

Indications for Liver Transplantation

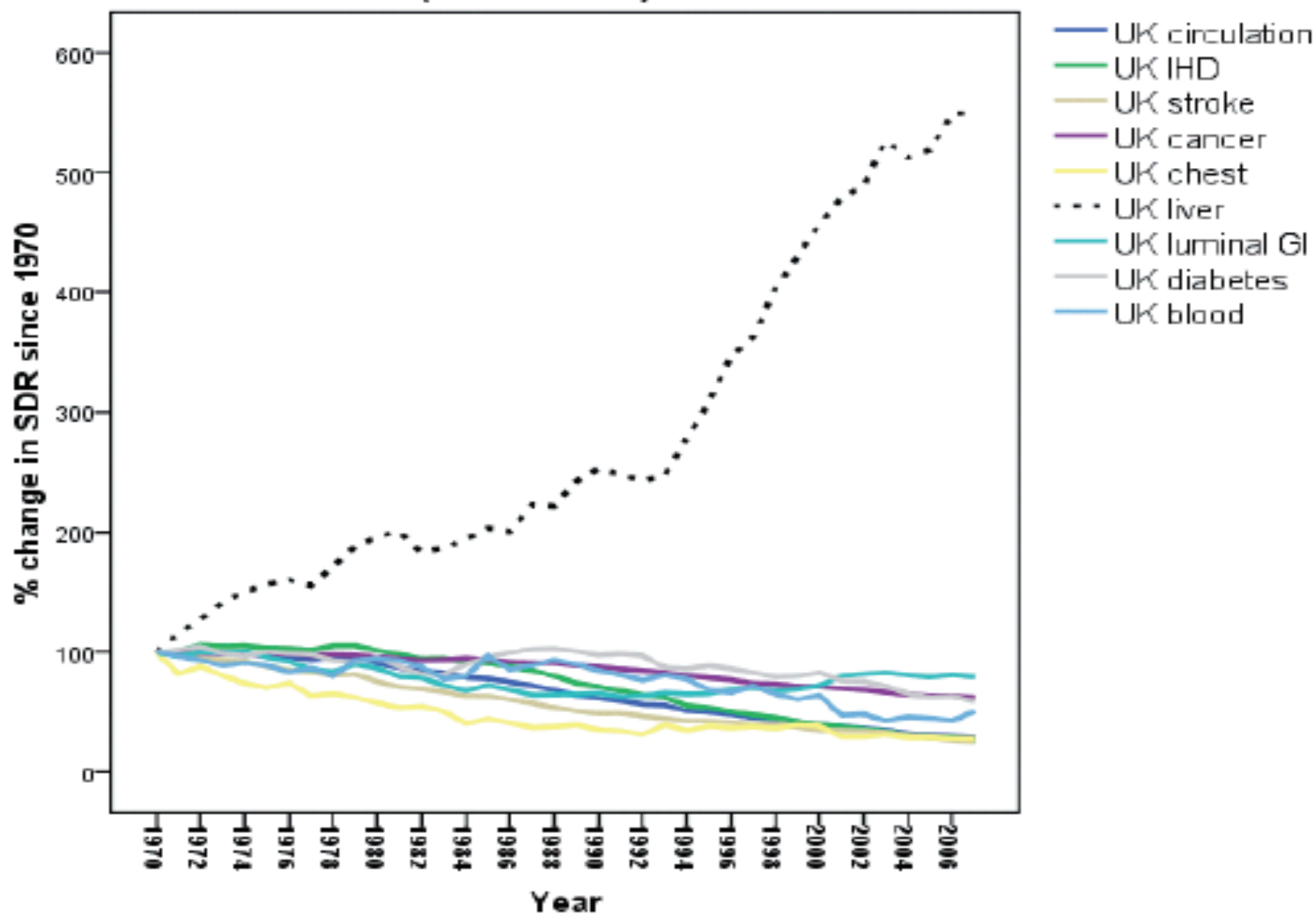
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Chelsea & Westminster Hospital / King's College Hospital



UK under 65 standard death rate for various diseases
(1970 = 100%)

