

Greenland: DANHEP: clinical hepatitis database in  
Denmark and Greenland

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# The Danish Database for Hepatitis B and C

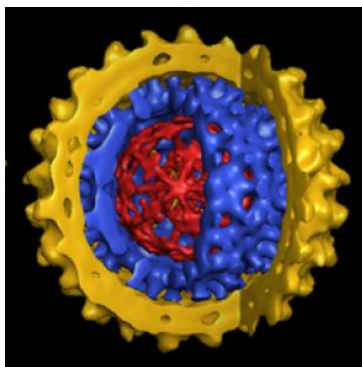
- Established in 2002
- Patients registered via Internet and Central Person Registry (CPR) number
- Approved by The Danish Regions & The Danish National Board of Health as a national, clinical database
- Biobank at Aalborg University Hospital – annual collection of blood samples
- Purpose: Clinic quality, scientific activity & participation in clinical trials

# Patients with chronic hepatitis B and C, followed at hospital departments in Denmark

- Number of patients
- Gender and age
- Mode of transmission
- Country of origin
- Hepatitis B: HBeAg & HBV DNA
- Hepatitis B: Genotypes
- Hepatitis C: Genotypes
- HIV co-infection
- Liverbiopsy
- Treatment
- Conclusion and Perspective

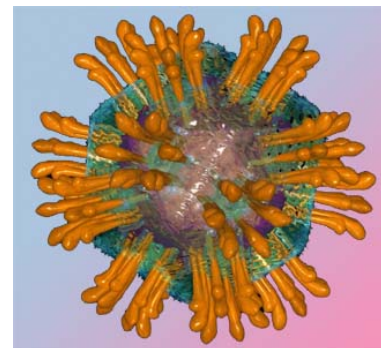
# Patients with chronic hepatitis B og C, followed at hospital departments in Denmark 2002-2009

- Chronic hepatitis B:



- 1902 patients

- Chronic hepatitis C:



- 4480 patients

Registreringsår	Hepatitis B		Hepatitis C		Hepatitis B og C		Ingen Hepatitis		I alt	
	Antal	%	Antal	%	Antal	%	Antal	%	Antal	%
<=2001	369	23.3	1140	72.1	24	1.5	49	3.1	1582	24.4
2002	124	27.9	305	68.5	4	0.9	12	2.7	445	6.9
2003	154	26.9	399	69.6	5	0.9	15	2.6	573	8.8
2004	152	27.5	382	69.2	9	1.6	9	1.6	552	8.5
2005	156	27.4	404	70.9	7	1.2	3	0.5	570	8.8
2006	170	27.3	440	70.6	4	0.6	9	1.4	623	9.6
2007	217	29.8	476	65.3	10	1.4	26	3.6	729	11.2
2008	237	35.0	414	61.1	8	1.2	19	2.8	678	10.4
2009	244	33.1	441	59.8	8	1.1	44	6.0	737	11.4
I alt	1823	28.1	4401	67.8	79	1.2	186	2.9	6489	100.0

