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# Prediction of HCV-related morbidity and mortality burden in France

Sylvie Deuffic-Burban  
CNRS URA 362 Lille, France

# Introduction

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- HCV burden depends on
  - Number of subjects infected with HCV
  - Stage of disease for these subjects
  - Natural history of HCV and treatment
- Difficult to measure directly
- Epidemiological data are limited
- ➔ Mathematical modeling is an useful approach

# Backcalculation method

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Age at disease diagnosis

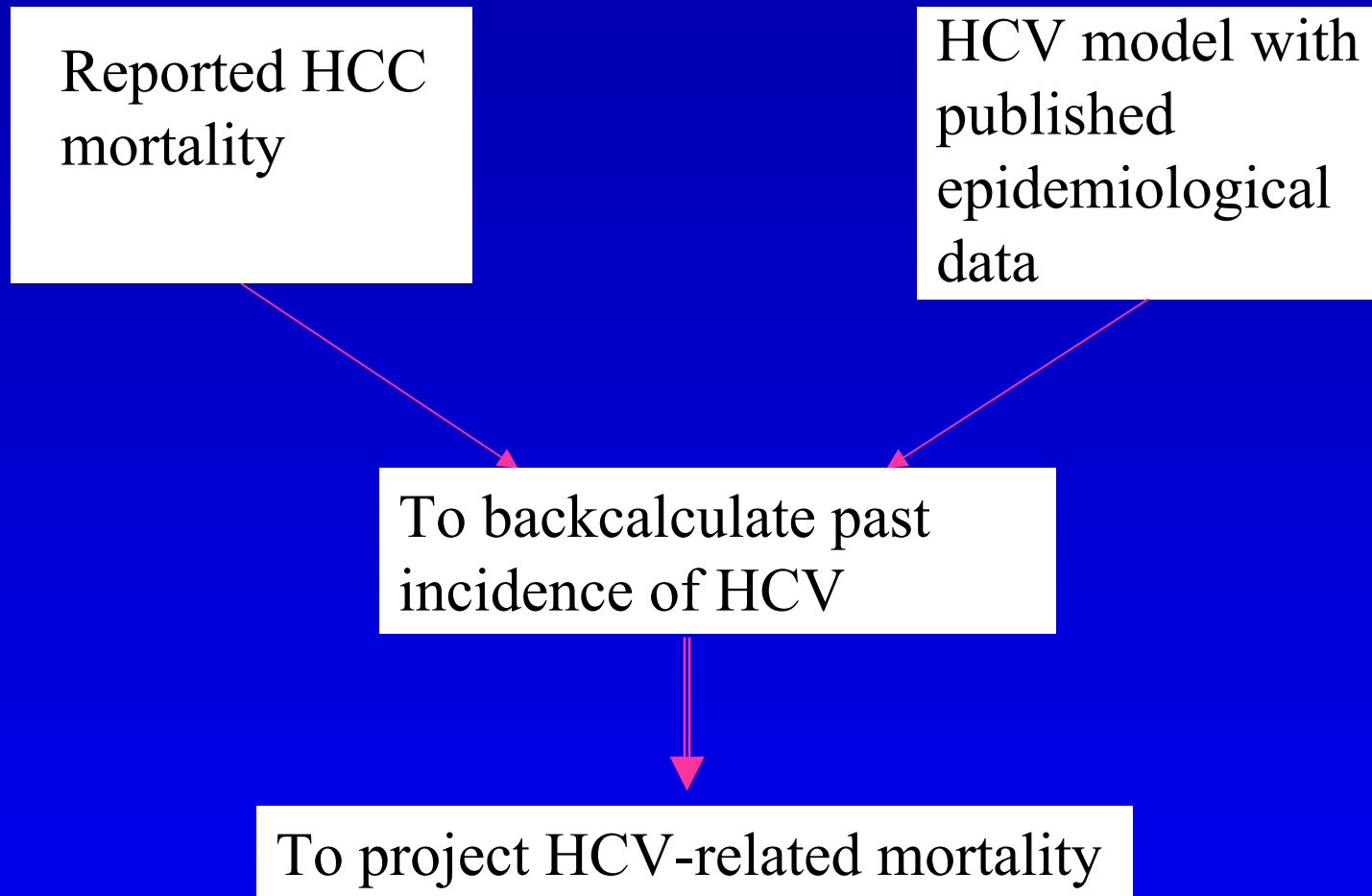
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Age at infection + Time to disease development

