 8.0 | 0.6 |
| 30–34.9 kg/m$^2$ | (14.2) | 10.9 | 0.9 |
| 35 kg/m$^2$ | (7.6) | 16.8 | 1.5 |

**Table 1. Prevalence of Elevated Aminotransferase Levels in the United States Population by Various Demographic Characteristics and Body Mass Index**

**The prevalence and etiology of elevated aminotransferase levels in the United States**

Jeanne M Clark MD, MPH[1,2], Frederick L Brancati MD, MHS[1,2] and Anna Mae Diehl MD[1]

*The American Journal of Gastroenterology* (2003) **98**, 960–967




Prevalence of aminotransferase elevation and likely etiologies in the United States (aminotransferase elevation defined as AST >37 IU/L or ALT >40 IU/L in men and AST or ALT >31 IU/L in women.

Sherwood et al BMJ 2001;332:276

# Abnormal LFTs in Primary Care

**342 Abnormal results**

185 no further tests required

**157 needed further investigations**

58% no further tests done
42% some further tests

Diagnostic test not acted on in 4%
(AMA+ve, High ferritin, Dilated CBD, SMA+ve)

## Findings on investigation

23% normal LFTs on retesting

11% normal serology, declined biopsy

27% alcoholic liver disease

17% NASH/fatty liver

18% viral/autoimmune metabolic/biliary

Skelly et al. J Hepatol 2001;35:195-199

# Findings on Liver biopsy for abnormal LFTS

- Abnormal liver enzymes
- Negative diagnostic serology
- careful exclusion of alcohol

Again abnormal =2x ULN

**397 patients**

43 declined biopsy

**354 underwent biopsy**

| **Stage of liver disease** | |
|---|---|
| Cirrhosis | 6% |
| Bridging | 9% |
| Portal | 12% |
| None | 73% |

# Causes of raised ALP

- Physiological
  - Pregnancy (1st and 3rd trimester)
  - Adolescents
  - Benign familial (intestinal ALP)

- Pathological
  - Biliary obstruction
  - PBC/PSC
  - Drugs
  - Adult ductopaenia
  - Metastatic liver disease
  - Bone disease

# Drugs associated with raised transaminases

NSAIDS
Statins (probably no good evidence for this)
Anti-epileptics
Anti-tuberculous therapy
Herbal remedies
Illicit drug use (cocaine, ecstasy)

# GGT –gamma glutamyltransferase

- Cell membrane glycoprotein enzyme
- Maintains intracellular glutathione concentrations
- Found in kidney brain spleen and heart

- Only 30-50% excessive alcohol consumers in community have raised GGT
- PPV of GGT is only 32%!!

