

# Economic issues in Hepatitis C

Richard Grieve

London School of Hygiene and  
Tropical Medicine

# Acknowledgements

- Mild Hepatitis C study
- Principal Investigators:
  - Howard Thomas, Janice Main
- Centre co-ordinators
  - William Rosenberg; Maggie Bassendine
- Statisticians
  - Daniela DeAngelis; Michael Sweeting

# Summary of talk

- Cost-effectiveness analysis (CEA) of antiviral treatment
- CEA of antiviral treatment for mild hepatitis C
- Emerging issues
  - Sub groups
  - Changing treatment regimens

# Challenges for Cost-effectiveness analysis in hepatitis C

- Slowly progressive disease
- Antiviral treatment has high initial cost
  - (48 weeks pegylated interferon+ ribavirin~20,000 Euro)
- Are initial treatment costs offset by?
  - Improved life expectancy
  - Gains in quality of life (QOL)
  - Lower costs of subsequent disease
- Estimation of quality-adjusted life years (QALYS)
- Lifetime costs per QALY gained from intervention
  - NICE <30,000 per QALY

# Cost-effectiveness analysis in hepatitis C requires evidence..

- Interventions' effectiveness in routine clinical practice (RCTs)
- Disease progression (observational studies)
- QOL and costs (RCTs, observational studies or expert opinion)
- *Lifetime* costs/QALY (from a model)

# Previous studies in hepatitis C

- Interferon alpha + ribavirin cost-effective for chronic hepatitis C (<15,000 Euro per QALY)
  - Younossi et al (1999); Wong et al (2000ab); Shephard and Waugh (2000); Stein et al (2002)
- Pegylated Interferon alpha + ribavirin is cost-effective for chronic hepatitis C (<20,000 Euro per QALY)
  - Shephard et al (2004); Siebert et al (2003); Wong et al (2003)

# Cost-effectiveness analysis and policy

- NICE concluded for patients with moderate to severe chronic hepatitis C
  - a) Interferon alpha and ribavirin is cost-effective and should be provided (2000)
  - b) Pegylated interferon alpha and ribavirin cost-effective and should be provided (2003)
  - c) Decision on mild chronic hepatitis C delayed (Guidance expected August 2006)
    - Lack of evidence
    - Currently not recommended for treatment