- Combination of
  - Existing statistics about the number of reported cases
  - Mathematical representation of the time course between infection and disease diagnosis

# HCV backcalculation

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# Process

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- **Initialization:** Set the unknown parameters to initial values
- **Estimation:** Age- and sex- stratified cohorts simulated by year through the model of HCV progression until death
- **Minimization**
  - To fit the 500,000 HCV chronic carriers in 1994, a standardization factor applied to all estimated numbers
  - Observed and predicted HCV-related deaths from HCC compared using the weighted least squares criterion
- **Iteration:** The process repeated until a minimum value of the weighted least squares criterion was obtained

# Predictions

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- Estimated parameters are used to predict
  - HCV-related deaths from HCC due to pre-1996 infections and in the absence of effective therapy (preliminary model)
  - HCV-related deaths from HCC and liver failure due to pre-1999 infections, taking into account treatment effects (updated model)

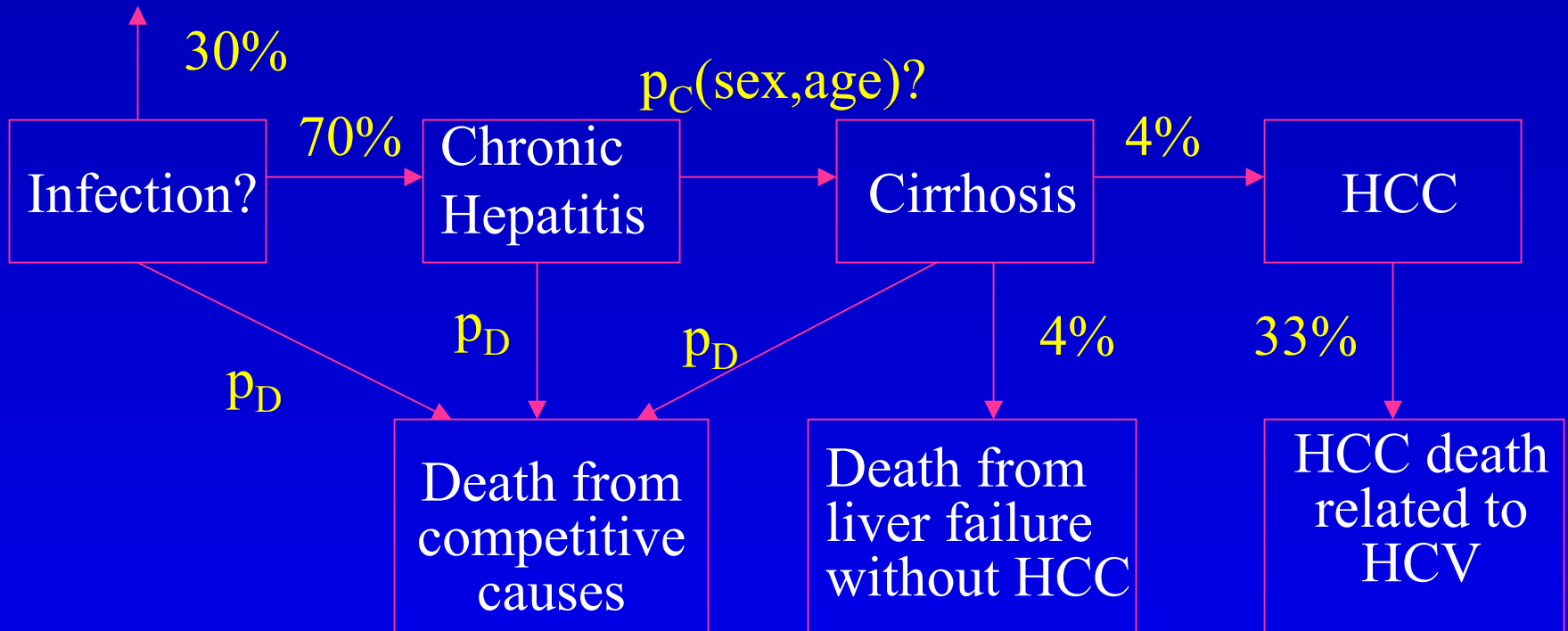
# Plan

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- 1) Preliminary HCV model (Deuffic et al, Hepatology 1999)
  - 1979-1995 data
  - No treatment
- 2) Updated HCV model (Deuffic-Burban et al, J Hepatol 2004)
  - 1979-1998 data
  - Including treatment effects

# Preliminary HCV model

Recovery from infection



# Assumptions

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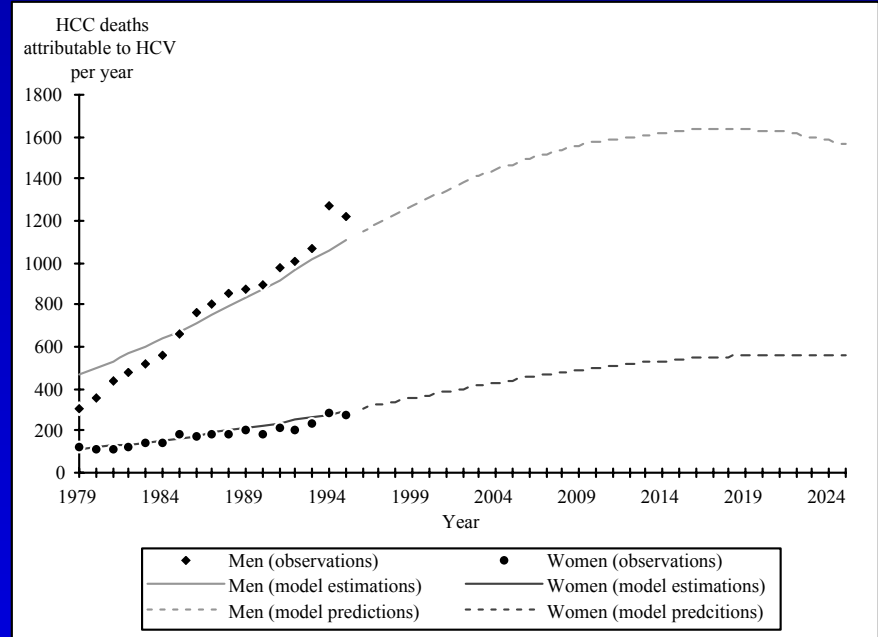
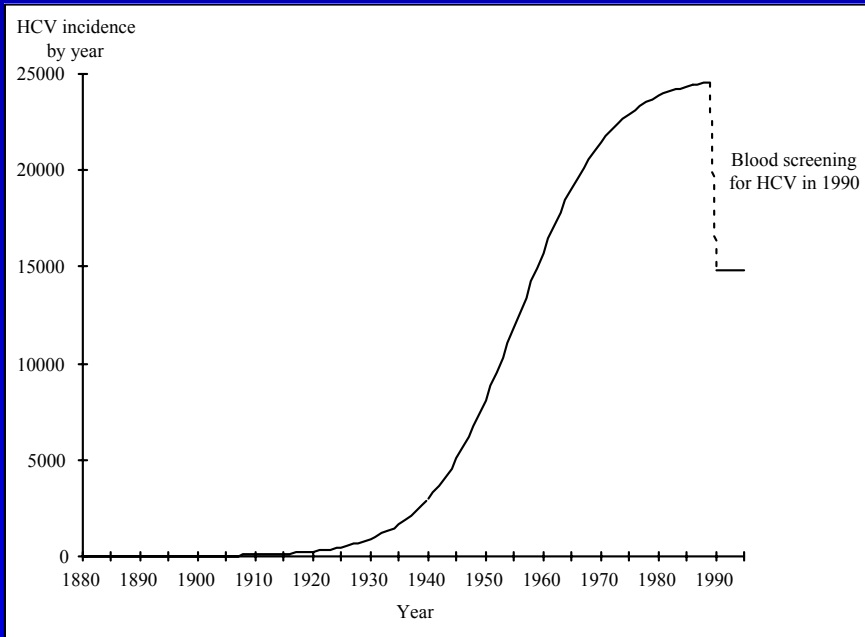
- Past incidence curve modeled by a logistic function
  - modified in 1990 by a 60%-factor to account for the screening of blood donations
- Age and sex distribution at infection obtained from three French cohorts (Poynard et al, Lancet 1997)