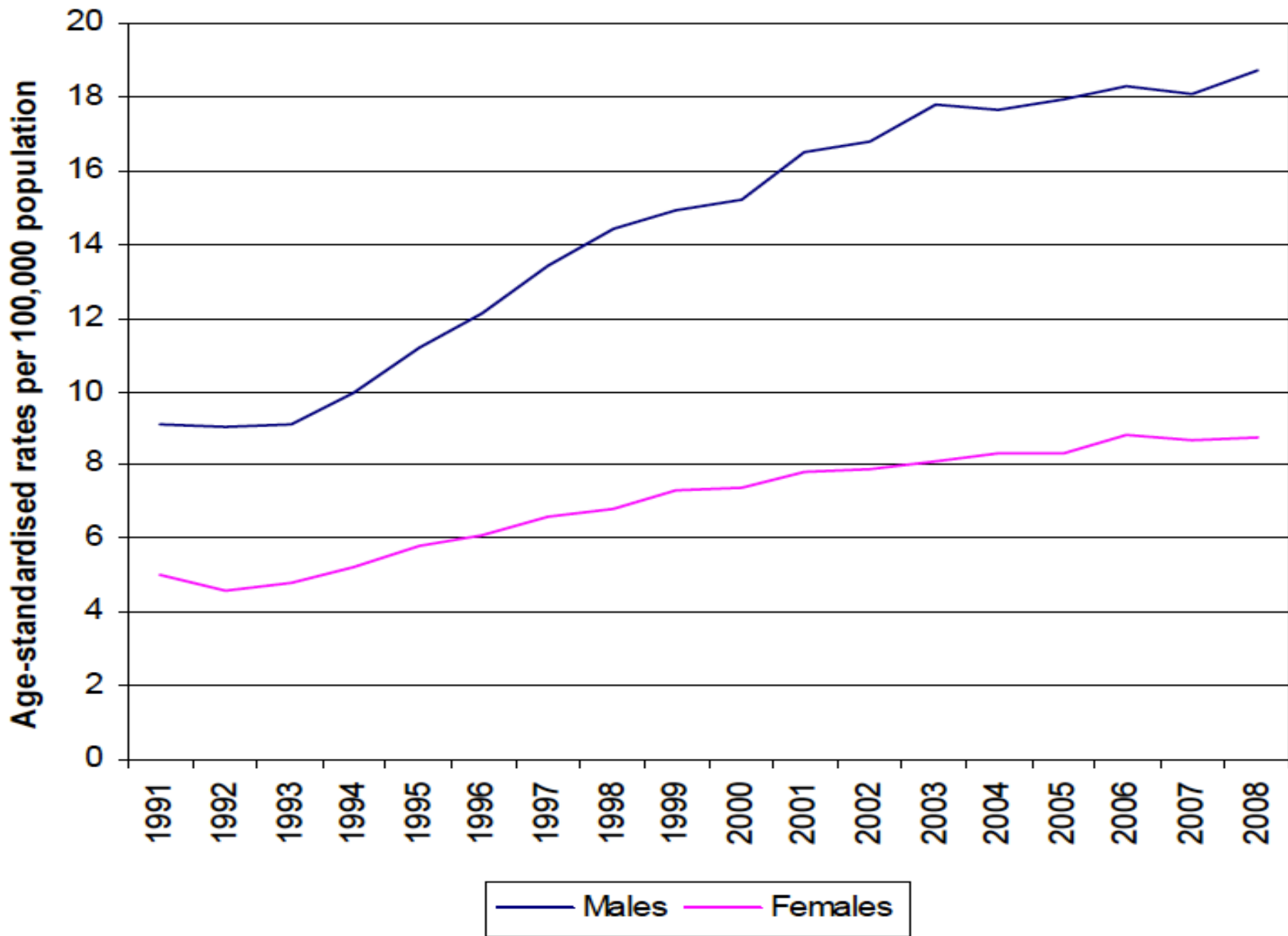


WWW.ABSOLUTAD.COM

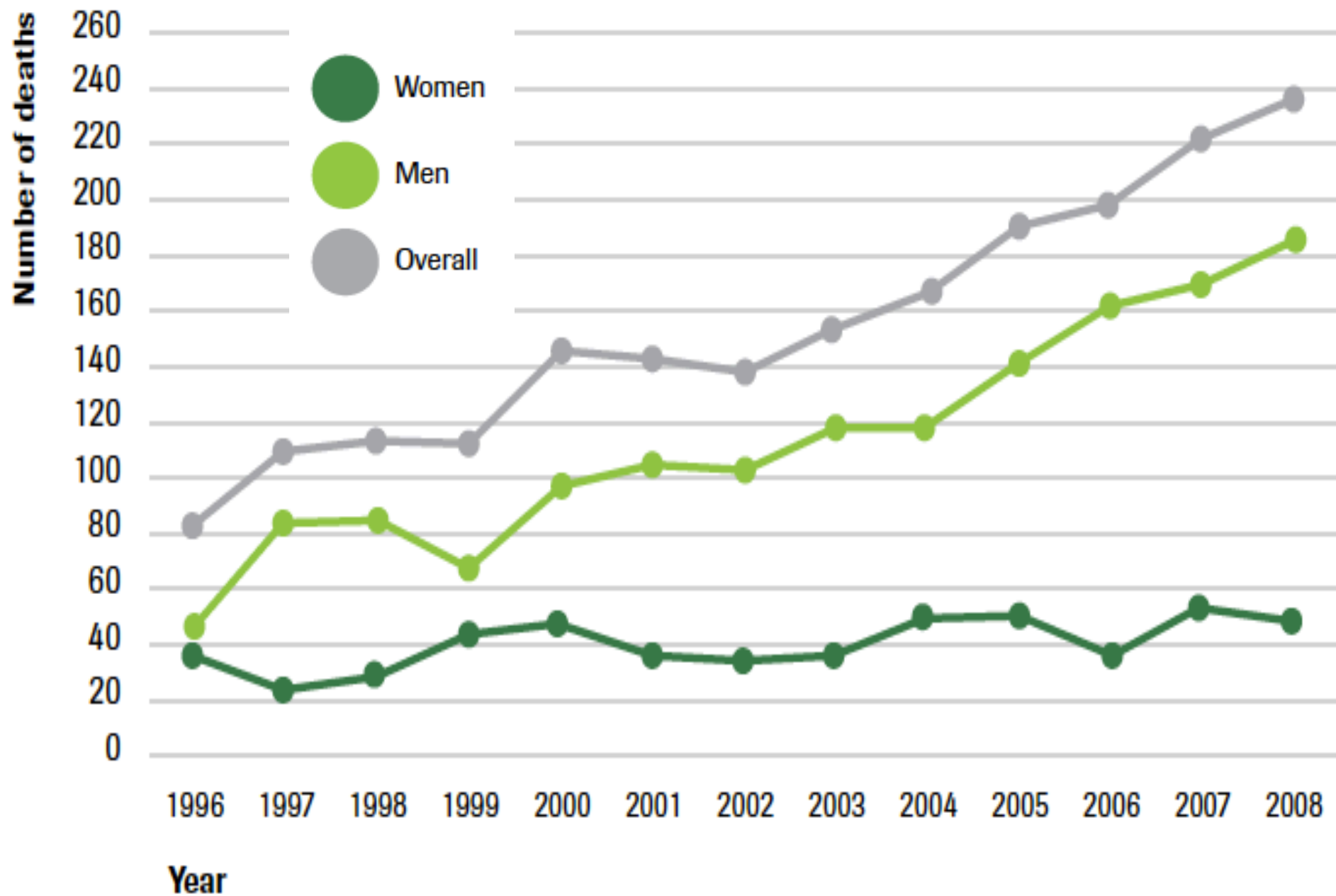


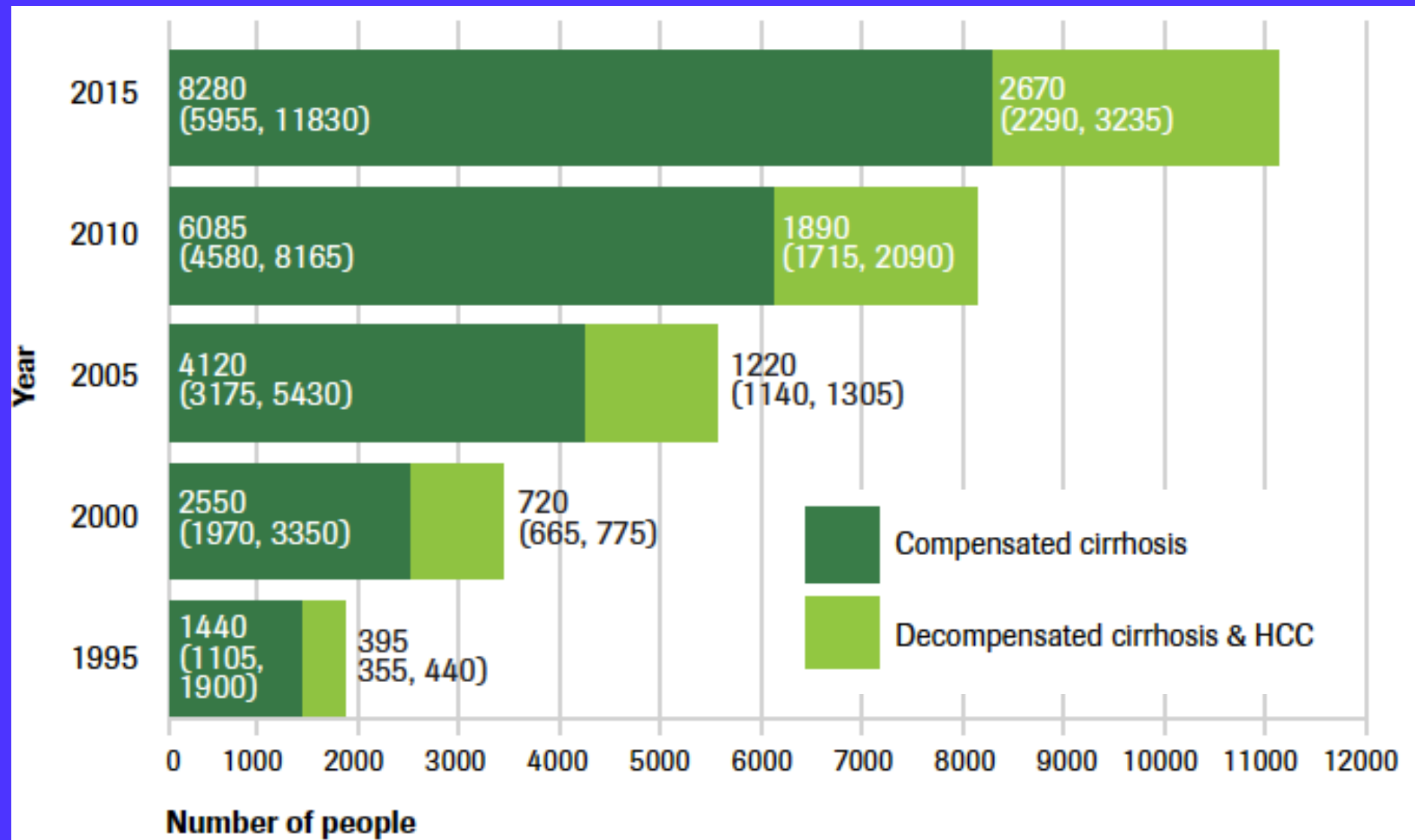
ABSOLUTE CIRRHOSIS.

The alcohol industry spends nearly \$2 billion a year on advertising and promotion and has been successful in creating more than 10 million alcoholic Americans. Each year in this country, alcohol accounts for 20,000 deaths by disease, 25,000 traffic deaths and 15,000 homicides and suicides. Alcohol-related problems cost the nation \$80 billion annually in lost productivity and health care. Congratulations to the alcohol industry on a job well done. Bottoms up!



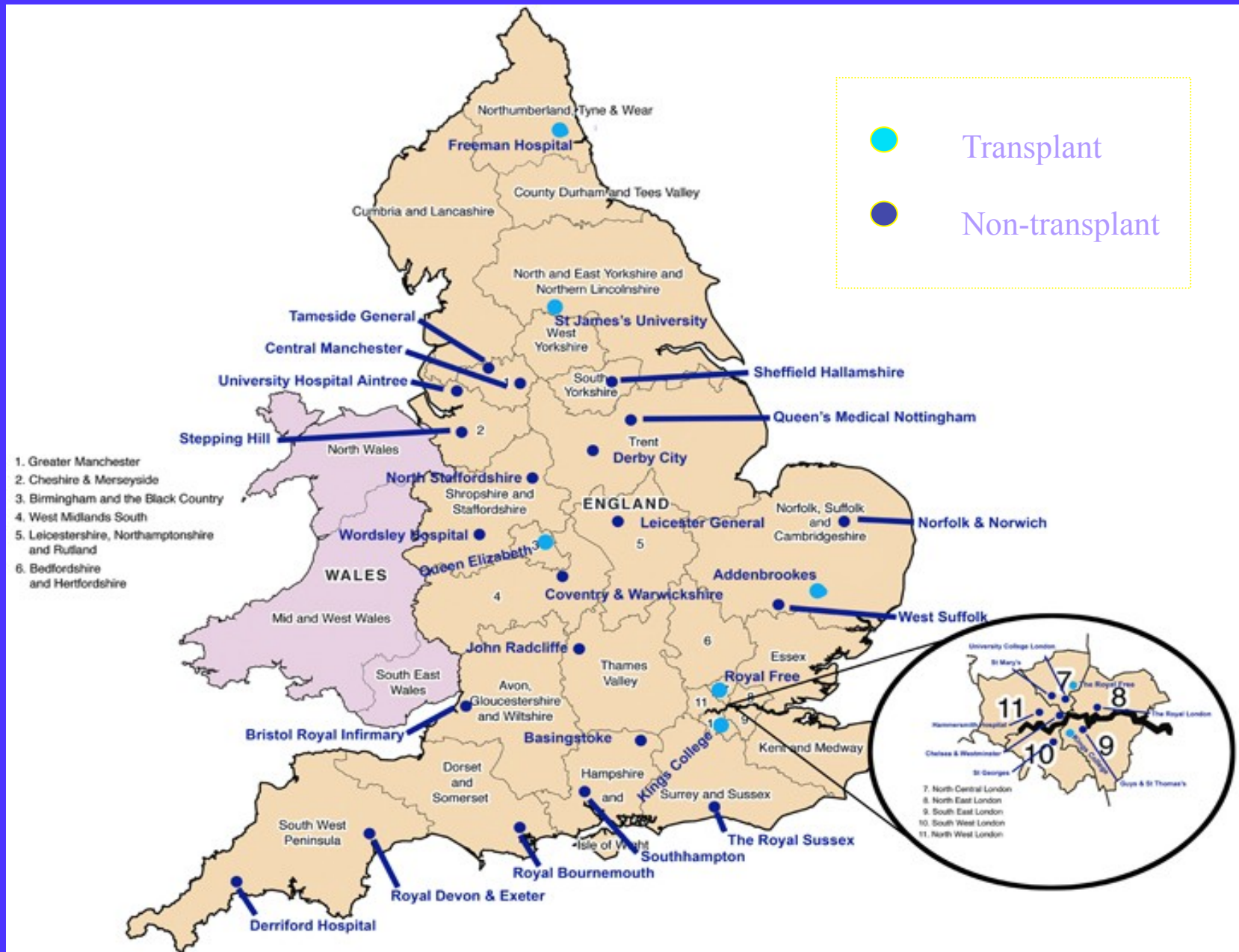
Alcohol-related death rates by sex, United Kingdom, 1991-2008



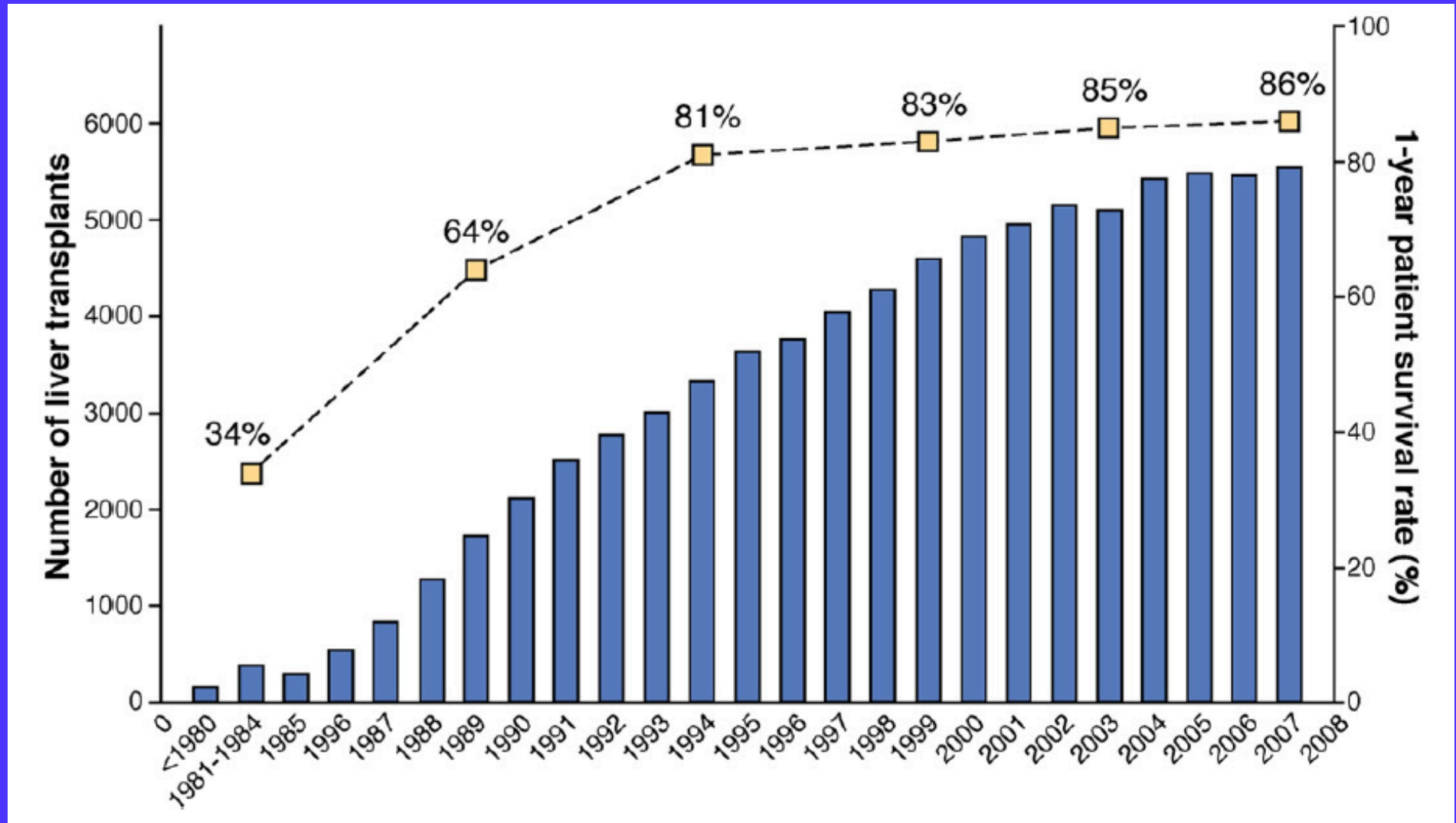


History of Liver Transplant

- 1963 – 1st Liver Transplant - Denver USA
- 1967 – 1st Liver transplant in UK
- 1977 – Preservation solutions
- 1980 – Introduction of cyclosporin
- 1981 – Multi-organ donor cards
- 1983 – UK Liver Transplant Programme



