

ADDITIONAL FILE - Included Studies

Table 1: Hepatitis C transmission in injecting drug users

Author (year)	Country	Population (n)	Follow up period	Incidence (per 100 person years)
Backmund et al (2004) ¹	US	(18)	2.8 years (mean)	4.1 (reinfection)
Cox et al (2005) ²	US	(179)	3 years (median)	27.2
Currie et al (2008) ³	US	HCV clearers	5.1 years (median)	0.49 reinfection (1.8 in continuing IDU)
Foley & Abou-Saleh (2009) ⁴	UK	(95)	1.0 year	9.1
Fuller et al (2004) ⁵	US	(114)	0.25 years (mean)	35.9
Grebely et al (2006) ⁶	Canada	(1072)	5.2 years (median)	8.1 (re-infections in 1.8)
Hahn et al (2002) ⁷	US	(195)	0.25 years (minimum)	25.1
Hallinan et al (2004) ⁸	Australia	ORT (195)	2.4 years (mean)	3.8 (1.3 in continuous ORT)
Holtzman et al (2009) ⁹	US	(1288)	1.0 year (retrospective)	11.6
Jittiwutikam et al (2006) ¹⁰	Thailand	IDU & non-IDU (515)	2.0 years	44.3 (1.9 in non-IDU)
Judd et al (2005) ¹¹	UK	(241)	1.0 year	41.8
Kim et al (2009) ¹²	Canada	(533)	≥ 0.5 years	16.9
Maher et al (2007) ¹³	Australia	(377)	≤ 3.0 years	45.8
Micallef et al (2007) ¹⁴	Australia	(423)	1.0 year (retrospective)	17.0 (re-infections in 31.0)
Page et al (2009) ¹⁵	US	(522)	≥ 0.25 years	26.7 (re-infections in 24.6)
Roy et al (2009) ¹⁶	Canada	(858)	≤ 4.0 years	15.4
Ruan et al (2007) ¹⁷	China	(333)	3.0 years	33.3
van den Berg et al (2009) ¹⁸	Netherlands	non-IDU at entry (352)	6.4 years (median)	0.049 (0.79 in IDU initiates)

Notes : **IDU** – Injecting Drug Use(r); **ORT** – Opium Replacement Therapy

Table 2: Hepatitis C transmission in various initially hepatitis C negative population groups.

Author (year)	Country	Population (n)	Follow up period	Incidence (*per 100 person years)
<u>General population:</u>				
González et al (2005) ¹⁹	Chile	(959)	≤ 7.0 years	0.02
**Grebely et al (2009) ²⁰	Canada	IDU (758)	5 years	7.4
Kondili et al (2002) ²¹	Italy	(2032)	7.0 years (median)	0.01
Mazzeo et al (2003) ²²	Italy	(1646)	10.0 years	0.05
Okayama et al (2002) ²³	Japan	(973)	11 years	0.36
<u>Haemodialysis patients:</u>				
**Di Napoli et al (2006) ²⁴	Italy	(6412)	9.0 years	2.0