# HCC mortality data

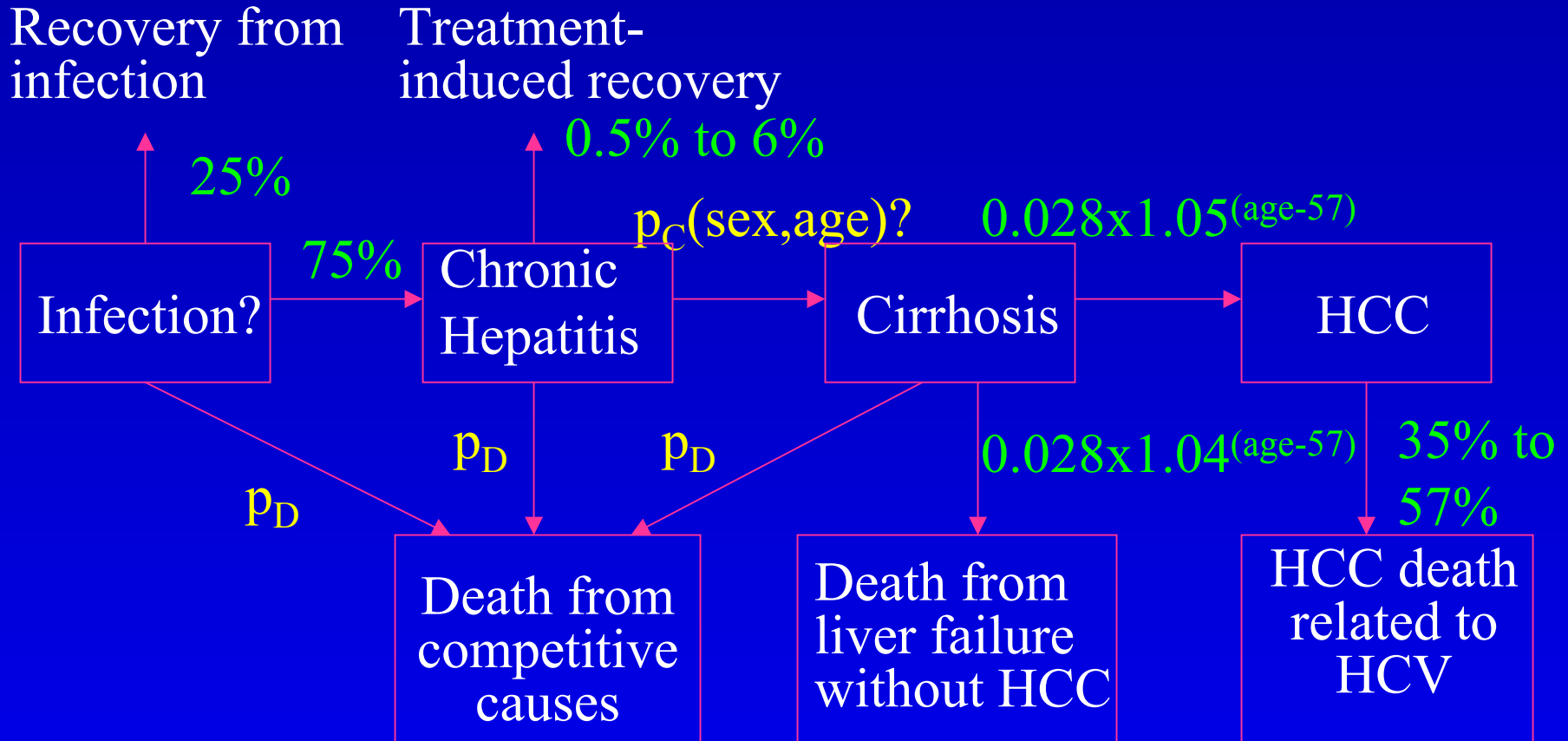
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- By age and gender, between 1979 and 1995 (French national database CeperDC)
- Assuming that 36% were attributed to HCV = weighted mean of the estimate of three studies
  - Zarski et al, J Hepatol 1991 (20%)
  - Ducreux et al, Lancet 1990 (28%)
  - Nalpas et al, J Hepatol 1991 (58%)