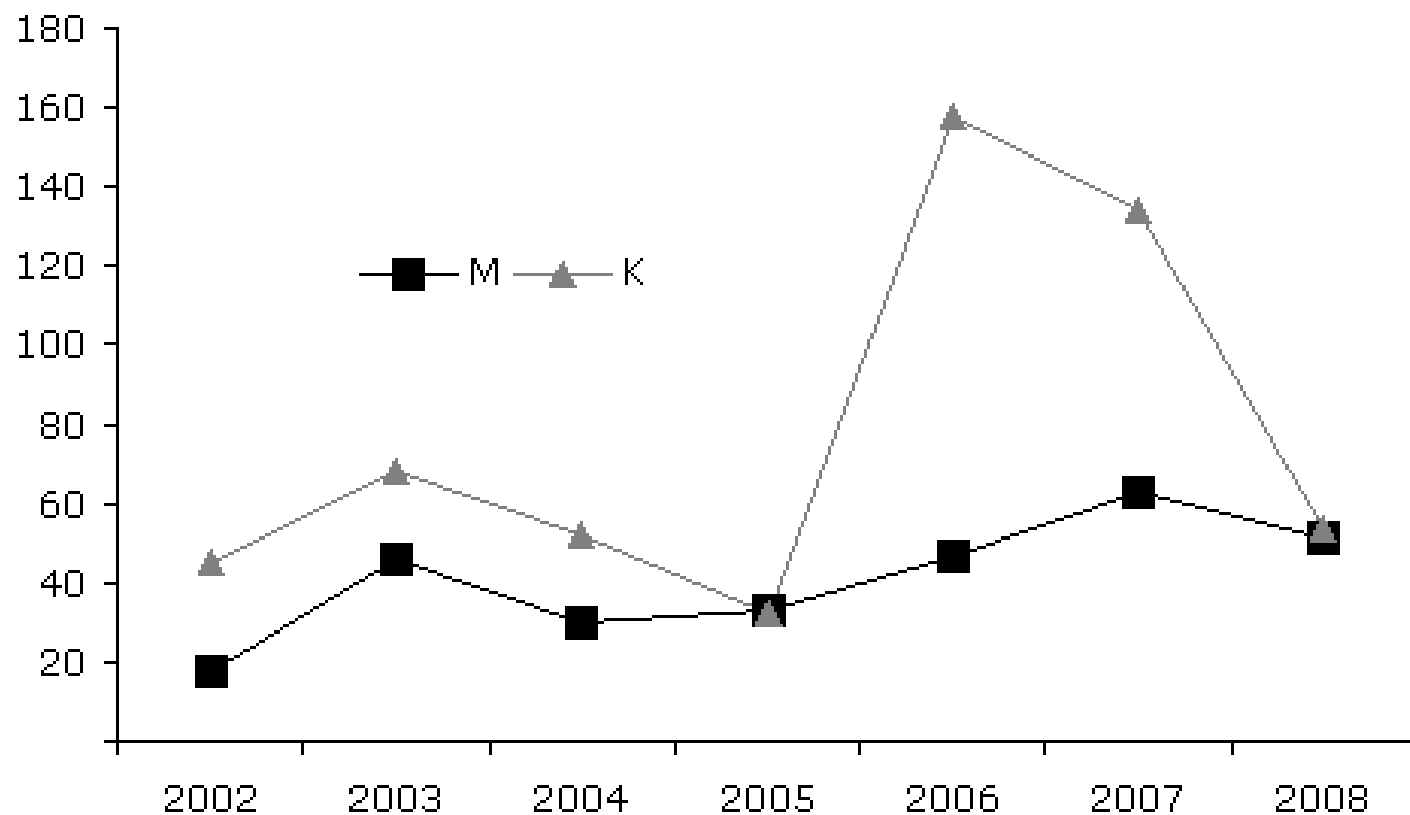
1902

4480

# Number of 20-39 year-old individuals, notified with chronic hepatitis B during 2002-2008, distributed in relation to gender

(M=males: K= females)

Figur 1. Antal 20-39-årige anmeldt med kronisk HBV-infektion i perioden 2002-2008, fordelt på køn



# Gender and Age

- **Hepatitis B**
  - Males/Females  
50%/50%
  - Median age
  - M: 37 years
  - F: 31 years
- **Hepatitis C**
  - Males/Females  
64%/36%
  - Median age
  - M: 42 years
  - F: 42 years

# Mode of Transmission

- Hepatitis B
- Vertical Transmission  
26%
- Sexual Contact 6,6%
- IVDU 5,5%
- Hepatitis C
- IVDU 61%
- Bloodtransfusion 5%
- Sexual Contact 3%