Author (year)	Country	Population (n)	Follow up period	Incidence (*per 100 person years)
Furusyo et al (2001) ²⁵	Japan	(169)	6.6 years (mean)	2.6% per year
Kamagai et al (2005) ²⁶	Japan	(2114)	3.5 years	0.3
Moreira et al (2003) ²⁷	Brazil	(240)	1.0 year	3.7
Ross et al (2009) ²⁸	Germany	(1986)	1.0 year	0.0
<u>Medical procedure:</u>				
Mikhail et al (2007) ²⁹	Egypt	Endoscopy (149)	0.8 years	2.7
<u>Perinatal populations:</u>				
Mast et al (2005) ³⁰	US	Live births (244)	5.0 years	5% infants of HCV-PCR ⁺ mothers (0 in PCR ⁻); 25% HIV ⁺ mothers.
Mok et al (2005) ³¹	UK	Live births (54)	0.25 years	31% infants
Saleh et al (2008) ³²	Egypt	Mothers (2,171)	2.2 years	0.5 (post partum); 1.2 (peri-natal)
Sbebl et al (2009) ³³	Egypt	HCV ⁺ mothers (329)	3 years	2.4% infants
<u>People with HIV:</u>				
Augenbraun et al (2003) ³⁴	US	Females (1517)	3.5 years (mean)	0.3
Palacios et al (2009) ³⁵	Spain	(1231)	8.1 years (mean)	0.2
Rauch et al (2005) ³⁶	Switzerland	(3327)	4.4 years (median)	0.64 (7.4 in IDU)
<u>Men who have sex with men:</u>				
Alary et al (2005) ³⁷	Canada	(1,054)	2.5 years (mean)	0.04 (only in one IDU)
Ruan et al (2009) ³⁸	China	(507)	1.0 year	0.2
<u>Prisoners:</u>				
Champion et al (2004) ³⁹	Scotland	(307 males)	0.5 years	3.3
Christensen et al (2000) ⁴⁰	Denmark	(158 males)	0.5 years (median)	25.0
Dolan et al (2005) ⁴¹	Australia	(382 male heroin users)	4.2 years (median)	21.3
Miller et al (2009) ⁴²	Australia	(148)	0.3 years (median)	4.6

*unless otherwise indicated

** study also included in other study category

Table 3: Studies investigating the health outcomes in hepatitis C mono-infection and co-infection with other blood borne viruses.

Authors (year)	Country	Population (n)	Follow up period	Outcomes measured
<u>Hepatitis C monoinfection:</u>				
Bruno et al (2007) ⁴³	Italy	Cirrhosis patients (163)	10.7 years	HCC, mortality.
*Bruno et al (2009) ⁴⁴	Italy	Cirrhosis patients (352)	14.4 years	Progression, HCC, mortality.
Casiraghi et al (2004) ⁴⁵	Italy	Blood recipients (31)	35 years	Progression, fibrosis.

Authors (year)	Country	Population (n)	Follow up period	Outcomes measured
Delladetsima et al (2006) ⁴⁶	Greece	Renal patients (17)	7.2 years	Progression, fibrosis.
*Di Napoli et al (2006) ²⁴	Italy	Renal patients (6412)	9.0 years	Cumulative survival
Federici et al (2006) ⁴⁷	Italy	Blood disorders patients (696)	6 years	HCV, disease activity, cirrhosis, HCC.
Fong et al (2009) ⁴⁸	US	Heart transplant patients (10,630)	≤5 years (retrospective)	Survival.
Forns et al (2001) ⁴⁹	Spain	HCV patients (114)	27 years (retrospective)	Cirrhosis, HCC, survival.
Harris et al (2006) ⁵⁰	UK	Blood recipients (1,399)	16 years (lookback)	All cause & liver mortality.
Hirofumi et al (2009) ⁵¹	Japan	HCV patients (1,125)	8.2 years	All cause & liver mortality.
Hui et al (2007) ⁵²	China	HCV patients with normal ALT (82)	8.1 years	Fibrosis, disease activity.
*Ikeda et al (2009) ⁵³	Japan	Elderly HCV patients (1,917)	6 years	HCC & survival.
Jauncey et al (2004) ⁵⁴	Australia	Newly infected IDU (57)	1.8 (retrospective)	Viral clearance.
Keating et al (2005) ⁵⁵	Ireland	Newly infected IDU (289)	2 years	Viral clearance.
Kumada et al (2009) ⁵⁶	Japan	HCV patients with normal ALT (398)	8.8 years	HCC.
Martinot-Peignoux et al (2001) ⁵⁷	France	HCV patients with normal ALT (135)	3.6 years	Fibrosis, disease activity.
Miyakama et al (2009) ⁵⁸	Japan	Cirrhosis patients (132)	7.9 years	HCC.
Monica et al (2006) ⁵⁹	Italy	Elderly HCV patients (35)	10 years	HCC, liver mortality.
Nagao et al (2004) ⁶⁰	Japan	Community sample (509)	12 years	HCC, liver mortality.
Nakagawa et al (2009) ⁶¹	Japan	HCV patients (333)	9 years	HCC.
Neal et al (2007) ⁶²	UK	HCV patients (2,285)	≥ 1 year	All cause & liver mortality.
Okuda & Yokosuka (2004) ⁶³	Japan	Renal patients (189)	> 4 years	Viral activity, cirrhosis.
Pergam et al (2008) ⁶⁴	US	Obstetric patients (2,528)	To delivery	Obstetric/maternal outcome.
Persico et al (2006) ⁶⁵	Italy	HCV patients (64)	10 years	Viral activity, cirrhosis.
Posthouwer et al (2007) ⁶⁶	Netherlands	Haemophilia patients (847)	≥15 years	ESLD.
*Pradat et al (2007) ⁶⁷	**8 Euro centres	HCV patients (962)	≤7 years	Cirrhosis, HCC, liver transplant, mortality
Prasad et al (2009) ⁶⁸	Switzerland	HCV patients (1,645)	2 years	All cause mortality
Punyagupta & Siwadune (2001) ⁶⁹	Thailand	Blood recipients (38)	≤24 years	Cirrhosis, HCC, mortality.
Rumi et al (2005) ⁷⁰	Italy	HCV patients (206)	5.9 years	Disease (ALT) activity.
Sangiovanni et al (2006) ⁷¹	Sweden	HCV patients (214)	17 years	HCC, progression, mortality.
Sanyal et al (2006) ⁷²	US	HCV-cirrhosis/NASH Patients (302)	10 years	All cause & liver mortality.
Solá et al (2006) ⁷³	Spain	HCV/alcohol cirrhosis patients (377)	3.3 years	HCC, mortality & survival.
Strauss et al (2008) ⁷⁴	Sweden	HCV patients (36,126)	6.8 years	Primary liver Ca, HCC.
Tarao et al (2004) ⁷⁵	Japan	Cirrhosis patients (63)	>10 years	HCC.
Toshikuni et al (2009) ⁷⁶	Japan	HCV/alcohol cirrhosis	4.9 years	HCC, survival.