Evolution of Liver Tx

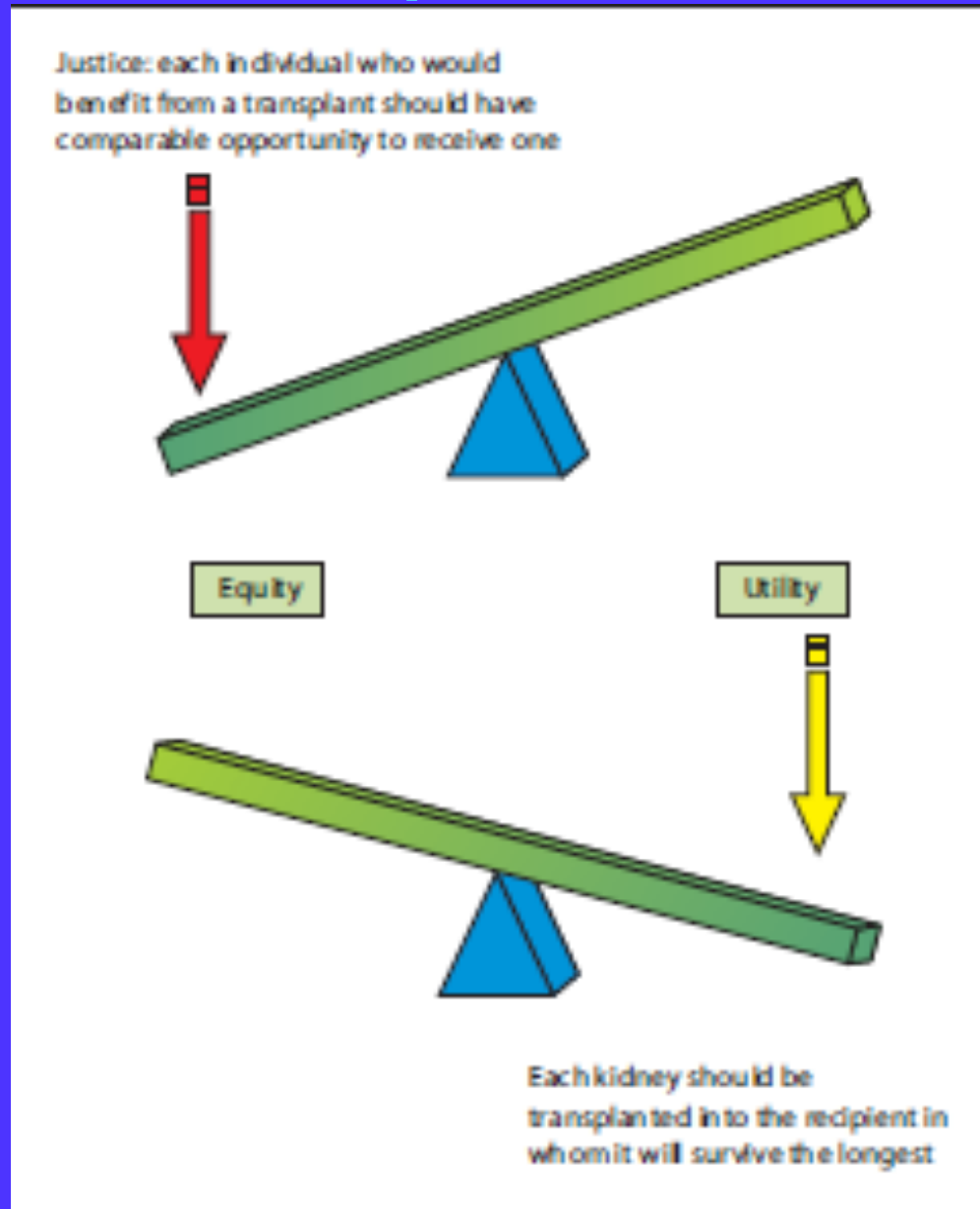


WHO guiding principles

- Consent
- Separate physicians
- Related live donation
- Protect vulnerable
- Money
 - Selling organs
 - Advertising for organs
 - Paying doctors
 - Paying organisations
- Governance
- Transparency & Privacy
- Allocation rules
 - equitable
 - justifiable
 - transparent
 - utility

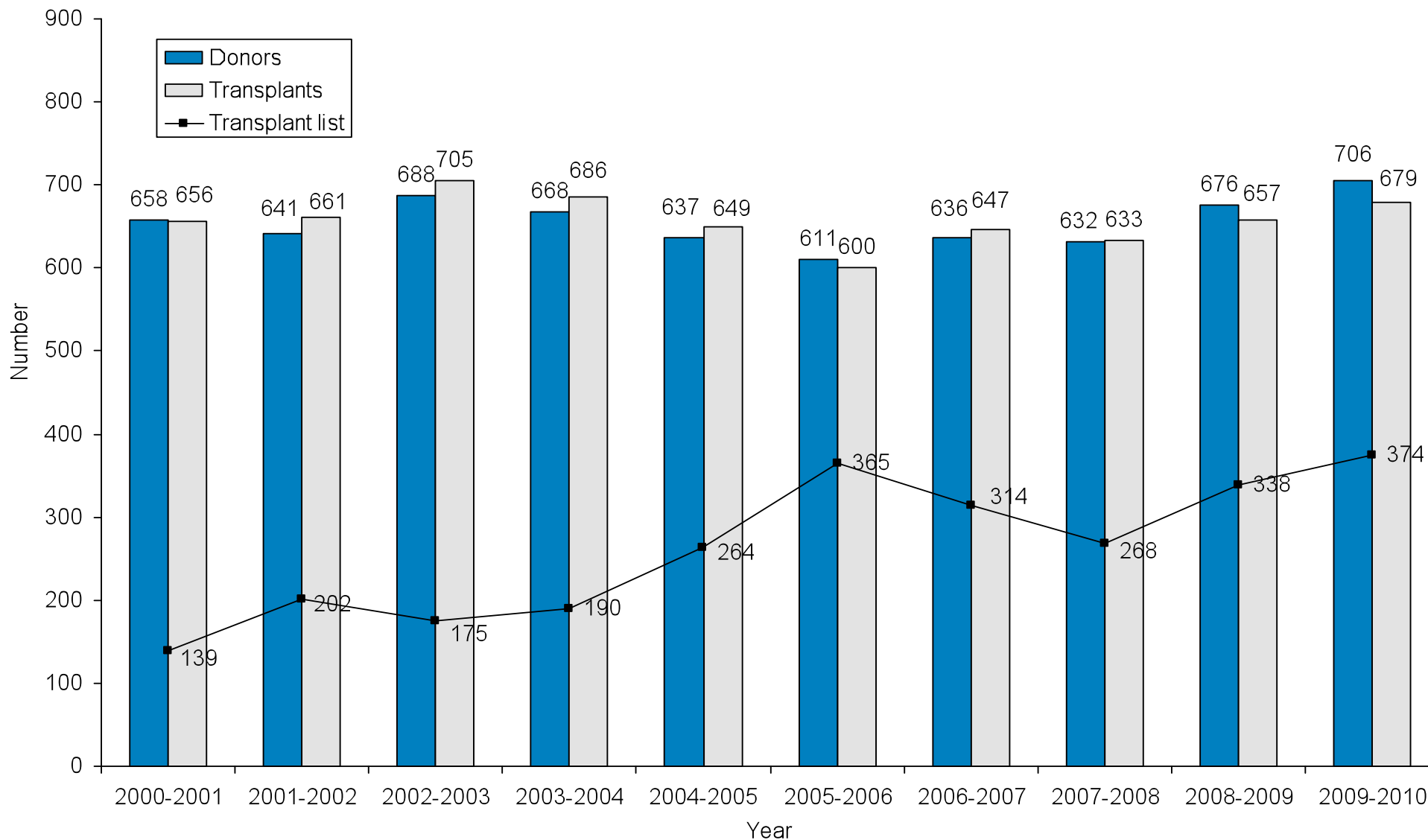
Principles of Transplantation

- Justice
- Utility
- Equity
- Benefit



Deceased donor liver programme in the UK, 1 April 2000 - 31 March 2010

Number of donors, transplants and patients on the active transplant list at 31 March



Source: Transplant activity in the UK, 2009-2010, NHS Blood and Transplant

Priorities for liver transplant (1)

1. 68 year old woman looks after her 92 year old father at home. She has a serious liver disease and will die within 6 months without the transplant
2. 9 month old boy has liver disease. Without a transplant he will die in 18 months. He has three older brothers and one older sister
3. 21 year old woman is diagnosed with liver cancer when 8 months' pregnant. She will die in 6 months without the transplant. If transplanted, she has only a one in two chance of being present at her daughter's 1st birthday party but a one in 10 chance of a cure and living for 10 or more years
4. 17 year old woman takes a paracetamol overdose after a row with her boyfriend. It is the first time she has done this. Without the transplant she will be dead in 4 days

Priorities for liver transplant (2)

5. 45 year old garage owner with a wife and two young children has drunk heavily since he was 18. This has led to liver and kidney failure. He has 2 months to live if he is not transplanted
6. 35 year old unemployed man lives alone. His liver disease will kill him within 9 months unless he receives a transplant
7. 45 year old woman used drugs in the 1970s during which she contracted a virus which resulted in liver failure. She has not used drugs since and unless transplanted is unlikely to live more than a year
8. 50 year old man is in prison serving a long sentence for grievous bodily harm. He has a serious liver disease from which he will die in 9 months

Results

	BSc
68 yr old carer	
9 mth old boy	
21yr old cancer	
17yr old O.D.	
45yr old drinker	
35yr old unemployed	
45yr old ex-IVDU	
50yr old prisoner	

Results

	Public	GPs	Gastro
68 yr old carer	38	26	21
9 mth old boy	78	82	64
21yr old cancer	74	57	45
17yr old O.D.	47	81	95
45yr old drinker	16	18	19
35yr old unemployed	56	67	74
45yr old ex-IVDU	17	41	76
50yr old prisoner	2	7	9

Scoring systems for liver disease

- Child-Pugh score
- MELD score
- UKELD score

Child-Pugh scores (CPS)

	1	2	3
Encephalopathy	0	Grade I/II	Grade III/IV
Ascites	None	Mild	>Moderate
Bilirubin	<34	34-51	>51
Albumin	>35	28-35	<28
INR	<1.3	1.3-1.5	>1.5

Model for End-Stage Liver Disease (MELD)