# NHS Health Technology assessment on mild hepatitis C

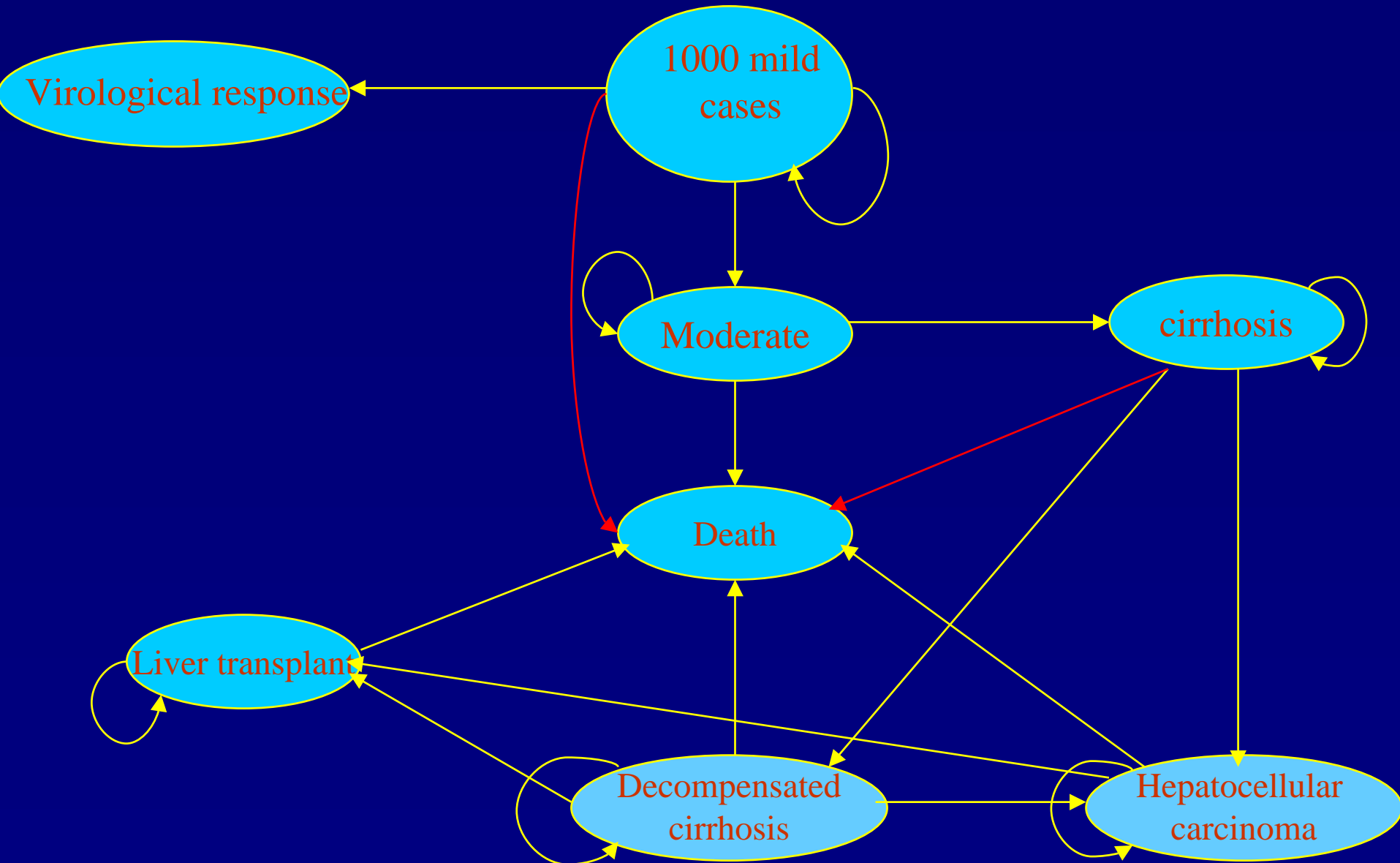
- Cost-effectiveness of antiviral treatment at a *mild* stage vs only treating those who progress to *moderate disease*?
  - Interferon alpha and ribavirin
  - Pegylated interferon alpha and ribavirin
- Final results