# Results



# Updated HCV model



# Treatment

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- Antiviral treatment effects (one-line therapy)
  - Likelihood of treatment was 5 % in 1991-1994, 10% in 1995-1998, 15% in 1999
  - Likelihood of becoming viral negative was 10% in 1991-1994, 20% in 1995-1998, 40% in 1999
- Hypothetical scenario of mass screening and treatment with PEG-IFN+RIBAVIRIN in 2001
  - 50% of treatment coverage and PVR=60%
  - 100% of treatment coverage and PVR=60%

# Assumptions

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- Past incidence curve modeled by a logistic function until 1990
  - Reduced in 1990 by a 60%-factor and constant from 1990 to 1994
  - Reduced again in 1995 by a 50%-factor and constant from 1995 to 1998
- Age and sex distribution at infection (Poynard et al, Lancet 1997)

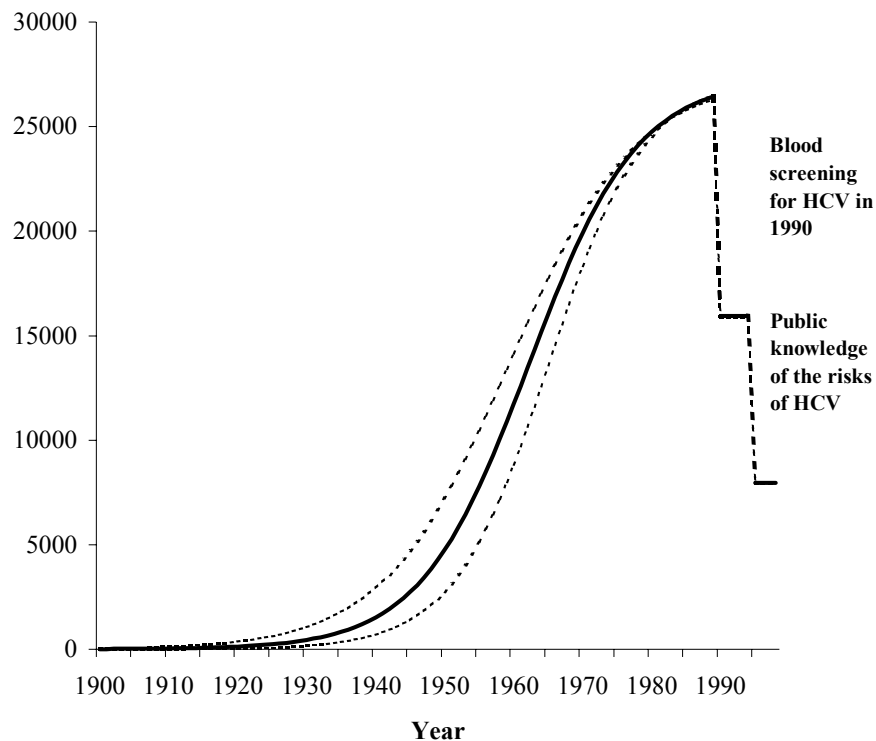
# HCC mortality data

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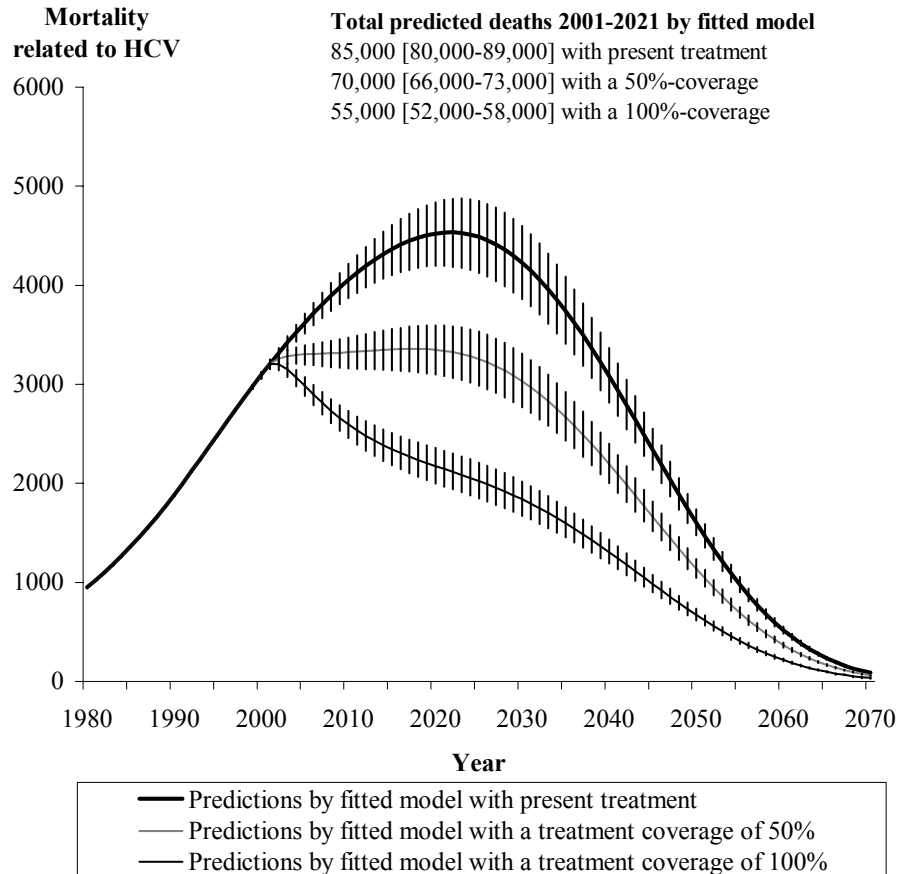
- By age and gender, between 1979 to 1998 (CepiDC)
- Assuming that 27% were attributed to HCV (Bréchet 1998)
- Sensitivity analysis
  - Constants: 15% and 40%
  - Increasing functions taking the values of 5% in 1979 and 27% in 1998: linear and exponential