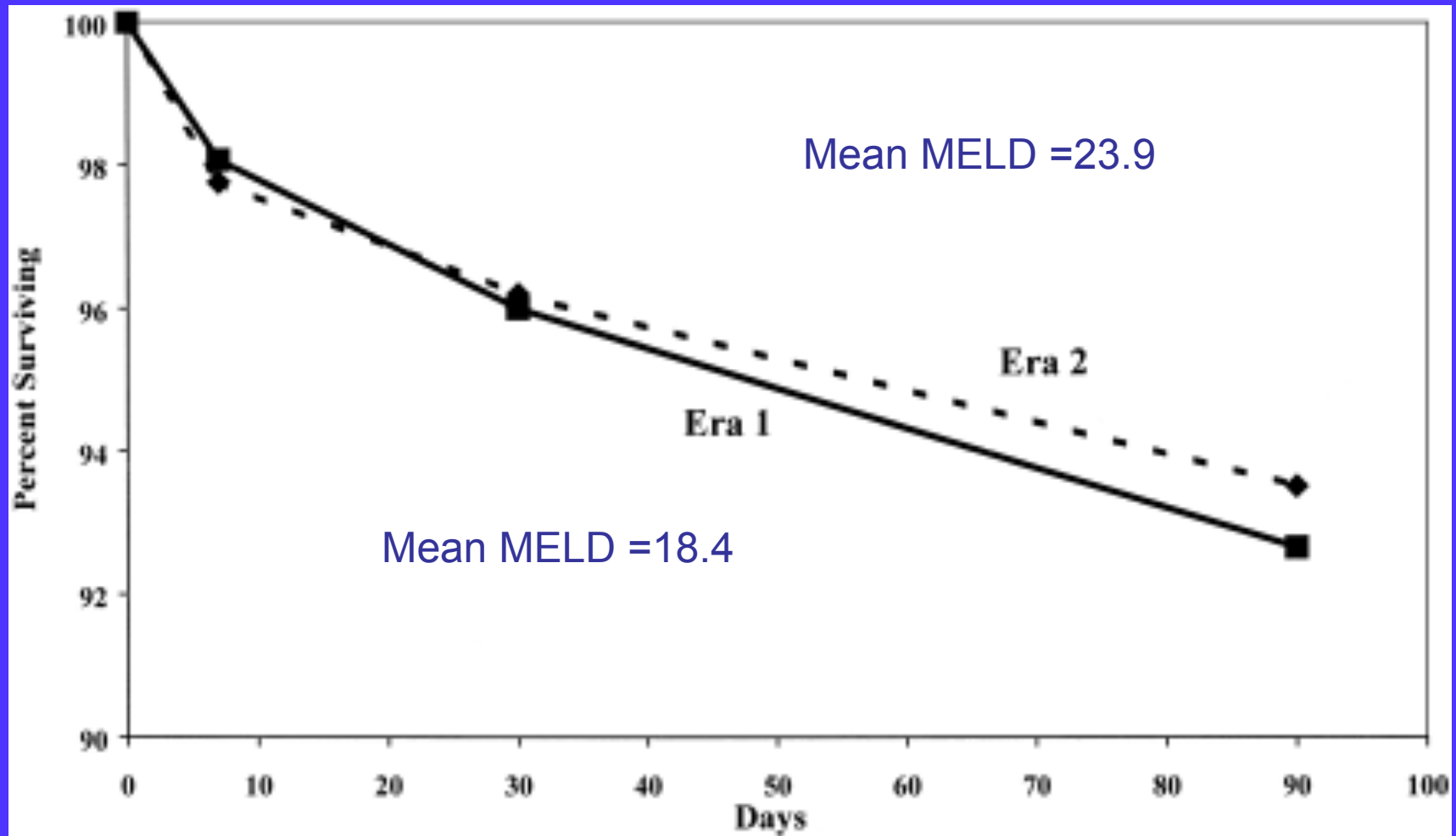
- Introduced as means of organ allocation in USA in Feb 2002
- Originally devised for survival post TIPSS¹
- Modified for use as tool for predicting 3 month mortality on LT waiting list²

$$\text{MELD} = 11.2 \text{ Ln(INR)} + 3.78 \text{ Ln(Bilirubin)} + 9.57 \text{ Ln(Creatinine)} + 6.43$$

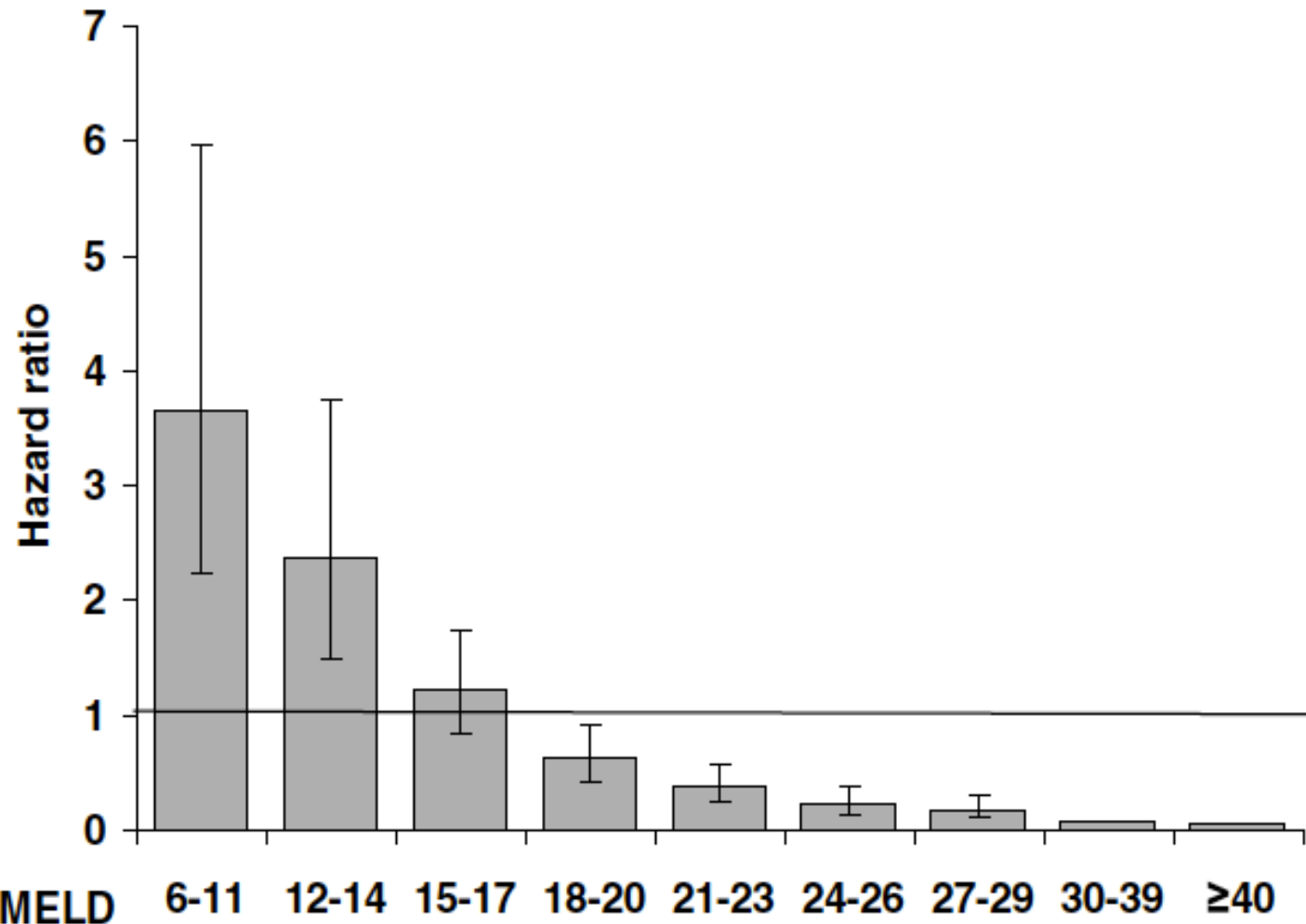
¹ Malinchoc M *et al* *Hepatology* 2000; **31**: 864-871

² Wiesner R *et al*. *Gastroenterology* 2003; **124**: 91-96.

Use of the MELD system



Benefit of Liver Tx



Hazard Ratio	3.64	2.35	1.21	0.62	0.38	0.22	0.18	0.07	0.04
p-values	<0.001	<0.001	0.41	<0.01	<0.001	<0.001	<0.001	<0.001	<0.001

UKELD

$$= 5x \{1.5x \ln (\text{INR}) + \\ 0.3x \ln (\text{creatinine } (\mu\text{mol/L})) + \\ 0.6x \ln (\text{bilirubin } (\mu\text{mol/L})) - \\ 13x \ln (\text{Na } (\text{mmol/L}) + 70)\}$$

UKELD >49 = 9% mortality at 1 year

Indications for LT

- 1968 – ‘. . . are too ill for an independent existence outside hospital’
- 1991 – ‘when their chances of surviving the procedure are greatest, rather than in the final throes of their illness’
- 1999 – ‘a survival probability of at least 50% at 5 years with the quality of life acceptable to the patient and life expectancy of less than 1 year’

Indications for Liver Transplant

1. Acute liver failure
2. Chronic liver failure
3. Metabolic liver disease
 - Inborn errors of metabolism
4. Hepatocellular carcinoma

Contra-indications to LT

ABSOLUTE

- AIDS
- Extrahepatic malignancy
- Advanced cardiopulmonary disease
- Cholangiocarcinoma

RELATIVE

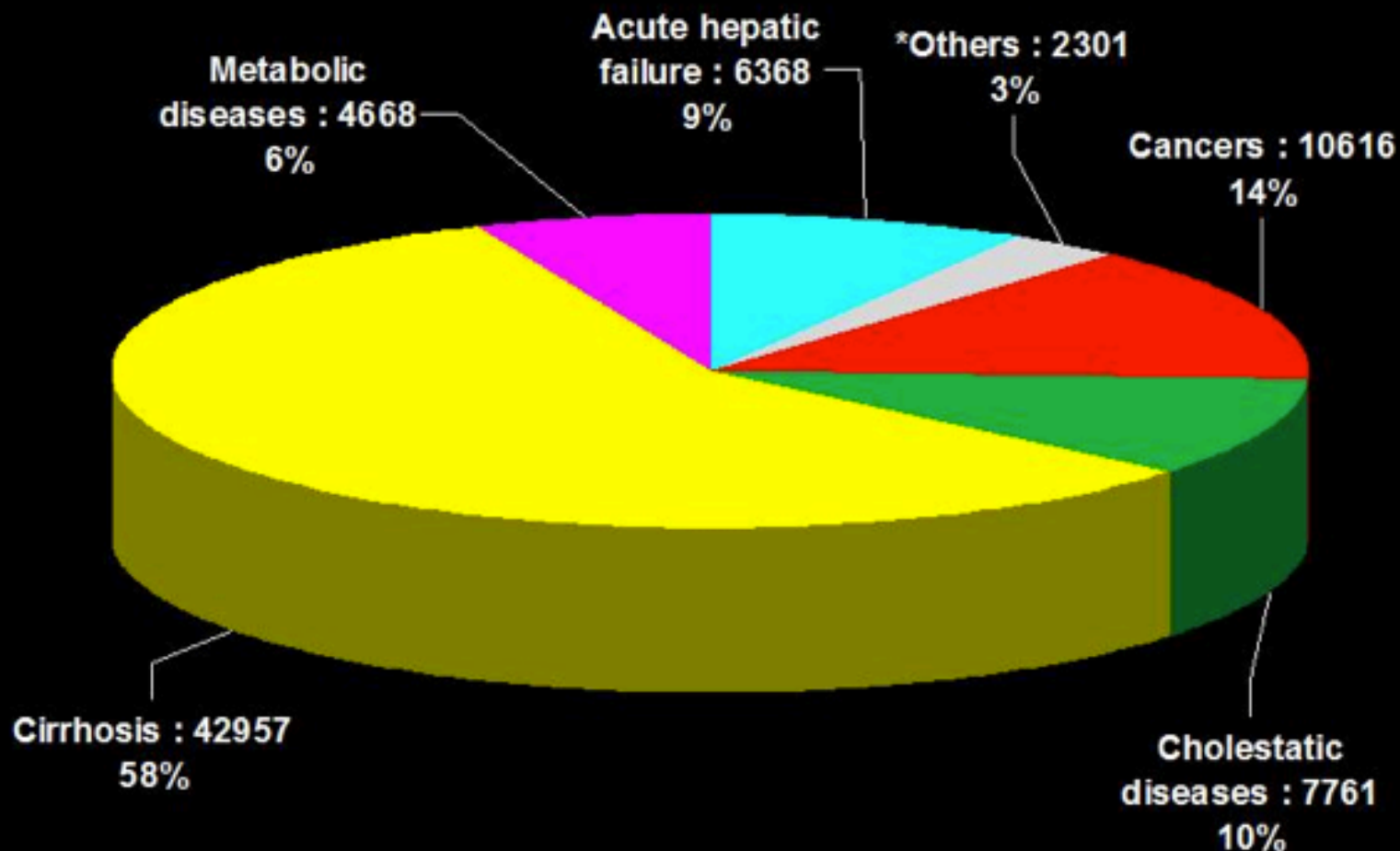
- HIV positivity
- Age above 70 years
- Significant sepsis outside the extrahepatic biliary tree
- HBV DNA positivity
- Active alcohol/substance misuse
- Severe psychiatric disorder
- Portal venous system thrombosis
- Pulmonary hypertension