# Evidence to address study questions

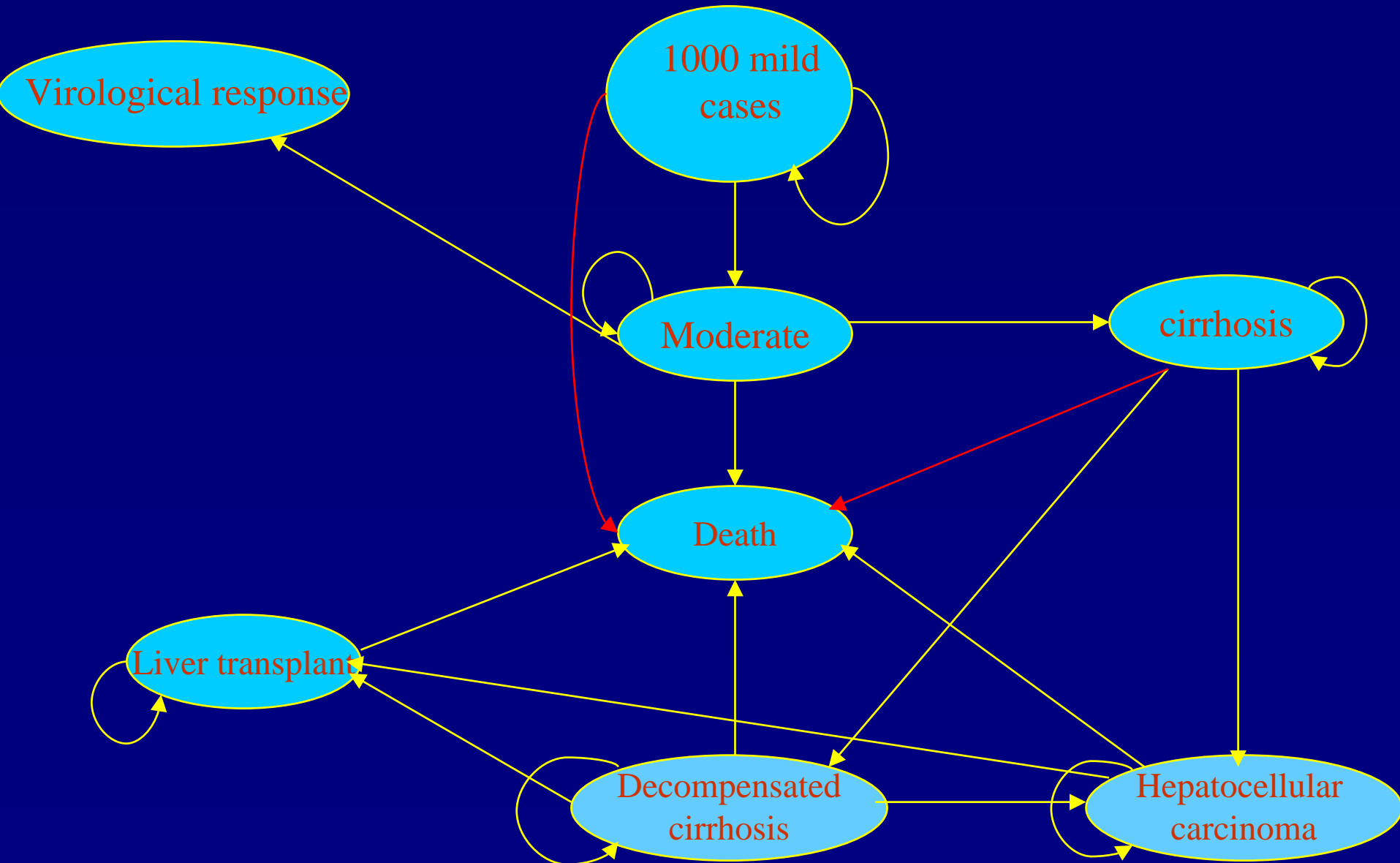
- Interventions' effectiveness:
  - Alpha interferon and ribavirin NHS RCT (Wright et al 2005)
  - Pegylated interferon and ribavirin: multinational RCTs adjusted estimates (Manns et al)
- Disease progression
  - Reanalysis of observational studies (Wright et al 2005; Sweeting et al 2005)
- HRQOL and costs
  - NHS RCT, observational study (Wright et al 2005)
  - *Lifetime* costs/QALY from model (Grieve and Roberts 2002)

# Markov Model for Hepatitis C

## Treatment for mild HCV



# Markov Model for Hepatitis C Treatment for moderate HCV



# Model inputs

## Transition Probabilities

	Mean estimate	Source
Mild-moderate	0.025	Wright et al 2005
Moderate-cirrhotic	0.037	Wright et al 2005
Cirrhotic-decomp	0.039	Fattovitch 1997
Decompensated-HCC	0.01	Fattovitch 1997
Decompensated-death	0.13	Fattovitch 1997

# Model inputs: Effectiveness alpha interferon and ribavirin

- Overall sustained viral response (SVR) of 33% (Wright et al 2005)
  - 18% genotype 1
  - 49% genotype non-1
- Previous estimates higher SVRs (Manns et al 2001, McHutchison et al 1998)
- No evidence lower SVR because mild rather than moderate HCV (Manns et al 2001)
- So used overall SVR of 33% for moderate disease
- Context NHS pragmatic RCT vs multinational RCT

# Effectiveness: pegylated interferon and ribavirin

- No available estimates from NHS RCTs
- Effectiveness of pegylated interferon +ribavirin vs alpha interferon+ riba from multinational RCT (Manns et al)
- Used to derive 'NHS' effectiveness of pegylated interferon and ribavirin
  - Genotype 1 SVR: 24%
  - Genotype non-1 SVR: 55%

# Quality of life at different stages of hepatitis C

(Euroqol EQ-5D scores; scale: 0 death to 1 perfect health)

Stage	source	N	Mean (SD)
Mild HCV	RCT	185	0.77(0.25)
Treatment mild HCV	RCT	80	0.66(0.32)
Post SVR	RCT	24	0.82(0.21)
Moderate HCV	Observational	71	0.66(0.21)
Cirrhosis	Observational	40	0.55(0.34)

## Mean Health service costs (£) per year at different stages of hepatitis C

Stage	source	N	Mean (SD)
Mild HCV	RCT	39	138 (170)
Treatment* mild HCV	RCT	44	7,141 (2,852)
Moderate HCV	Observational	183	717 (1,029)
cirrhosis	Observational	24	1,138 (2,479)
Decompensated Cirrhosis	Observational	64	9,121(9,610)