# Results

**HCV incidence per year**

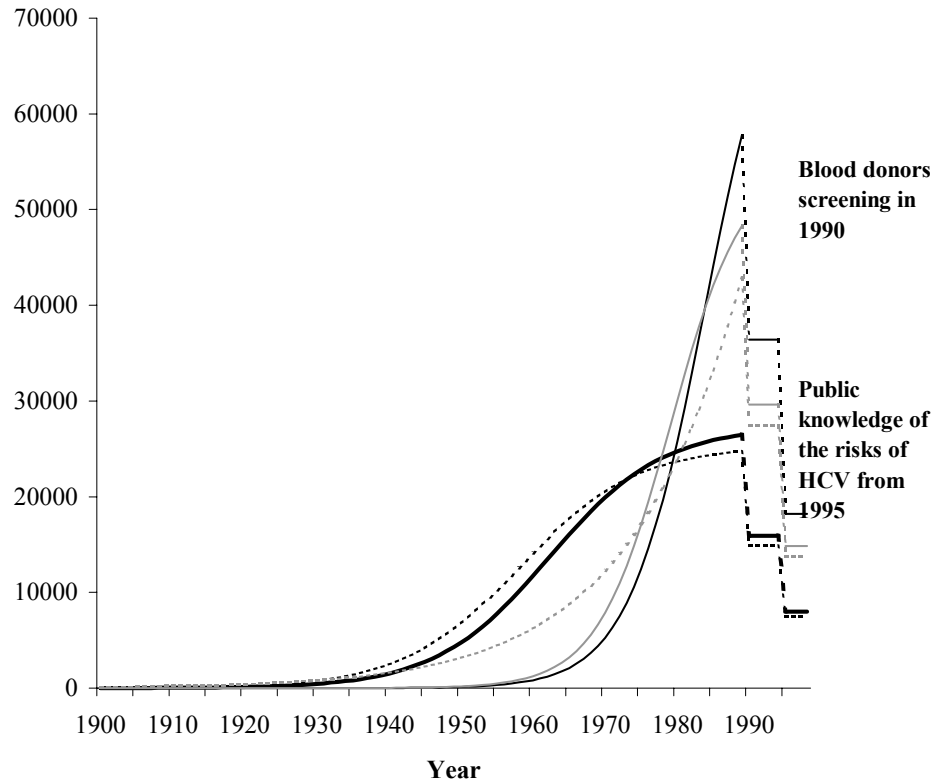


**Mortality related to HCV**

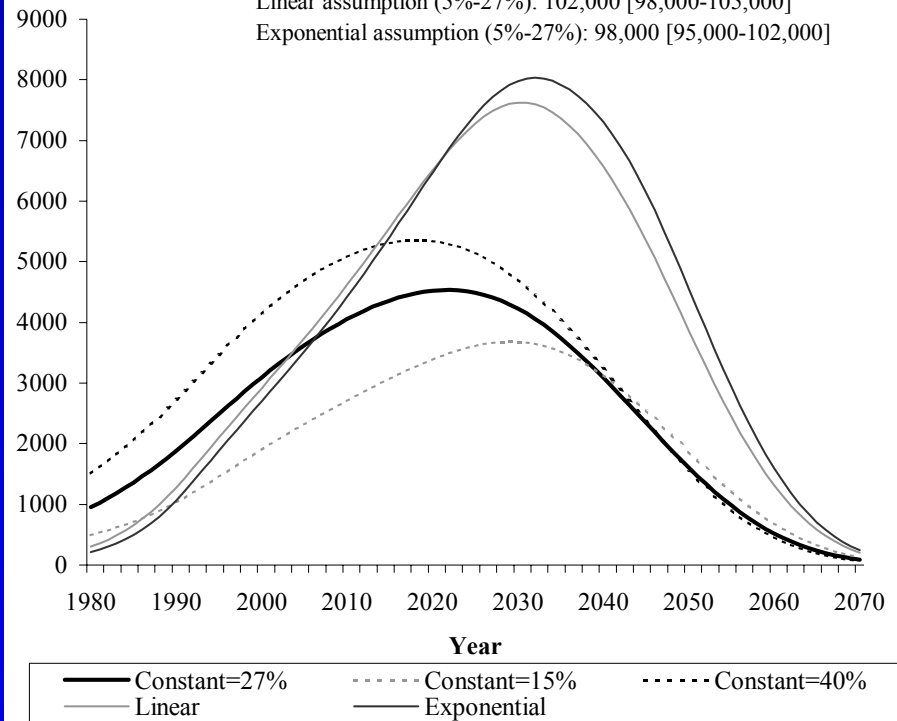


# Sensitivity analysis

**HCV incidence per year**



**Mortality related to HCV**



# Morbidity and mortality in 2002 and 2022

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- Estimates with updated model
- Two scenarios tested
  - S1: no treatment of cirrhosis
  - S2: hypothetical treatment of 100% of subjects with cirrhosis in 2002 that would cure 50% of them

# Results (Expertise Collective INSERM 2003)

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	2002	2022	
		S1	S2
Prevalence	478,000	282,000	261,000
Chronic hepatitis	431,000	234,000	234,000
Cirrhosis	45,000	45,000	26,000
HCC	2,000	2,800	1,600
HCV-related deaths	3,300	4,500	2,500

# Conclusion

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- Mathematical models provide back and future projections of HCV burden
- Projections need to be updated when new data become available
- Limitations:
  - Inadequacy or lack of data
  - Delay due to « time-modeling »