Primary Diseases leading to Liver Transplantation in Europe

01/1988 - 06/2009



06/2009



* Others : Budd Chiari : 683
Parasitic diseases : 71

Benign liver tumors or Polycystic diseases : 982
Other liver diseases : 565

Acute Liver Failure

- Jaundice to encephalopathy time
- Hyperacute
 - ≤ 1 week
- Acute
 - 1 – 4 weeks
- Subacute
 - 4 -12 weeks

Superurgent Listing

Paracetamol Poisoning

- 1) pH < 7.25 more than 24 h after overdose and after fluid resuscitation
- 2) Co-existing PT > 100 s (or INR > 6.5) and serum creatinine > 300 μmol/l (or anuria) and grade 3–4 encephalopathy
- 3) Serum lactate more than 24 h after overdose > 3.5 mmol/l on admission or > 3.0 mmol/l after fluid resuscitation
- 4) Two of the three criteria from category 2 with clinical evidence of deterioration (e.g. increased ICP, FiO₂ > 50%, increasing inotrope requirements) in the absence of clinical sepsis

Superurgent Listing

Seronegative hepatitis, hepatitis A or B, or an idiosyncratic drug reaction

- 1) PT >100 seconds (or INR >6.5) and any grade of encephalopathy
- 2) Any grade of encephalopathy, and any three from the following:
 - i. unfavourable aetiology (idiosyncratic drug reaction, seronegative hepatitis)
 - ii. age >40 years
 - iii. jaundice to encephalopathy time >7 days
 - iv. serum bilirubin >300 mmol/l
 - v. PT >50s (or INR >3.5)

Superurgent Listing

Acute presentation of Wilson's disease, or
Budd–Chiari syndrome

A combination of coagulopathy, and any
grade of encephalopathy

Superurgent Listing

Post-LT

- 1) Hepatic artery thrombosis on days 0 to 21 after liver transplantation
- 2) Early graft dysfunction on days 0 to 7 after liver transplantation with at least two of the following:
 - i. AST > 10 000 IU/l
 - ii. INR > 3.0
 - iii. serum lactate > 3 mmol/l
 - iv. absence of bile production
- 3) Any patient who has been a live liver donor who develops severe liver failure within 4 weeks of the donor operation

Chronic Liver Failure

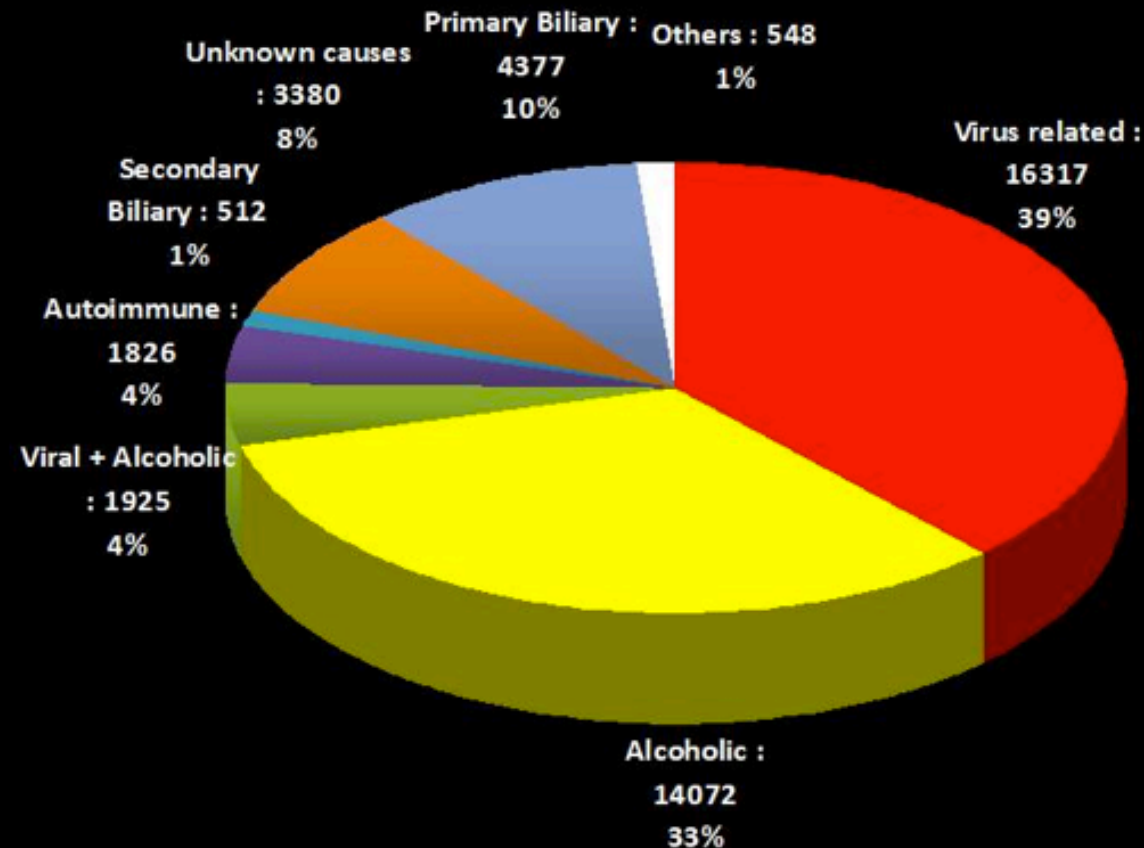
- Alcoholic
- Viral
 - HCV
 - HBV
- Cholestatic
 - Primary biliary cirrhosis
 - Secondary biliary cirrhosis
 - Primary sclerosing cholangitis
 - Secondary sclerosing cholangitis
- Cryptogenic
 - Non-alcoholic fatty liver disease
- Autoimmune Hepatitis
- Primary hepatocellular cancer in cirrhotic liver
- Metabolic
 - Alpha - 1-antitrypsin deficiency
 - Haemochromatosis
 - Wilson's disease
- Budd-Chiari syndrome
- Paediatric
 - Biliary atresia
 - Other congenital biliary abnormalities
 - Inborn errors of metabolism not in CLF group
- Cystic Fibrosis
- Polycystic liver disease
- Familial Amyloidosis syndromes
- Congenital hepatic fibrosis

Liver Transplantation in Europe Indications in 42957 Cirrhosis

01/1988 - 06/2009



06/2009



Indications for LT

- Unacceptable quality of life (because of liver disease) *AND / OR*
- Anticipated length of life without transplantation that is shorter than that with transplantation
- >50% probability of survival at 5 years after transplantation with a quality of life that is acceptable to the patient

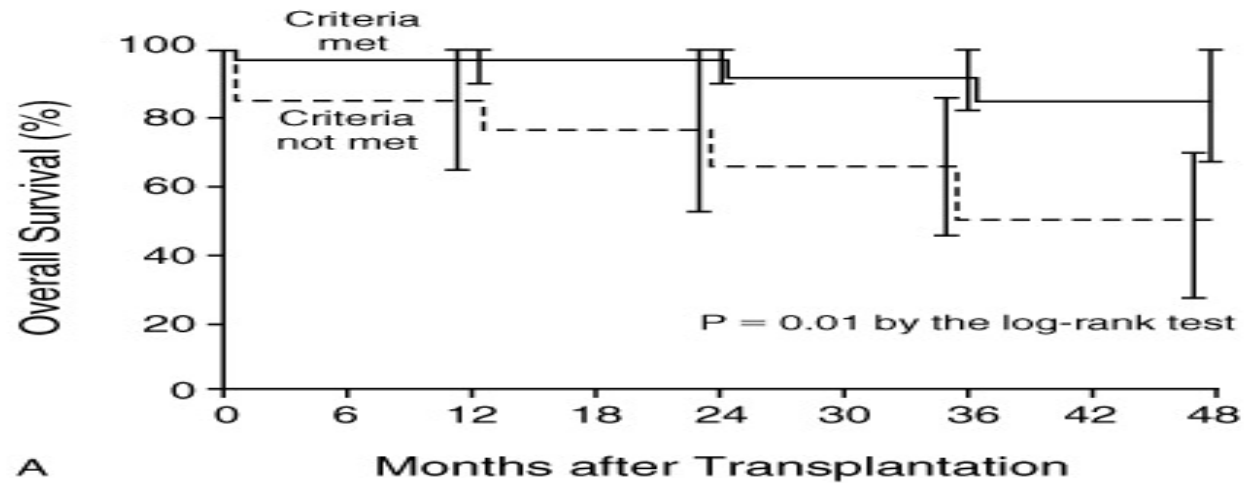
Indications for LT

- 1) Projected 1-year liver disease mortality without transplantation of >9%
 - UKELD
- 2) Hepatocellular carcinoma (HCC)
 - Size and number
- 3) Variant syndromes
- 4) National appeals panel

Variant Syndromes

- Diuretic resistant ascites
- Hepato-pulmonary syndrome
- Chronic hepatic encephalopathy
- Persistent and intractable pruritus
- Familial amyloidosis
- Primary hyperlipidaemia
- Polycystic liver disease
- Recurrent cholangitis

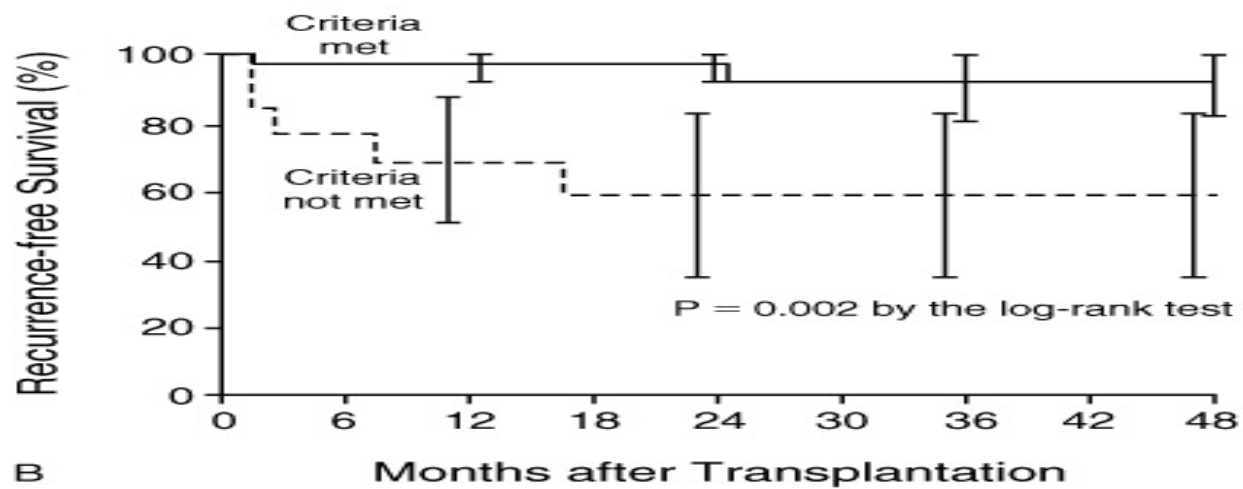
HCC



A

PATIENTS AT RISK

Criteria met	35	34	31	24	21	16	13	6	3
Criteria not met	13	13	11	8	6	6	4	4	3



B

PATIENTS AT RISK

Criteria met	35	34	31	24	21	15	12	6	3
Criteria not met	13	10	9	5	5	5	4	3	3

HCC

- Single tumour ≤ 5 cms diameter OR
- Up to 5 tumours all ≤ 3 cms OR
- Single tumour >5 cms and ≤ 7 cms with $<20\%$ change over 6/12
- Contraindications:
 - Tumour rupture
 - AFP $>10,000$ iu/ml
 - Extra-hepatic spread
 - Macrovascular invasion