# Country of Origin

- Hepatitis B

- 20% Denmark



- 33% Asia

- 11% Turkey

- Hepatitis C

- 80% Denmark



- The rest evenly distributed between other countries

ORIGINAL ARTICLE

**HBeAg and not genotypes predicts viral load in patients with hepatitis B in Denmark: A nationwide cohort study**

HENRIK KRARUP<sup>1,5</sup>, STIG ANDERSEN<sup>2</sup>, POUL HENNING MADSEN<sup>1</sup>,  
PEER BREHM CHRISTENSEN<sup>3</sup>, ALEX LUND LAURSEN<sup>4</sup>, ANNE BENTZEN-PETERSEN<sup>1</sup>,  
JØRN M. MØLLER<sup>5</sup>, NINA WEIS<sup>6,7</sup> & THE DANHEP GROUP<sup>8</sup>

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Table I. Region of origin and distribution of age and gender among 1025 individuals of the study population.

	Total		Men		Women	
	<i>n</i> (%)	Age <sup>a</sup>	<i>n</i> (%)	Age <sup>a</sup>	<i>n</i> (%)	Age <sup>a</sup>
Origin <sup>b</sup>						
N Europe	150 (15)	45	96 (18)	47	54 (11)	40
S Europe	39 (4)	40	23 (4)	39	16 (3)	40
E Europe	33 (3)	26	20 (4)	24	13 (3)	29
Middle East	254 (25)	31	146 (27)	32	108 (22)	29
NE Asia	76 (7)	28	27 (5)	30	49 (10)	27
SE Asia	220 (21)	30	70 (13)	32	150 (30)	29
N Africa	78 (8)	32	51 (10)	32	27 (6)	32
S Africa	49 (5)	28	28 (5)	27	21 (4)	29
N America	5 (0)	50	5 (1)	50	0 (0)	Na
Unknown	121 (12)	33	68 (13)	40	53 (11)	29
Total	1025 (100)	32	534 (100)	36	491 (100)	30

<sup>a</sup>Median age, years.

<sup>b</sup>N = north; S = south; E = east. S Africa is Sub-Saharan Africa.