Authors (year)	Country	Population (n)	Follow up period	Outcomes measured
		Patients (227)		
Töz et al (2009) ⁷⁷	Turkey	Renal patients (197)	7.1 years	Progression, fibrosis.
Tsui et al (2007) ⁷⁸	US	Veterans (474,369)	4 years (retrospective)	HCV & ESRD.
Uto et al (2009) ⁷⁹	Japan	HCV patients (1,125)	8.2 years	All cause & liver mortality.
Wilson et al (2006) ⁸⁰	US	IDU (119)	4.2 years	Progression, fibrosis.
Wright et al (2003) ⁸¹	**8 Euro centres	HCV patients (917)	11 years	Progression, cirrhosis.
Yawn et al (2002) ⁸²	US	HCV patients (355)	10 years (retrospective)	Referral to service patterns.
<u>Hepatitis C and B</u>				
Adachi et al (2008) ⁸³	Japan	Cirrhosis patients (123)	4.4 years	HCC.
Amin et al (2006) ⁸⁴	Australia	Case notifications (117,547)	12 years	HCC, other HC related Ca.
Duberg et al (2008) ⁸⁵	Sweden	Case notifications (45,353)	≤7.9 years	All cause & liver mortality.
Fujiwara et al (2008) ⁸⁶	Japan	BBV patients (70)	3.4 years	Fibrosis rate.
*Gannon et al (2009) ⁸⁷	US	BBV patients (10,263)	≤5.0 years	HCC, survival
Ikeda et al (2003) ⁸⁸	Japan	Cirrhosis patients (892)	7.5 years	HCC, survival and Ca treatment outcome.
*Ikeda et al (2007) ⁸⁹	Japan	BBV patients HBV ^{+/-} (846)	8.5 years	HCC.
Inoue et al (2009) ⁹⁰	Japan	Community sample (17,590)	12.7 years	HCC.
Mori et al (2000) ⁹¹	Japan	Community sample (3,059)	4.8 years	HCC, viral/lifestyle factors.
Sasaki et al (2006) ⁹²	Japan	HCC post-surgery (417)	≤0.9 years	Survival, HCC recurrence
Sun et al (2003) ⁹³	Taiwan	Community sample males (12,008)	9.2 years	HCC.
Tanaka et al (2004) ⁹⁴	Japan	Blood donors (1,927)	8.3 years	HCC.
Tanaka et al (2006) ⁹⁵	Japan	HCV+ community sample (74)	12 years	HCC.
Wang et al (2007) ⁹⁶	Taiwan	Community sample (4,958)	7 years	Diabetes Type 2.
Zampino et al (2009) ⁹⁷	Italy	BBV patients (54)	23 years	HCC & cirrhosis.
<u>Hepatitis C and HIV</u>				
Anderson et al (2006) ⁹⁸	US	HIV patients (970)	4 years	Survival to AIDS, death.
Cheng et al (2007) ⁹⁹	US	HIV patients with Alcohol problems (396)	3.5 years	HCV impact on CD4 count
García-García et al (2006) ¹⁰⁰	Spain	Cirrhosis patients (1,217)	1.1 years	HCC.
Giordano et al (2004) ¹⁰¹	US	HCV/ HIV patients (16,439)	10 years	HCC.
Grebel et al (2007) ¹⁰²	Canada	Community sample	6 years	HCV clearance, persistence