\*alpha interferon and ribavirin for mean of 38 weeks

# Results of cost-effectiveness analysis: Overview

- Projected results are based on the trial population
- Results are based on lifetime analysis
- Presented for “average” 40 year old trial patient
- Costs and outcomes discounted at 3.5%
- Key Assumptions tested in subsequent sensitivity analysis

# Costs per QALY gained (£)

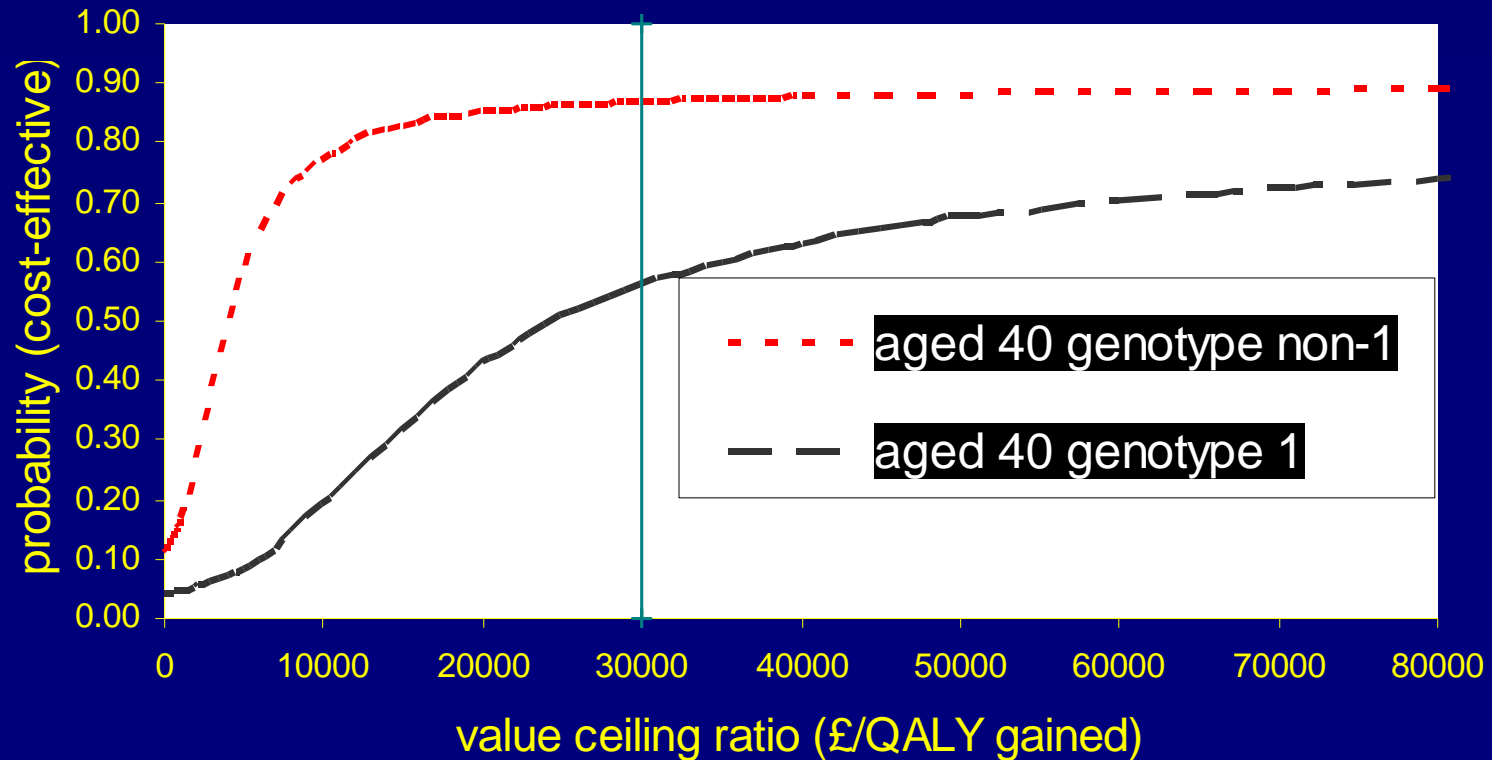
- Interferon alpha+ ribavirin at mild vs moderate stage
  - Overall £9,535 per QALY
  - genotype non-1 £4,535 per QALY
  - genotype 1 £25,188 per QALY