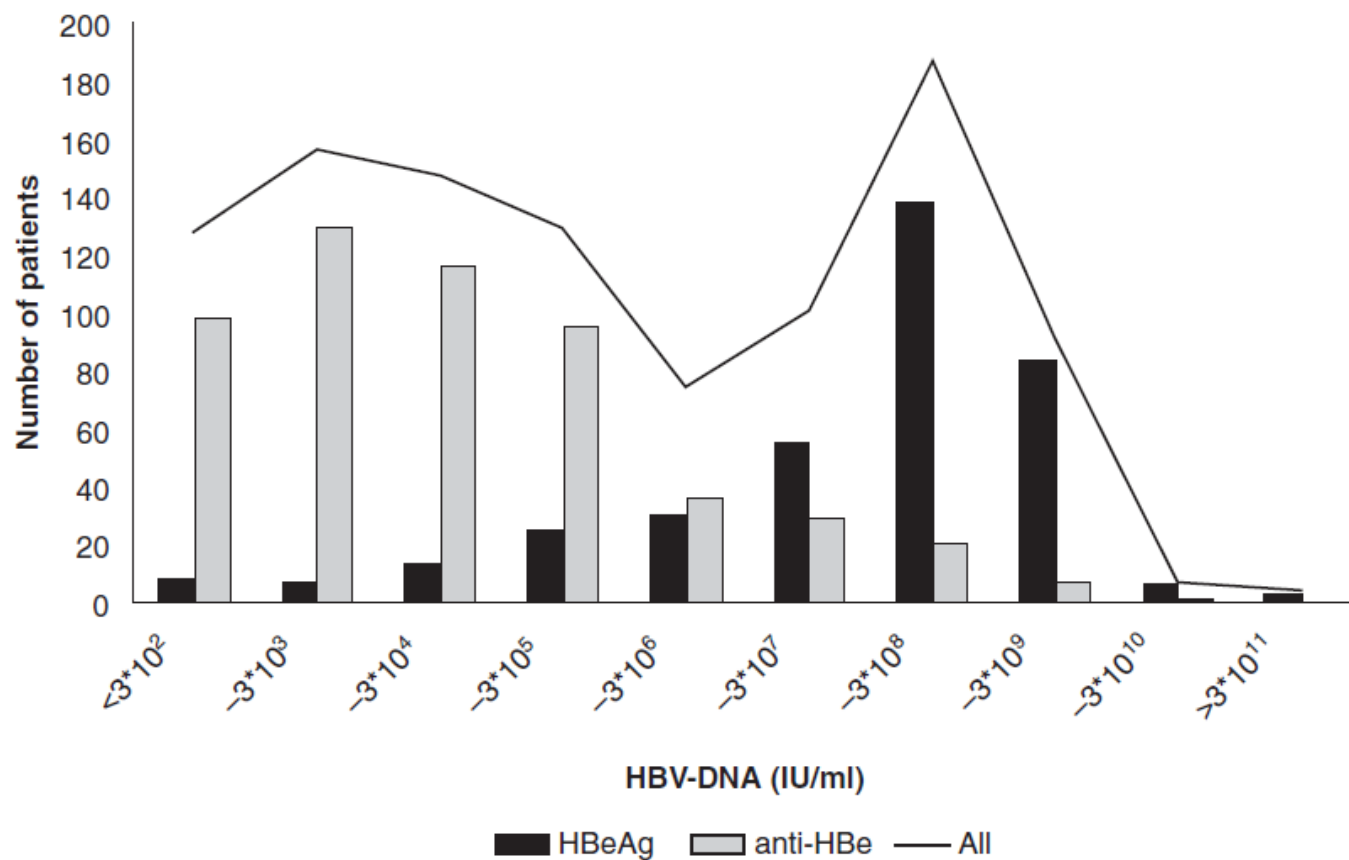
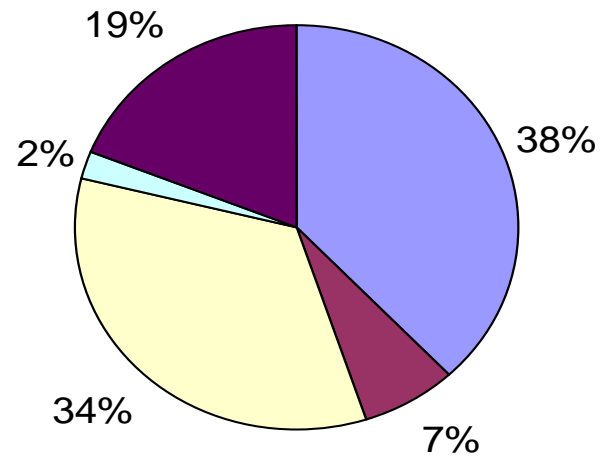


Figure 2. Distribution of viral load among 1025 patients with hepatitis B (line) and for each of anti-HBe and HBeAg positive patients (bars). Anti-HBe = antibodies against HBeAg; HBeAg = hepatitis B e antigen.

## Distribution of HCV genotypes



GT1	
GT2	
GT3	
GT4	
GT unknown	

# Hepatitis and HIV co-infection

- Hepatitis B
- 7% co-infected with HIV, but this number reduced from 12% (<2005) to 3% (2009)
- 55% HIV-negative
- 36% unknown HIV-status, but this number reduced from 44% (<2005) to 27% (2009)
- Hepatitis C
- 8% co-infected with HIV, but this number reduced from 10% (<2005) to 2% (2009)
- 68% HIV-negative
- 24% unknown HIV-status, but this number reduced from 30% (<2005) to 10% (2009)

# Liver biopsy

- Hepatitis B: 13 %
- Hepatitis C: 33 %
- Number of patients with a liver biopsy declining, due to the introduction of the Fibroscan