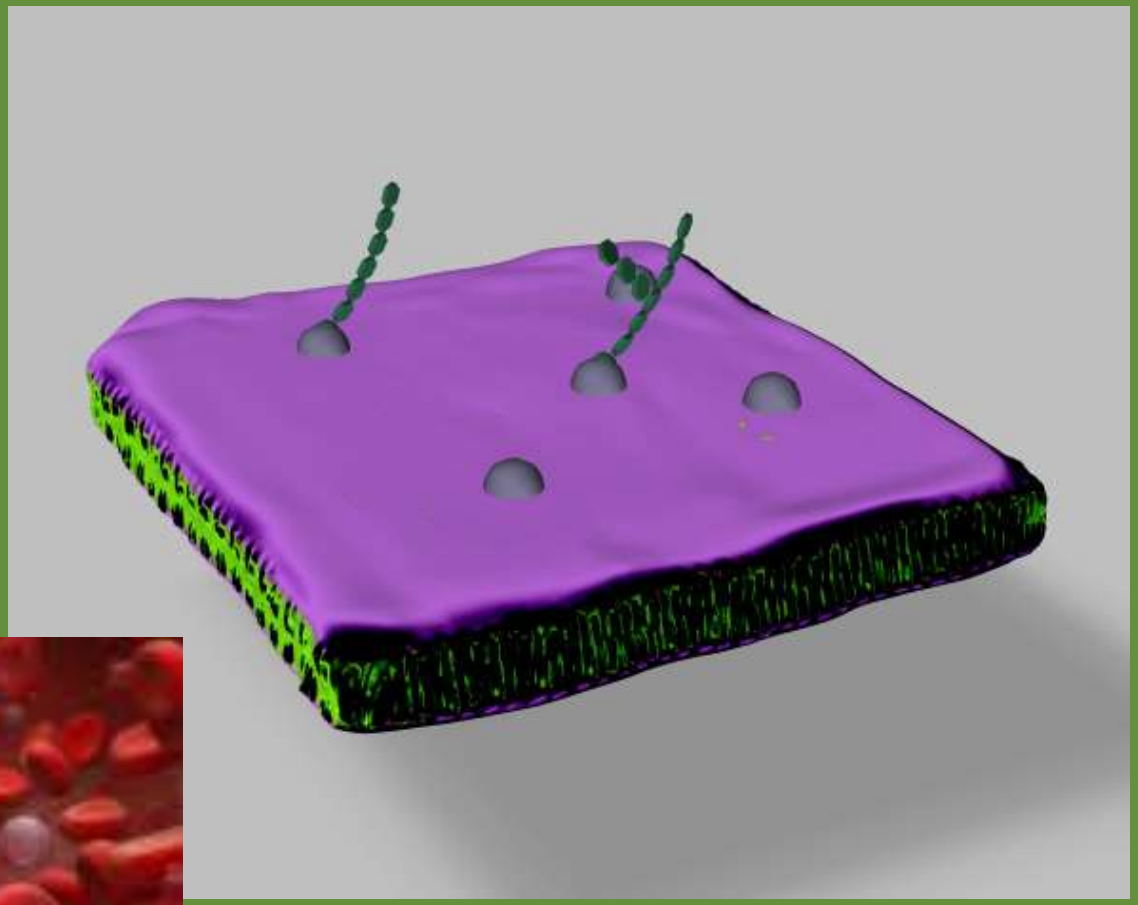
# Causes of raised GGT

- Hepatobiliary diseases
- Pancreatic disease
- Alcoholism
- COPD
- Renal failure
- Diabetes
- Myocardial disease
- Drugs