Assessment

- Hepatologist
 - Severity of liver disease
- Medical co-morbidities
 - DM / Cardiac / Respiratory / Previous cancer
- Anaesthetist / Intensivist
 - Will patient survive anaesthetic?
 - Will patient survive ITU?
- Surgical
 - Is the operation technically feasible?
- Psychologist / Social Worker / Tx Coordinator

Alcohol-induced liver disease

- Assessment by substance misuse team
- 6/12 abstinence
- Contraindications
 - Alcoholic hepatitis
 - Repetitive episodes (more than 2) of non-compliance
 - Return to drinking following full professional assessment and advice (this includes permanent removal from the list if found to be drinking while listed)
 - Concurrent or consecutive illicit drug use (except occasional cannabis use)

Illicit Drug Use

Assessment

- Substance misuse specialist
- Social support

Contraindications

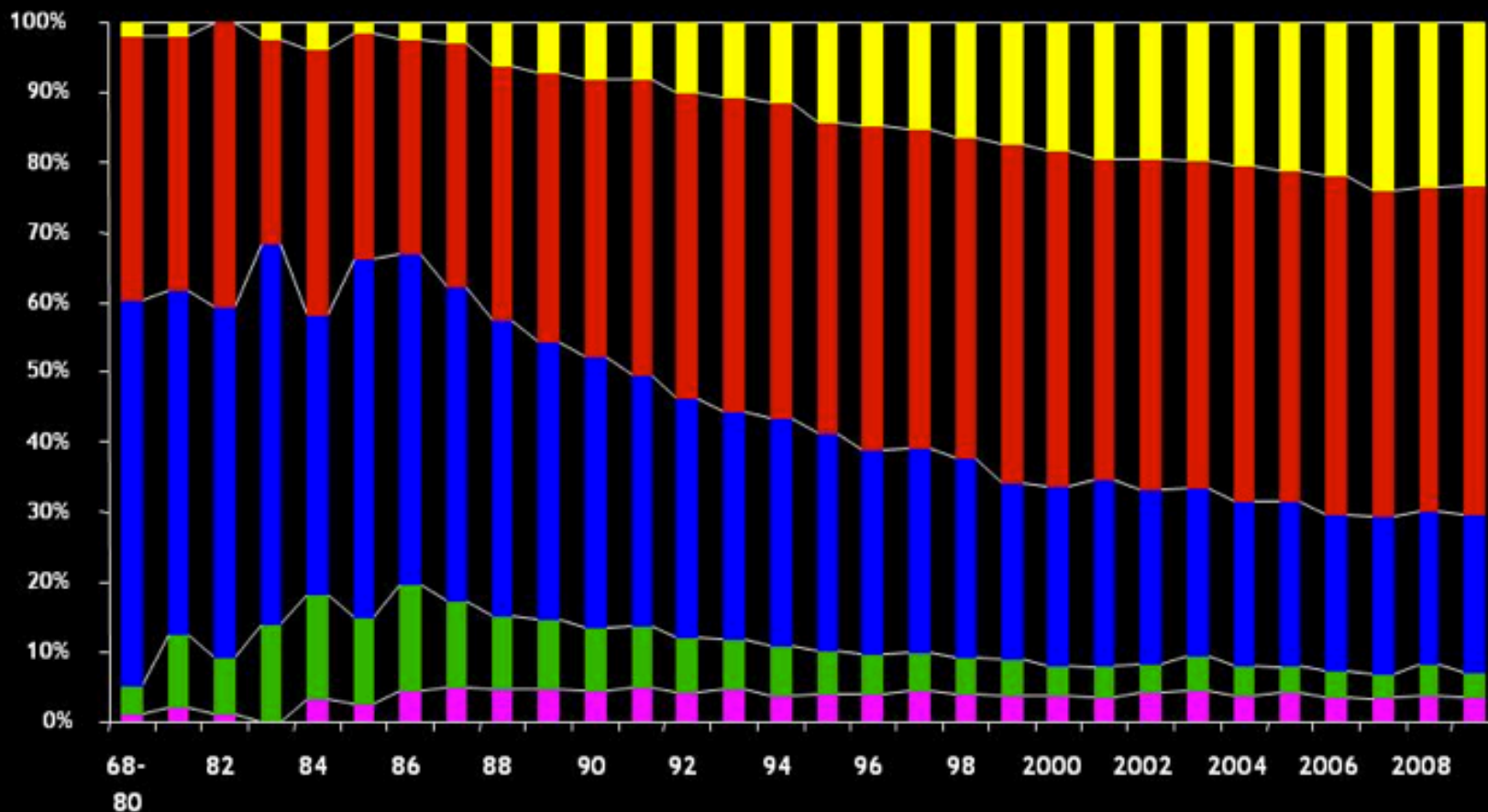
- Ongoing illicit use
- Poor compliance
- Cross-dependency
- Abstinence <6/12

Evolution of Recipient Age

05/1968 – 06/2009



06/2009



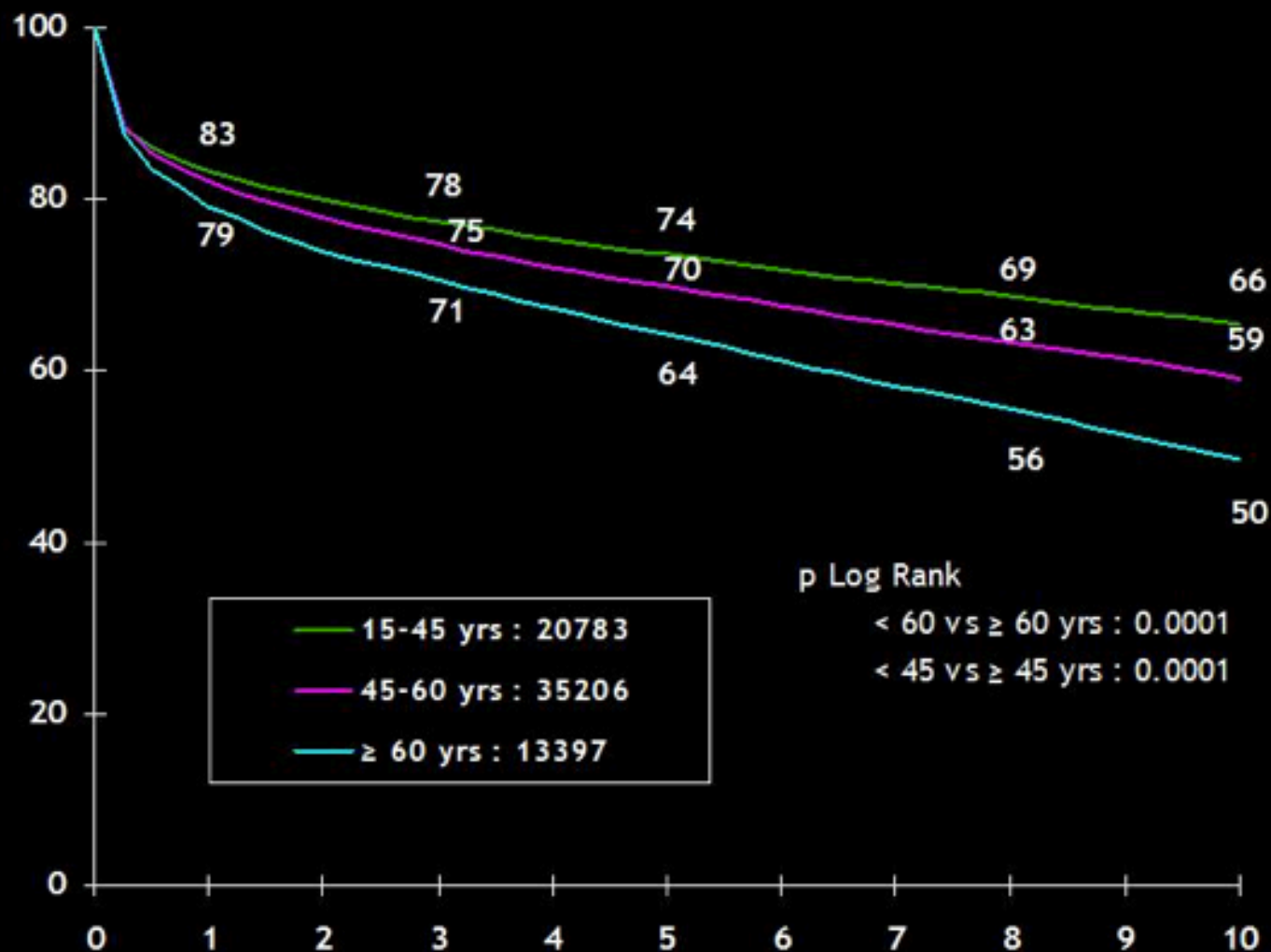
0 to 2 : 3187 2 to 15 : 4265 15 to 45 : 21798 45 to 60 : 36012 >=60 : 13480