Fibroscanner



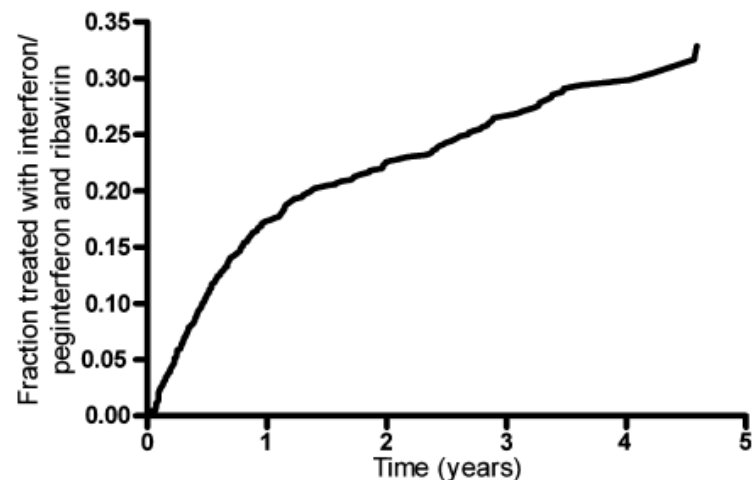
## Predictors of antiviral treatment initiation in hepatitis C virus-infected patients: a Danish cohort study

N. Hansen,<sup>1</sup> N. Obel,<sup>2</sup> P. B. Christensen,<sup>3</sup> H. Krarup,<sup>4</sup> A. L. Laursen,<sup>5</sup> M. R. Clausen,<sup>6</sup> S. Lunding,<sup>7</sup> A. Møller,<sup>8</sup> P. Schlichting,<sup>9</sup> H. Kromann-Andersen,<sup>10</sup> J. Bukh,<sup>11,12</sup> N. Weis<sup>1</sup> and the DANHEP group\* <sup>1</sup>Department of Infectious Diseases, Copenhagen University Hospital, Hvidovre, Denmark; <sup>2</sup>Department of Infectious Diseases, Copenhagen University Hospital, Rigshospitalet, Denmark; <sup>3</sup>Department of Infectious Diseases, Odense University Hospital, Denmark; <sup>4</sup>Department of Gastroenterology and Department of Clinical Biochemistry, Unit for Molecular Diagnostics, Aalborg University Hospital, Aalborg, Denmark; <sup>5</sup>Department of Infectious Diseases, Skejby University Hospital, Skejby, Denmark; <sup>6</sup>Department of Hepatology, Copenhagen University Hospital, Rigshospitalet, Denmark; <sup>7</sup>Department of Internal Medicine, Helsingør Hospital, Helsingør, Denmark; <sup>8</sup>Department of Internal Medicine, Kolding Hospital, Kolding, Denmark; <sup>9</sup>Department of Gastroenterology, Herlev University Hospital, Herlev, Denmark; <sup>10</sup>Department of Internal Medicine, Koege Hospital, Koege, Denmark; <sup>11</sup>Copenhagen Hepatitis C Program (CO-HEP), Department of Infectious Diseases and Clinical Research Centre, Copenhagen University Hospital, Hvidovre, Denmark; and Department of International Health, Immunology and Microbiology, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark; and <sup>12</sup>Hepatitis Viruses Section, LID, NIAID, NIH, Bethesda, MD, USA