## Costs per QALY gained (£)

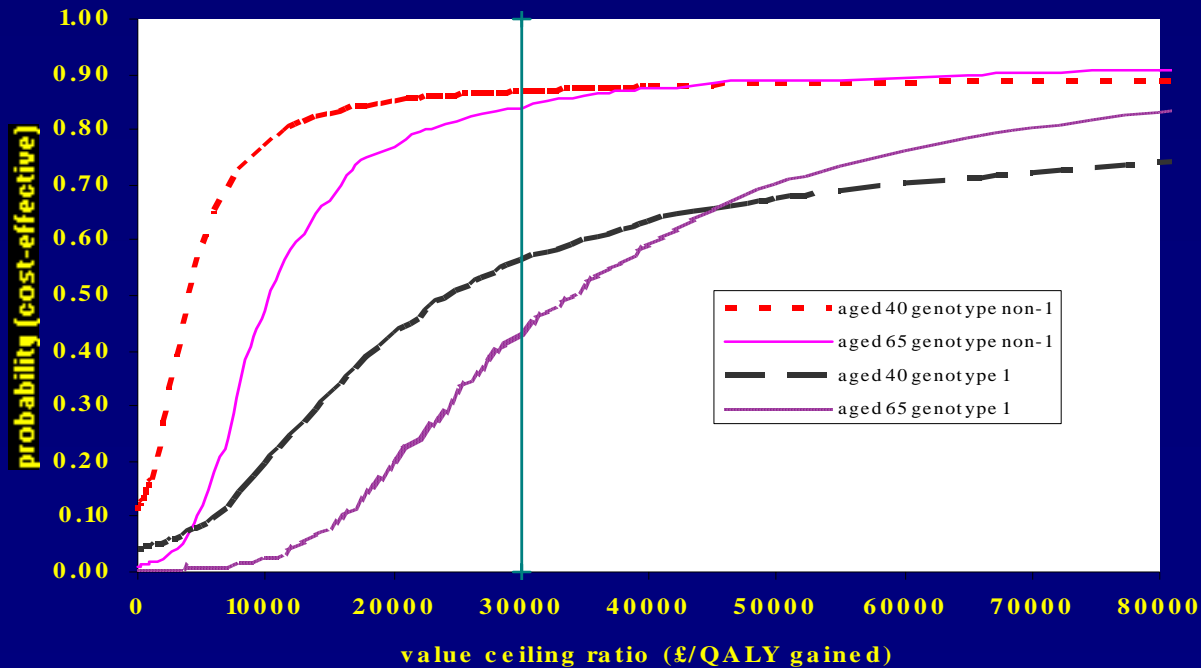
- Pegylated interferon alpha and ribavirin at mild vs moderate stage
  - genotype non-1            £7,821 per QALY
  - genotype 1                £28,409 per QALY



# Uncertainty in parameter estimates: Probabilistic sensitivity analysis



# Probabilistic sensitivity analysis by genotype and age



# Alternative scenarios: alpha interferon and ribavirin for mild HCV

Scenario	Genotype 1	Genotype non-1
Base	25,188	4,535
Viral kinetics	17,051	1,425
Transition probabilities from more gen popl'tion	36,040	6,604
Effectiveness McHutchison RCT	12,622	2,686

# Conclusions from HTA study

- Overall more cost-effective to provide antiviral treatment (either alpha or peg interferon combined with ribavirin) at a *mild* rather than a *moderate* stage
- Not cost-effective at a mild stage for older patients (>65) with genotype 1
- More conservative than previous estimates
  - Earlier stage of the disease
  - Lower estimates of disease progression
  - Lower SVRs based on pragmatic NHS RCT
  - Empirical estimates of QOL and cost

# Further areas research arising

- Which sub groups patients should have priority for antiviral treatment ?
  - Disease stage, age, genotype, co-morbidities
  - Efficiency vs equity
- How can treatment be made more cost-effective?
  - Shorter treatment regimens, nurse-led care, fewer liver biopsies
- HRQOL and cost data useful for cost-effectiveness of prevention strategies
  - How much should we invest in treatment vs prevention?