Patient Survival according to Adult Recipient Age

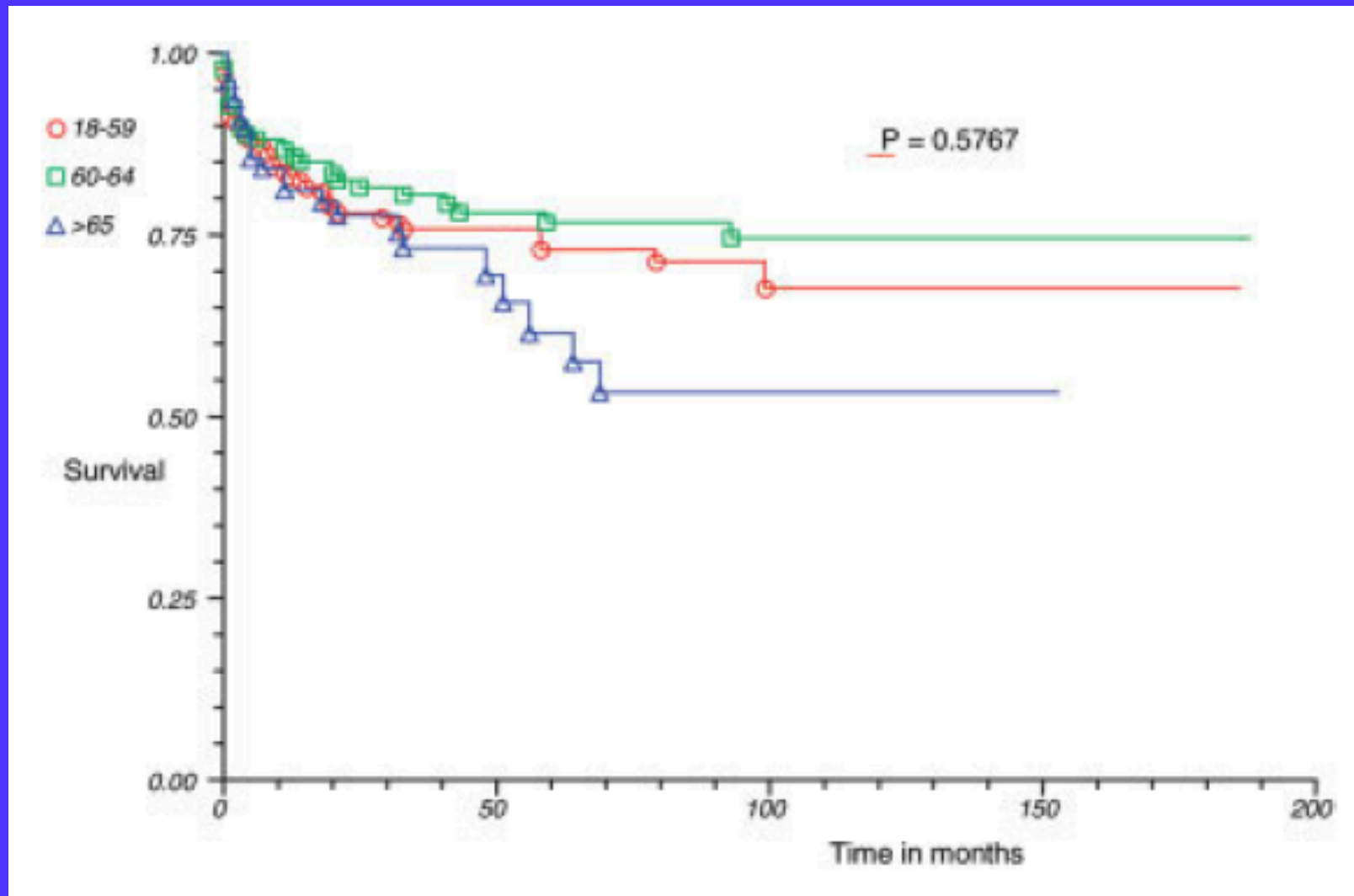


06/2009

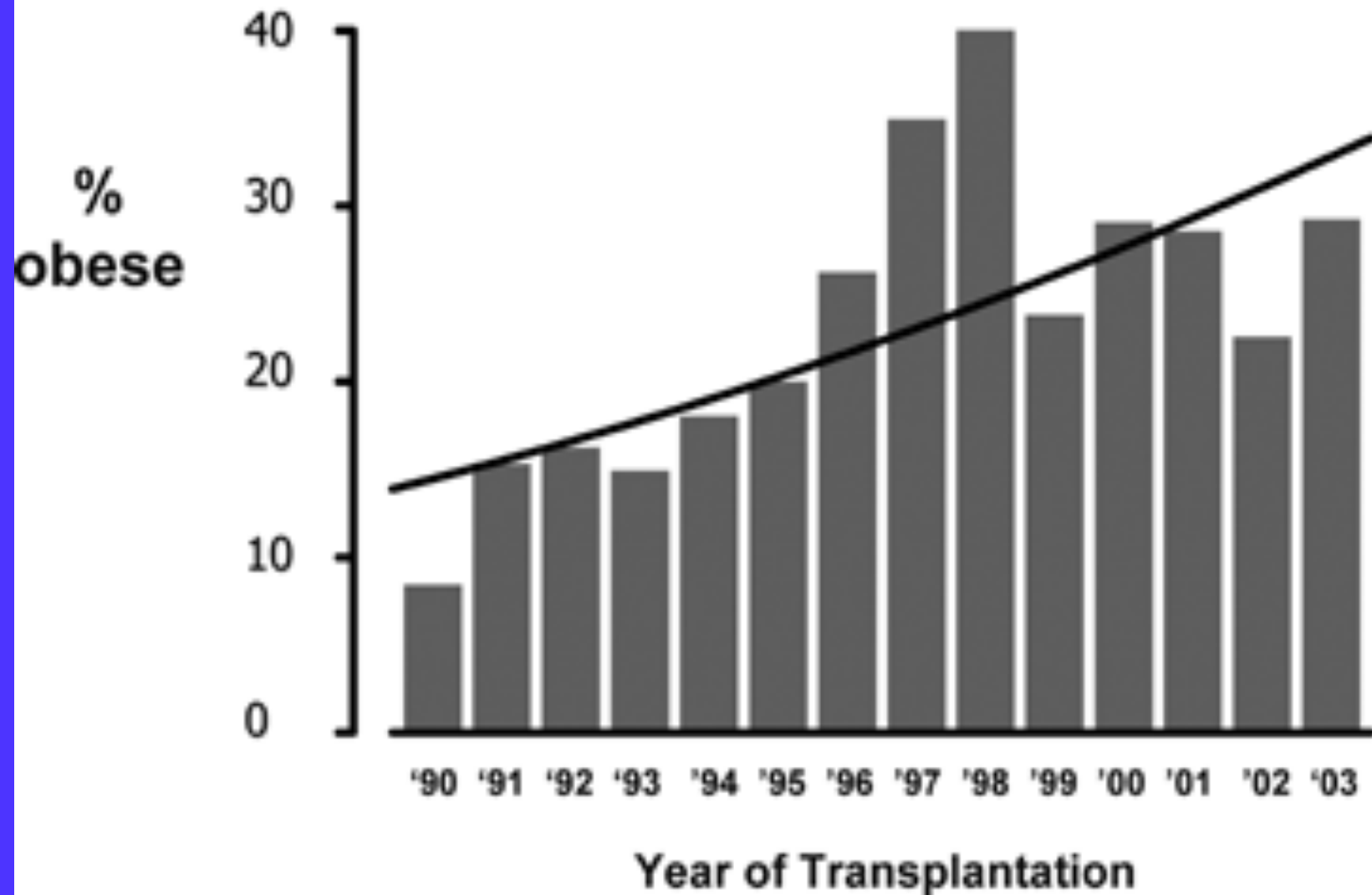
01/1988 - 06/2009



Age



Frequency of Obesity



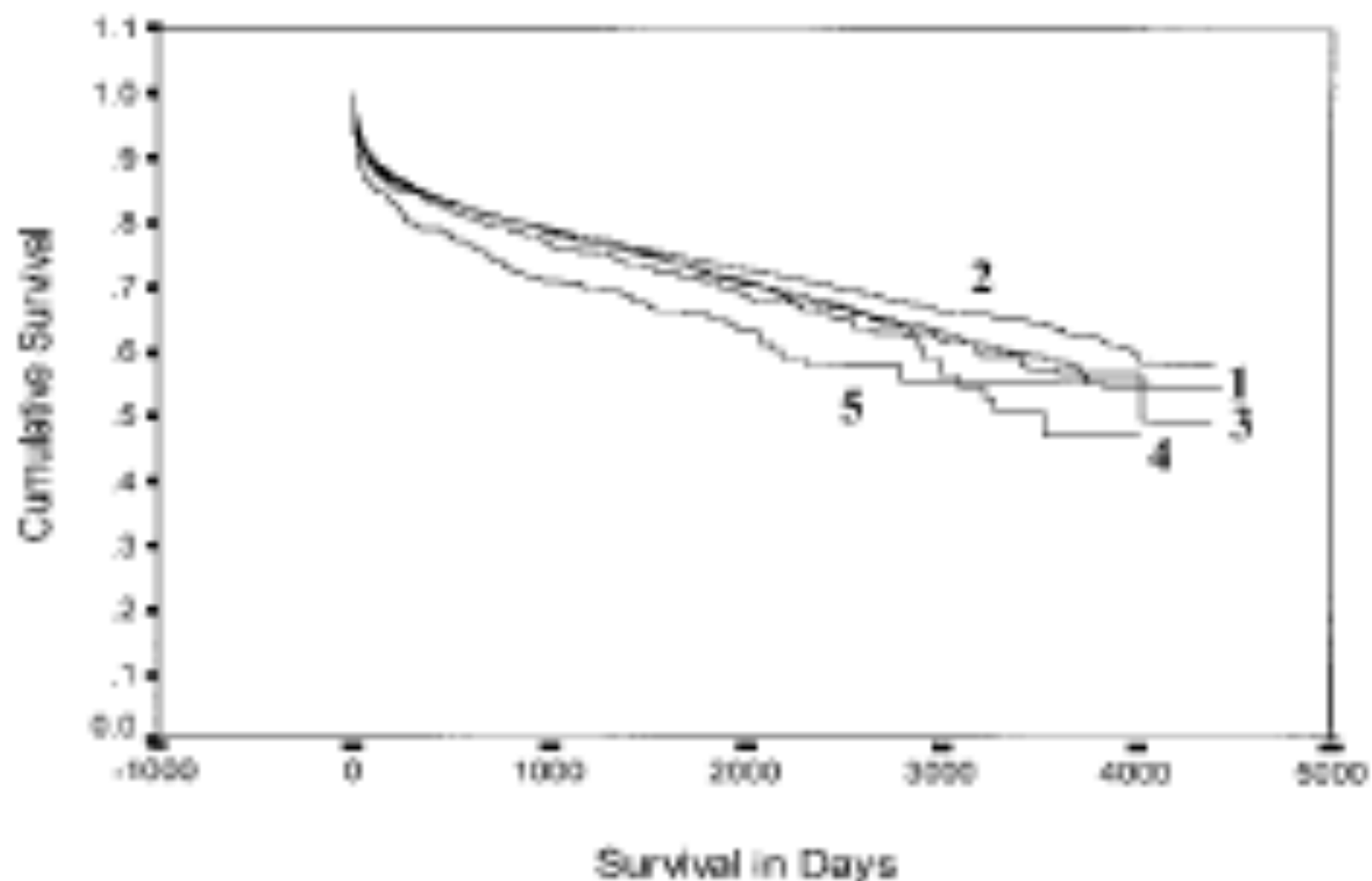
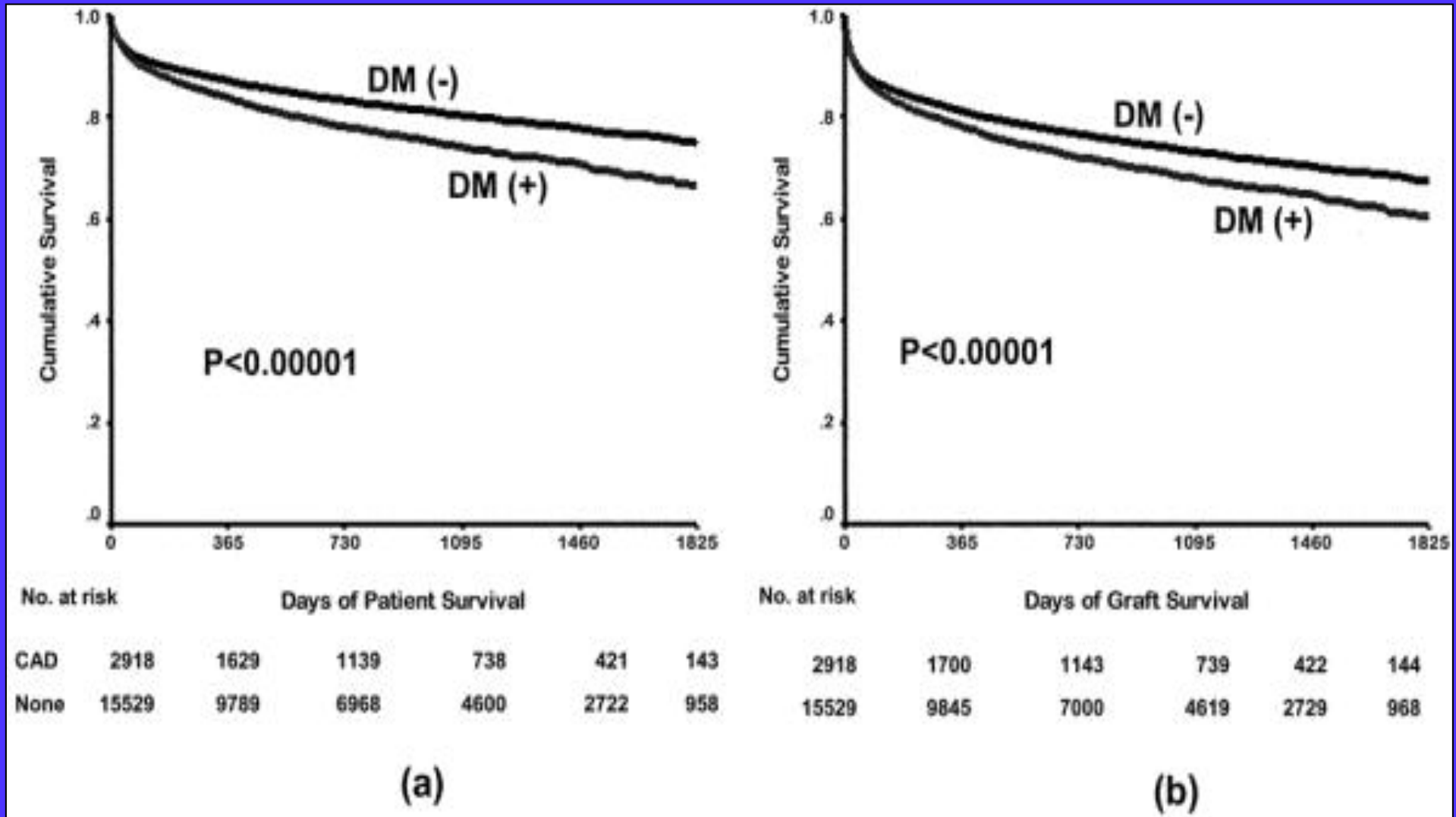
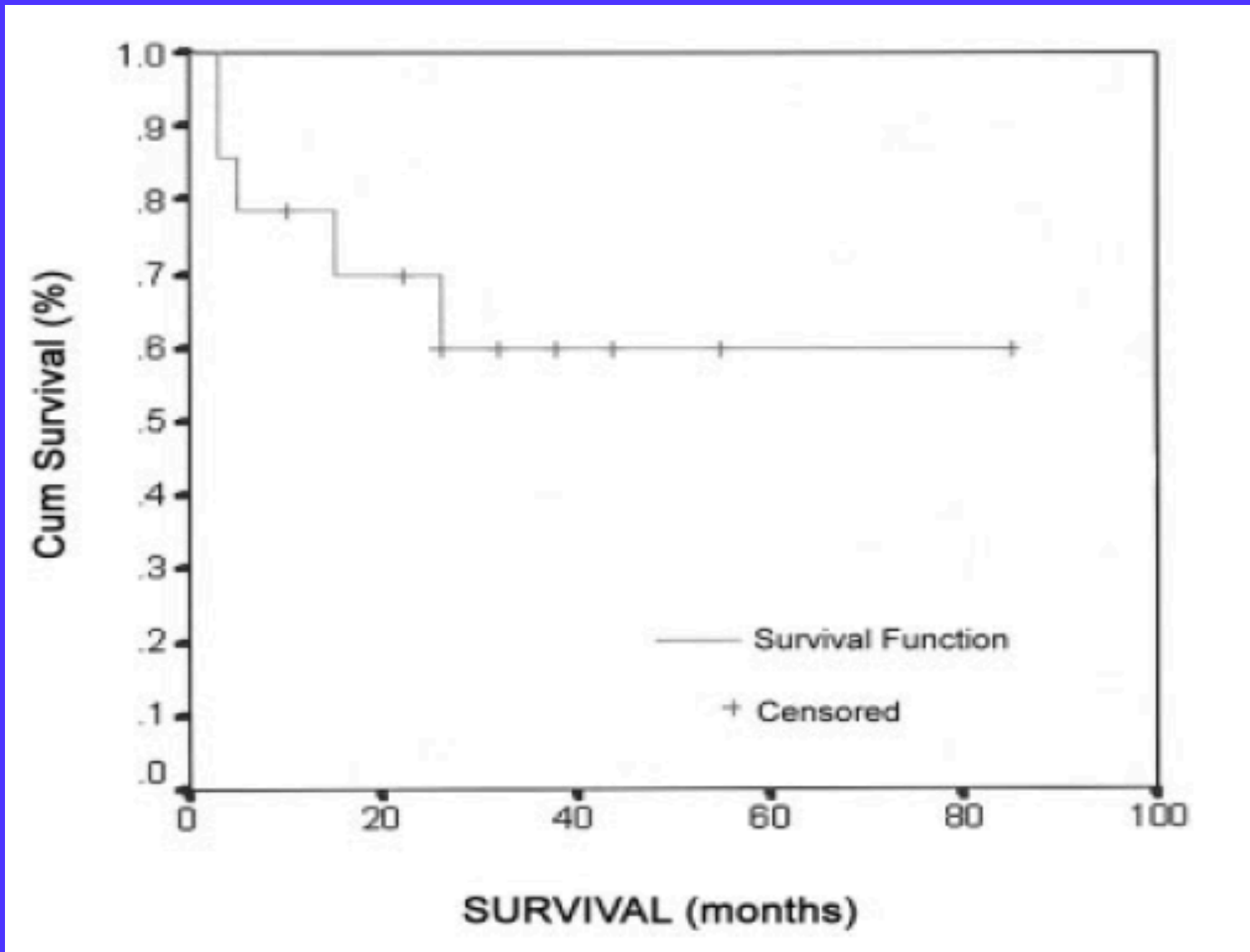