**Table 1** Baseline characteristics of the 1780 HCV-infected patients included in the study

	Not treated*	Treated*
Total	1401	379
Gender		
Male	924 (66.0)	252 (66.5)
Nationality		
Denmark	1128 (80.5)	271 (71.5)
Europe (not Denmark)	91 (6.5)	52 (13.7)
Africa	34 (2.4)	8 (2.1)
America	6 (0.4)	0 (0)
Asia	33 (2.3)	9 (2.4)
Turkey or Pakistan	25 (1.8)	15 (4.0)
Middle East	40 (2.9)	14 (3.7)
Greenland	8 (0.6)	2 (0.5)
Unknown	36 (2.6)	8 (2.1)
Age		
Age <40 years at date of inclusion in DANHEP	616 (44.0)	120 (31.7)
Route of infection		
Non-IVDU	137 (9.8)	62 (16.4)
IVDU	951 (67.9)	191 (50.4)
Unknown route of infection	313 (22.3)	126 (33.2)
Genotype		
1/4 <sup>†</sup>	666 (47.6)	132 (34.8)
2/3	614 (43.8)	239 (63.1)
Unknown genotype	121 (8.6)	8 (2.1)
ALT		
Normal ALT	639 (45.6)	80 (21.1)
ALT, 2× ULN <sup>‡</sup>	434 (31.0)	135 (35.6)
ALT, 3× ULN <sup>§</sup>	262 (18.7)	262 (38.3)
Unknown ALT	66 (4.7)	19 (5.0)
HIV status		
Anti-HIV negative	949 (67.7)	271 (71.5)
Anti-HIV positive	131 (9.4)	10 (2.6)
Anti-HIV unknown	321 (22.9)	98 (25.9)
Hepatitis B status		
HBsAg-neg	1256 (89.7)	332 (87.6)
HBsAg-pos	13 (0.9)	8 (2.1)
HBsAg unknown	132 (9.4)	39 (10.3)



**Fig. 1** Cause-specific cumulative probability of treatment initiation in a 5-year period in patients diagnosed with chronic HCV infection, attending specialist departments in Denmark.

UNL, upper normal limit.

Values in parentheses are given as percentages.

\*Treatment = interferon/peginterferon monotherapy or in combination with ribavirin.

<sup>†</sup>Three patients had double infection with genotypes 2 and 3, 14 with genotypes 1 and either 2, 3 or 4.

<sup>‡</sup>2× ULN = ALT 50–99 IU/L (female), 70–139 IU/L (male).

<sup>§</sup>3× ULN = ALT ≥100 IU/L (female), ≥140 IU/L (male).

Male gender was not a significant predictor of treatment initiation, but showed a clear trend as being so, especially in the adjusted analysis (RR = 1.22, 95% CI 0.98–1.51).

Only 21 individuals were co-infected with HBV. Of these, eight (38%) were treated for chronic HCV. Patients

**Table 2** Estimated incidence rate ratio (RR) (as measure of relative risk) and 95% confidence intervals (CI) for treatment initiation for chronic HCV in Denmark, according to predictor variables

	Relative risk (95% CI) unadjusted	Relative risk (95% CI) adjusted
<b>Gender</b>		
Female	Reference	Reference
Male	1.06 (0.86–1.31)	1.22 (0.98–1.51)
<b>Nationality</b>		
Denmark	Reference	Reference
Europe (not Denmark)	2.18 (1.61–2.93)	1.68 (1.24–2.28)
Africa	0.87 (0.43–1.77)	0.67 (0.32–1.39)
America	–	–
Asia	0.97 (0.50–1.89)	0.72 (0.37–1.43)
Turkey or Pakistan	2.32 (1.38–3.91)	1.73 (1.01–3.00)
Middle East	1.37 (0.80–2.35)	1.21 (0.70–2.08)
Greenland	0.99 (0.25–3.97)	1.42 (0.35–5.85)
<b>Age</b>		
Age <40 years at inclusion in DANHEP	Reference	Reference
Age >40 years at inclusion in DANHEP	1.62 (1.30–2.01)	1.70 (1.36–2.13)
<b>Route of infection</b>		
Non-IVDU	Reference	Reference
IVDU	0.49 (0.37–0.65)	0.45 (0.32–0.62)
<b>Genotype</b>		
1 or 4	Reference	Reference
2 or 3	1.88 (1.52–2.33)	1.86 (1.49–2.31)
<b>ALT</b>		
Normal ALT	Reference	Reference
ALT 2× UNL*	2.28 (1.73–3.01)	2.17 (1.64–2.87)
ALT 3× UNL†	4.08 (3.10–5.36)	3.64 (2.75–4.81)
<b>HIV-status</b>		
Anti-HIV negative	Reference	Reference
Anti-HIV positive	0.25 (0.13–0.46)	0.28 (0.15–0.53)
<b>Hepatitis B status</b>		
HBsAg-neg	Reference	Reference
HBsAg-pos	1.92 (0.95–3.88)	2.02 (0.99–2.13)

UNL, upper normal limit.