Authors (year)	Country	Population (n)	Follow up period	Outcomes measured
		(3,553)		
Hansen et al (2009) ¹⁰³	Denmark	HCV patients (1,780)	5 years (retrospective)	HCV treatment uptake.
Lumbreras et al (2006) ¹⁰⁴	Spain	IDU (3,247)	≤12 years	All cause mortality.
Merchante et al (2006) ¹⁰⁵	Spain	ESLD patients (153)	1.1 years	Decompensation, survival
Penida et al (2009) ¹⁰⁶	Spain	Cirrhosis patients (154)	3.0 years	Liver failure, liver mortality
Smit et al (2008) ¹⁰⁷	Netherlands	IDU (1,295)	≤11 years	Liver & all cause mortality.
Weis et al (2006) ¹⁰⁸	Denmark	HIV patients (2,734)	≤9 years	AIDS & all cause mortality.
<u>Hepatitis C, B and HIV</u>				
Bonacini et al (2004) ¹⁰⁹	US	HIV patients (472)	1.5 years	Liver mortality & HIV progression
Melendez-Morales et al (2007) ¹¹⁰	US	Haemophilia patients (478)	3.0 years	HCV clearance in HIV, HBV

* study also included in other study category

** cohort drawn from 'HENCORE' clinical database

Abbreviations: ALT – alanine aminotransferase; BBV – Blood Borne Virus (es); Ca – cancer; ESLD – end stage liver disease; ESRD – end stage renal disease; HCC – hepatocellular carcinoma; HCV – hepatitis C virus; HBV – hepatitis B virus; IDU – injecting drug user; NASH – non alcoholic steatohepatitis

Table 4: Health related quality of life associated with antiviral treatment

Author (year)	Country	Study period (n)	Main measures	Outcomes
*Bonkovsky et al (2007) ¹¹¹	US	72 weeks (1,144) [all cirrhosis]	HR-QoL (SF-36)	Decreased QoL at baseline associated with histology severity & depression; improved post Tx if SVR.
*Dan et al (2006) ¹¹²	US	72 weeks (271)	HR-QoL (SF-36)	Decreased SF-36 scores during Tx: associated with depression.
*Dan et al (2007) ¹¹³	US	72 weeks (87)	HR-QoL (SF-36), anger (STAEI)	Increasing anger during Tx: associated with depression & ↓HR-QoL.
Evon et al (2009) ¹¹⁴	US	72 weeks (114)	Depression (CES-D scale) social support (MOS)	12% depressed at baseline: most likely to exit early; low social support associated with new onset depression.
*Falasca et al (2009) ¹¹⁵	Italy	Pre-post (18)	HR-QoL (SF-12), depression (BDI)	BDI unchanged, but SF-12 improved.
*Hollander et al (2002) ¹¹⁶	Sweden	Pre-post (147)	HR-QoL (SF-36), Depression (CESD)	Baseline SF-36 reduced, reducing more in Tx, improving post Tx (best in SVR).
*McHutchison et al (2001) ¹¹⁷	US	Pre-post (905)	HR-QoL (SF-36),	Baseline SF-36 reduced, improved in SVR (predicted by ALT, viral load, improved histology).
*Şahingöz et al (2009) ¹¹⁸	Turkey	Pre-post (36)	HR-QoL (WHOQOL-BREF), anxiety (HARS), depression (HDRS)	High incidence of depression during IFN, associated with anxiety & reduced QoL