Fig. 1. Kaplan-Meier survival in patients based on their BMI. (1) Non-obese, (2) overweight, (3) obese, (4) severely obese, (5) morbidly obese.

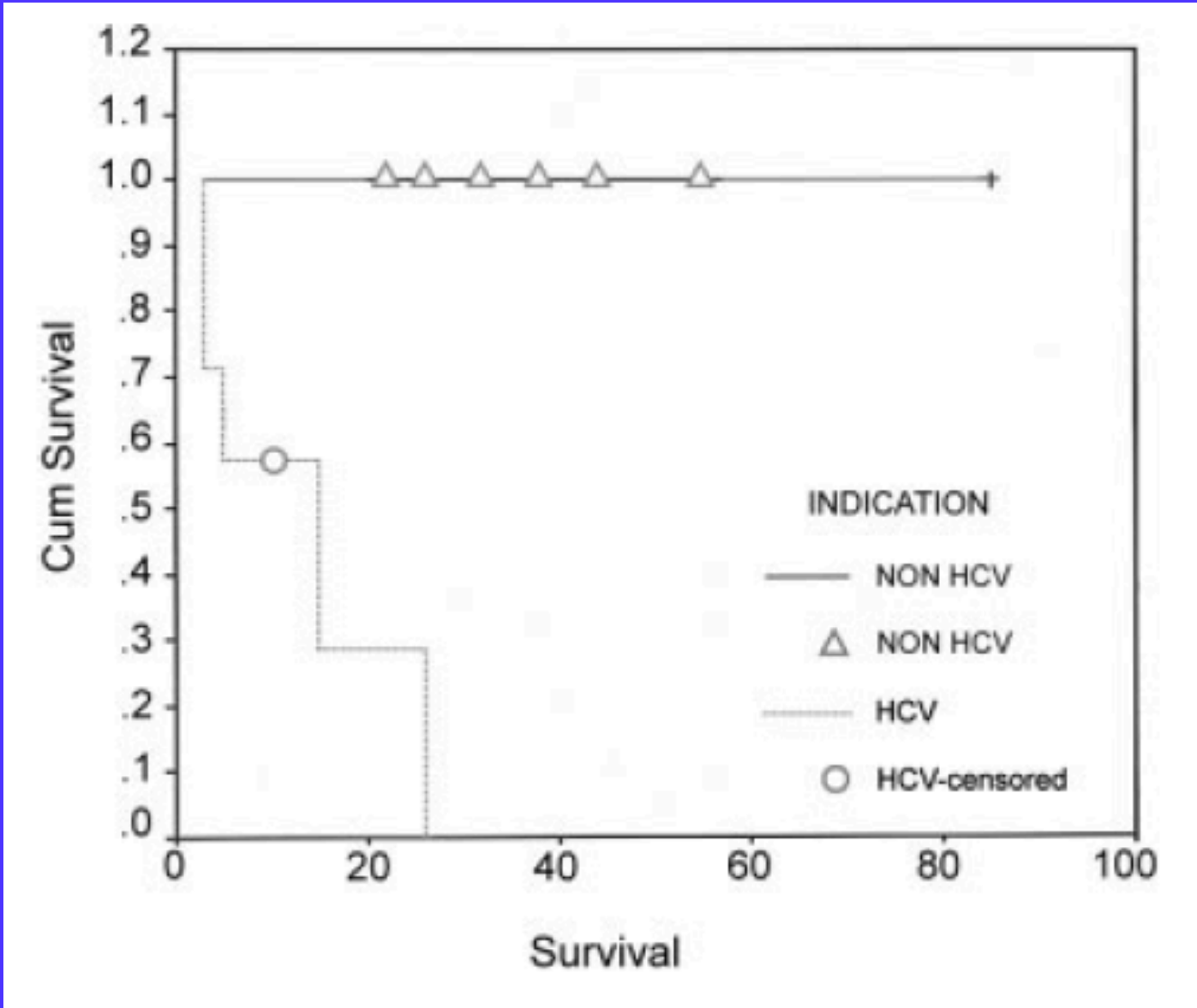
Diabetes mellitus



HIV



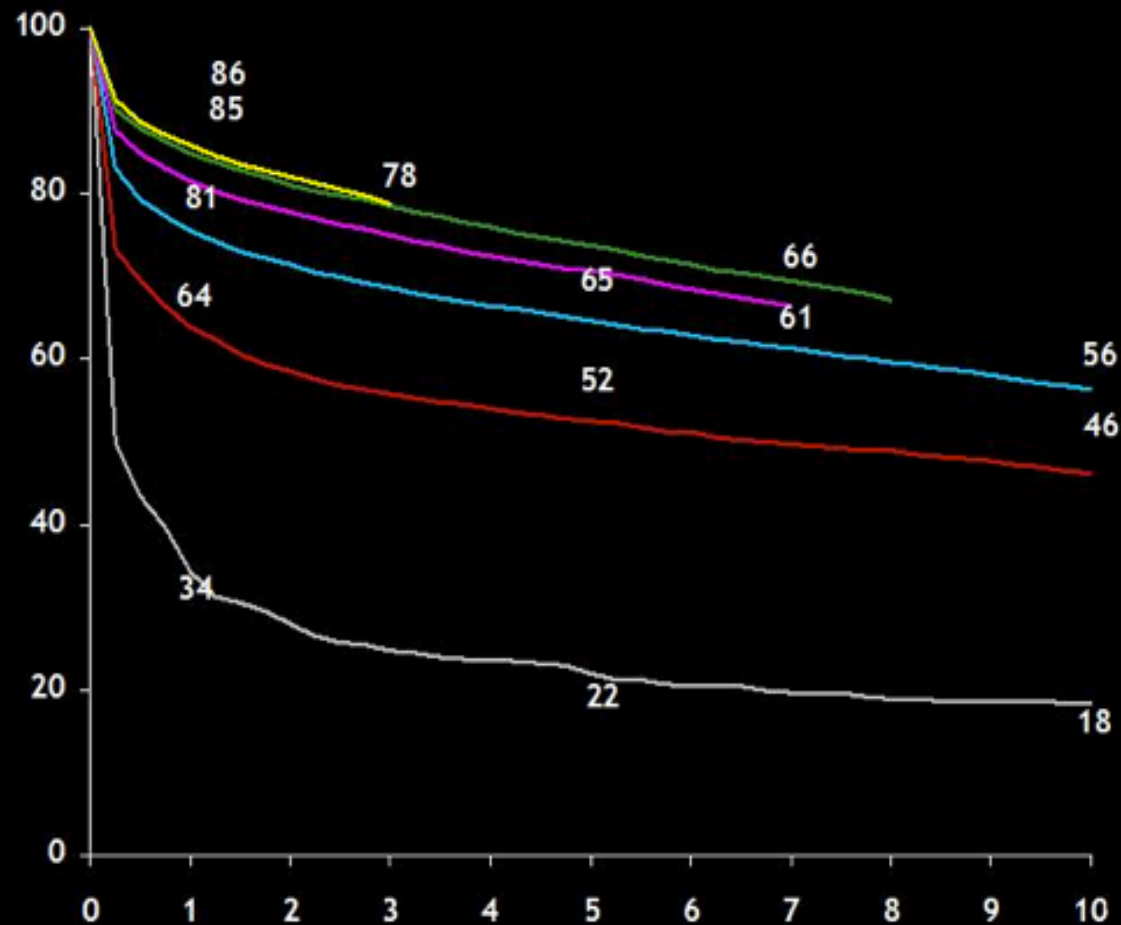
HIV and HCV



Patient Survival according to the Year of Liver Transplantation



06/2009



— <85 : 519 — 85-89 : 4130 — 90-94 : 12008
— 95-99 : 18166 — 2000-2004 : 22955 — >2004 : 21006

Donor Register

- How many of you think you should join the organ donor register?
- How many of you have joined!!

<https://www.organdonation.nhs.uk/ukt/RegistrationForm.do>