\*2× UNL = ALT 50–99 IU/L (female), 70–139 IU/L (male).

†3× UNL = ALT ≥100 IU/L (female), ≥140 IU/L (male).

**RESEARCH ARTICLE**

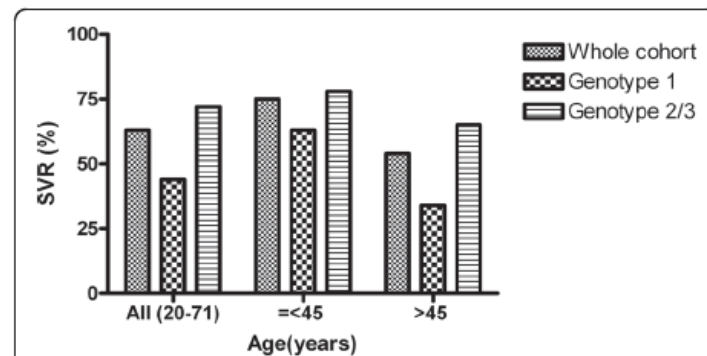
**Open Access**

# Effectiveness of treatment with pegylated interferon and ribavirin in an unselected population of patients with chronic hepatitis C: A Danish nationwide cohort study

Nanna Hansen<sup>1</sup>, Niels Obel<sup>2</sup>, Peer B Christensen<sup>3</sup>, Mette Kjær<sup>4</sup>, Alex L Laursen<sup>5</sup>, Henrik B Krarup<sup>6</sup>, Axel Møller<sup>7</sup>, Poul Schlichting<sup>8</sup>, Jens Bukh<sup>9</sup>, Nina Weis<sup>1,10\*</sup> and for the Danish Database for Hepatitis B and C (DANHEP)- group

## Conclusions

We conclude that in a routine clinical practice the treatment effectiveness of patients with chronic HCV with peginterferon and ribavirin is equivalent to the effectiveness observed in clinical trials. Furthermore, genotype 2 and 3, age  $\leq 45$  years at treatment initiation and completion of a non-modified treatment regimen is strongly associated with a sustained treatment response. Thus, our study on a nationwide Danish cohort shed new light on combination therapy of chronic HCV.



**Figure 1** Sustained virological response (SVR) as a function of age, at antiviral treatment initiation in patients with chronic hepatitis C. The figure illustrates SVR in the total cohort and SVR depending on genotype, in different age groups. In all, 274 of 432 achieved SVR. 197 patients were  $\leq 45$  years (148 achieved SVR) and 235 patients were  $> 45$  years (126 achieved SVR). Of the 133 patients with genotype 1 infection, 47 were  $\leq 45$  years (30 achieved SVR), and of the 285 genotype 2/3 infected patients, 144 were  $\leq 45$  years (113 achieved SVR).

# Conclusion and Perspectives

- DANHEP is a possible tool for registering data for patients with hepatitis; also in Greenland
- Available CPR number for all Citizens
- Requires Internet – and Manpower

# DANHEP steering committee

Nina Weis	Kim Krogsgaard	Jens Ole Nielsen
Toke Barfoed	Lone G. Madsen	Peter Nørregaard
Jens Bukh	Alex L. Laursen	Ove B. Schaffalitzky de Muckadell
Peer B Christensen	Jens Lindberg	Poul Schlichting
Mette Rye Clausen	Suzanne Lunding	Jesper Bach Hansen
Jan Gerstoft	Axel Møller	Britta Tarp
Karin Grønæk	Henrik Nielsen	Reimar W. Thomsen
Henrik Krarup		