* study also included in other study category

Abbreviations: BDI – Beck's Depression Inventory; CESD – Center for Epidemiological Studies Depression scale; HARS – Hamilton Anxiety Rating Scale; HCV – hepatitis C virus; HBV – hepatitis B virus; HDRS – Hamilton Depression Rating Scale; IDU – injection drug use; NVR – non viral response; HR-QoL – health related quality of life; SF-36 (or 12) – Short Form 36 (or 12); STAEI – State-Trait Anger Expression Inventory; SVR – sustained viral response; Tx – treatment; WHOQOL-BREF – World Health Organisation Quality Of Life assessment.

Table 5: Studies investigating the health outcomes after treatment.

Authors (year)	Country	Population (n)	Follow up period	Treatment outcome
<u>Hepatitis C monoinfection:</u>				
Bruggmen et al (2008) ¹¹⁹	Switzerland	IDU/nonIDU (500)	0.5 years	SVR 64% in both.
*Bruno et al (2009) ⁴⁴	Italy	Cirrhosis (352)	14.4 years	Tx → did not improve clinical outcome
Chavalitdhamrong & Tanwandee (2006) ¹²⁰	Thailand	Post SVR (171)	3 years	No relapse, 1 HCC in baseline cirrhosis
Dalgard et al (2002) ¹²¹	Norway	IDU/nonIDU post SVR (45)	5.3 years	No relapse, 1 IDU reinfected
Everhart et al (2009) ¹²²	US	Cirrhotic NVR (985)	3.8 years (retrospective)	50% long-term tx , increase progression in high BMI
Goodman et al (2009) ¹²³	US	NVR (535)	≤5 years	non-linear fibrosis (21-80%)
*Grebely et al (2009) ²⁰	Canada	High prevalence population (1,445)	5 years	1% tx uptake in HCV ⁺ →(SVR in 20%).
Ikeda et al (2005) ¹²⁴	Japan	Post SVR (1,056)	≥1 year	29 HCC (in med. 4.6 years)
*Ikeda et al (2009) ⁵³	Japan	Elderly (1,917)	6 years	HCC: Tx 11%; un-Tx 20%
Imazeki et al (2003) ¹²⁵	Japan	Treated/untreated (459)	8.2 years	SVR 80% fewer deaths.
Kobayashi et al (2007) ¹²⁶	Japan	Treated (1,124)	5.5 years	SVR 33%, HCC 6% (3.5% SVR)
Manesis et al (2009) ¹²⁷	Greece	Treated/untreated (1,738)	3.9 years (retrospective)	SVR 45%, HCC in 1.4% (lower in SVR)
Okanoue et al (2005) ¹²⁸	Japan	HCV (1,246)	7.7 years	13% HCC: ↑ in non- SVR
*Pradat et al (2007) ⁶⁷	**8 Euro centres	HCV (962)	≤7 years	SVR 25%, HCC 0.2 & death /transplant 0.4 /100 person years associated with NVR
Veldt et al (2007) ¹²⁹	Canada	Treated (479)	2.1 years	SVR 30%, 1/82 adverse outcomes in SVR
<u>Co-infection</u>				
De Bona et al (2007) ¹³⁰	Italy	HIV/HCV cirrhosis (50)	4.5 years	progression in NVR16% vs 52% un-treated
*Ikeda et al (2007) ⁸⁹	Japan	HBV/HCC	8.5 years	Tx response 41%: HCC only in HBV/HCV (11%)
Scott et al (2009) ¹³¹	US	HIV/HCV (248)	4.4 years	Tx evaluation 44% (Tx 16%)
Zinkernagel et al (2006) ¹³²	Switzerland	HIV/HCV treated (160)	0.5 years	SVR 28:52% (type 1/4:2/3)
<u>Liver transplant</u>				
Ananthakrishnan & Saeian (2008) ¹³³	US	various liver diseases (13,855)	2 years	Lower survival in HCV
Bizollon et al (2005) ¹³⁴	France	SVR/NVR (80)	4.8 years	SVR → ↑ graft survival
*Feurer et al (2002) ¹³⁵	US	HCV ⁺ / (75)	3 years	HCV recurrence in 10%, → ↓ functional performance
Gallegos-Orozco et al (2009) ¹³⁶	US	HCV	7 years (retrospective)	med. survival 3.5 years
*Gannon et al (2009) ⁸⁷	US	HBV & HCV (10,263)	≤5.0 years	HCC screen → ↑ survival post transplant