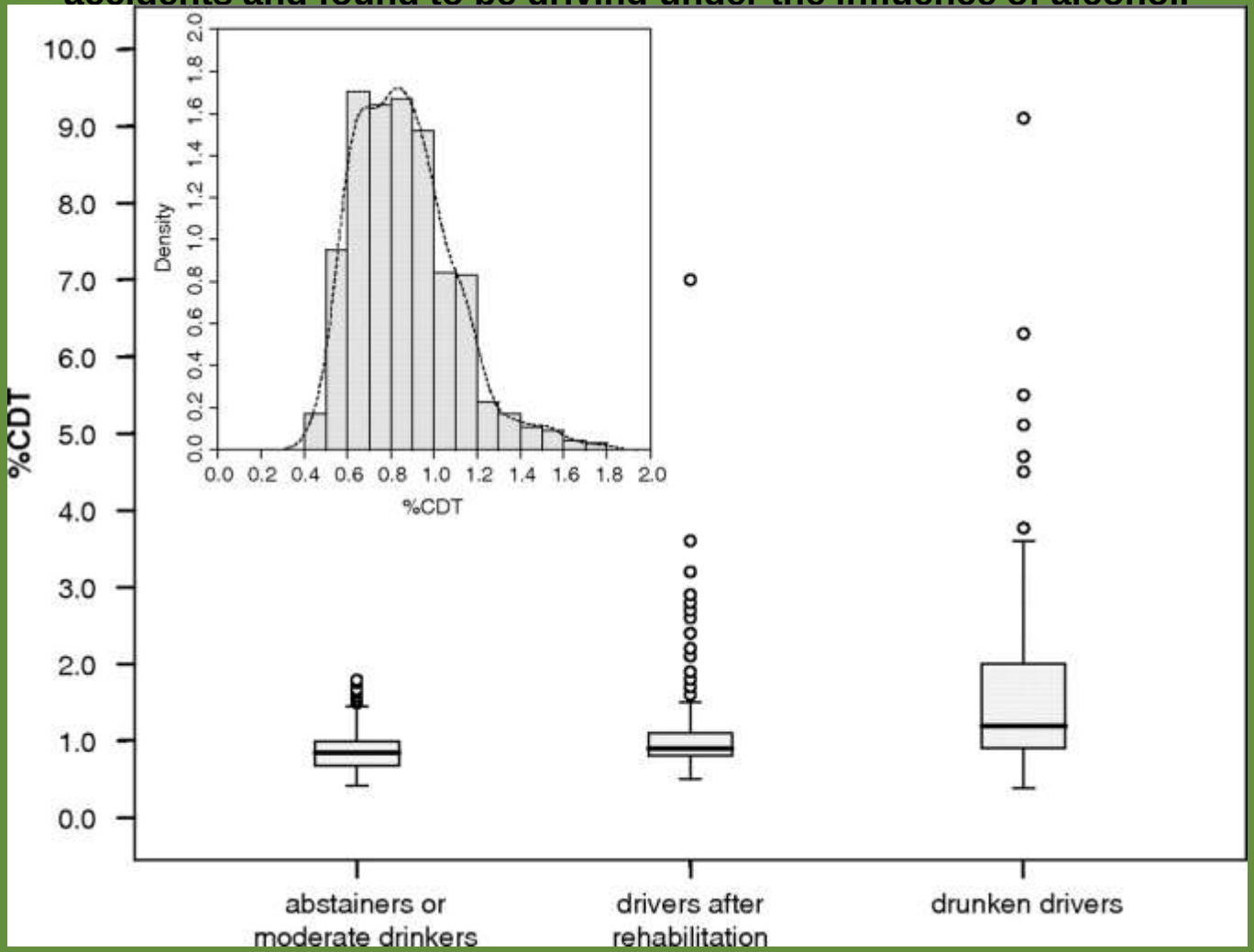

- 316 patients attending alcohol counselling services
  - 34% raised gamma GT
  - 18% raised AST
  - 7% raised alkaline phosphatase
- No correlation between abnormal LFTs and degree of current alcohol consumption

| Marker | Sensitivity (percent) | Diagnostic Specificity (percent) | Possible or Current Use |
|---|---|---|---|
| Gamma-glutamyltransferase (GGT) | 61[1] | n/a | Chronic alcohol abuse |
| Alanine aminotransferase (ALT) | Method-dependent | n/a | Chronic alcohol abuse |
| Aspartate aminotransferase (AST) | 56[1] | n/a | Chronic alcohol abuse |
| Carbohydrate-deficient transferrin (CDT) | 26–83[2]* | 92[3] | Heavy alcohol use** |
| N-acetyl-β-hexosaminidase | 94[2] | 91[2] | Heavy alcohol use |
| Whole blood–associated acetaldehyde (WBAA) | 100[4] | 95[4] | Recent alcohol consumption at all levels; monitoring abstinence |
| Mean corpuscular volume (MCV) | 47[1] | n/a | Heavy alcohol use |
| Apolipoprotein J | n/a | n/a | Heavy alcohol use |
| 5-hydroxytryptophol (5-HTOL) | n/a | n/a | Monitoring sobriety |
| Salsolinol | n/a | n/a | Chronic alcohol consumption |
| Fatty acid ethyl esters (FAEE) | 100[5] | 90[5] | Recent heavy alcohol use |
| Ethyl glucuronide (EtG) | n/a | Method-dependent | Monitoring sobriety; forensics |

# Carbohydrate-deficient transferrin



**Boxplots of %CDT values among 652 abstainers or moderate drinkers, 603 drivers applying for driving-license regranting after a rehabilitation programme and 105 drivers involved in car accidents and found to be driving under the influence of alcohol.**




**Bianchi V et al. Alcohol and Alcoholism 2010;45:247-251**



ALCOHOL AND ALCOHOLISM

The ineffectiveness of traditional markers to screen for alcohol consumption in the general population has been recognized for many years. Sensitivity and/or specificity rates are far too low to propose their systematic use as screening tests in unselected medical populations.

A biochemical marker with 60% sensitivity and 98% specificity rate for heavy drinking, when applied to a population with a 7% prevalence of alcohol misuse, has a positive predictive value of 0.66. This means that, if a patient has a positive test result, there is a 66% chance that this patient is a heavy drinker and a 34% chance that this patient is a false positive, rather than a true positive. Despite moderate sensitivity and specificity rates, this biochemical marker is not a good screening candidate.

Tests with moderate diagnostic performance have serious drawbacks in employment, legal and insurance settings where false positive results can have serious consequences. However, if false positive results could be eliminated or greatly reduced, these tests might find greater acceptance and use in these settings.

Alcohol and Alcoholism (2001) 36 (4): 349-353.

**MELD SCORE**

$3.78 \times \log_e$ serum bilirubin (mg/dL) +

$11.20 \times \log_e$ INR +

$9.57 \times \log_e$ serum creatinine (mg/dL) +

6.43 (constant for liver disease etiology)

NOTES:

If the patient has been dialyzed twice within the last 7 days, then the value for serum creatinine used should be 4.0

Any value less than one is given a value of 1 (i.e. if bilirubin is 0.8, a value of 1.0 is used) to prevent the occurrence of scores below 0 (the natural logarithm of 1 is 0, and any value below 1 would yield a negative result)

- Meld score
  - >9 2.9% 3 month mortality
  - 10-19 7.7%
  - 20-29 23.5%
  - 30-39 60%
  - >40 81%

Medscape® www.medscape.com

| Points | 1 | 2 | 3 |
|---|---|---|---|
| Encephalopathy | None | Minimal | Advanced (coma) |
| Ascites | Absent | Controlled | Refractory |
| Bilirubin (μmol/L) | <34 | 34–51 | >51 |
| Albumin (g/L) | >35 | 28–35 | <28 |
| Prothrombin (sec)* | <4 | 4–6 | >6 |

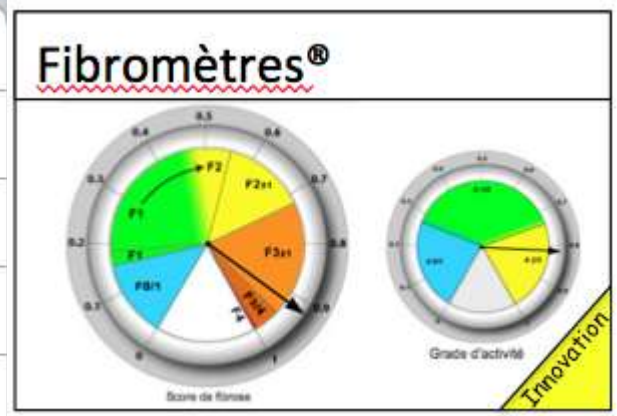
*Difference between the patient and the control. Differences of 4 to 6 seconds correspond approximately to a prothrombin ratio of ~50 to 40% of normal.

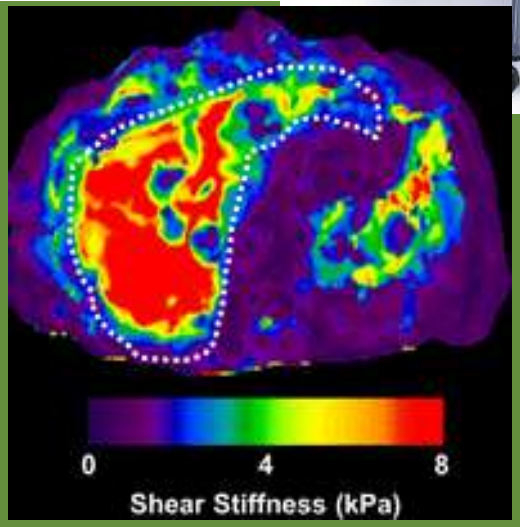
Source: Semin Liver Dis © 2008 Thieme Medical Publishers

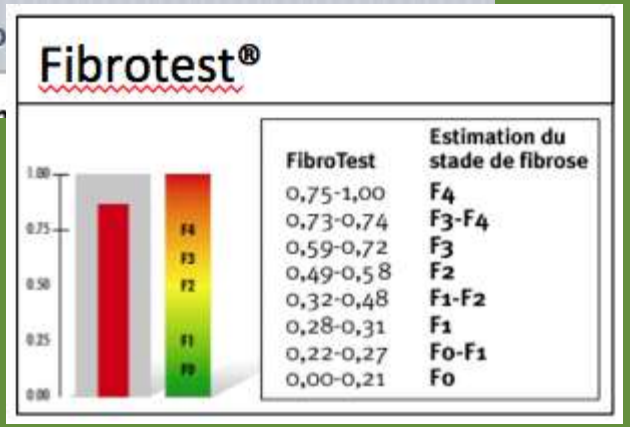
| Points | Class | One year survival | Two year survival |
|---|---|---|---|
| 5-6 | A | 100% | 85% |
| 7-9 | B | 81% | 57% |
| 10-15 | C | 45% | 35% |


Carrier
11:18 AM
Liver Calc
Search
Cancel
Progonstic Score
MELD
MELDNa
PELD
Child-Pugh
Maddrey Score (for Alocoholi...
Mayo Score (for PBC)
Diagno

ELF Testing


Fibromètres®
Innovation


0
4
8
Shear Stiffness (kPa)


Fibrotest®
FibroTest
Estimation du stade de fibrose
0,75-1,00 F4
0,73-0,74 F3-F4
0,59-0,72 F3
0,49-0,58 F2
0,32-0,48 F1-F2
0,28-0,31 F1
0,22-0,27 F0-F1
0,00-0,21 F0

Doh.....

Did I leave anything out??