Authors (year)	Country	Population (n)	Follow up period	Treatment outcome
Hong et al (2008) ¹³⁷	Canada	HCV ^{+/} (1,842)	5 years	↓ 2 & 5 year survival in HCV
Selzner et al (2009) ¹³⁸	Canada	HCV ^{+/} (822)	5 years	↓ 2 & 5 year survival in HCV & increasing age
Takada et al (2006) ¹³⁹	Japan	HCV (91)	2.1 years	69% 5-yr survival in living donors
Verna et al (2009) ¹⁴⁰	US	HCV ^{+/} (709)	3.4 years	Biliary complications 22%; ↓ 1-year survival in HCV

* study also included in other study category

** cohort drawn from 'HENCORE' clinical database

Abbreviations: ALT – alanine aminotransferase; Ca – cancer; ESLD – end stage liver disease; ESRD – end stage renal disease; HCC – hepatocellular carcinoma; HCV – hepatitis C virus; HBV – hepatitis B virus; IDU – injection drug use; NVR – non viral response; SVR – sustained viral response; Tx - treatment

Table 6: Health related quality of life in untreated chronic hepatitis C infection.

Authors (year)	Country	Population (n)	Main QoL measures	Outcomes
<u>Community and clinic populations:</u>				
Bailey et al (2009) ¹⁴¹	US	Clinic patients (135)	HR-QoL (adapted SF-36 & Cantrils Ladder); Depression (CESDS); illness uncertainty (MUIS)	Mod-high QoL, mild fatigue low depression - uncertainty main impact on QoL.
Balfour et al (2006) ¹⁴²	Italy	Clinic patients (123)	HR-QoL (SF-36); Depression (CESDC)	62% depressed; low QoL particularly in smokers.
Batista-Neves (2009) ¹⁴³	Brazil	Clinic patients (90)	HR-QoL (SF-36); Psych. diagnoses (MINI-Plus)	49% at least 1 psych. disorder; main association with reduced QoL
Coughlan et al (2002) ¹⁴⁴	Ireland	Female, medically acquired (93)	HR-QoL (SF-36, GHQ-30); mental health (HADS & SCAN)	High level psychological distress & reduced QoL not related to viraemia or liver histology.
Danoff et al (2006) ¹⁴⁵	US	Male, HCV ^{+/} (351)	HR-QoL (SF-36); depression (BDI); sexual function (BMSFI)	Reduced QoL in HCV - associated with sexual dysfunction (but not depression).
Gallegos-Orozco et al (2003) ¹⁴⁶	Mexico	Clinic patients (157)	HR-QoL (SF-36); depression (ZDS)	Reduced QoL in HCV, lower in low HCV knowledge.
*Gifford et al (2003) ¹⁴⁷	Australia	HCV ⁺ females (462)	HR-QoL (SF-12)	Reduced QoL in HCV, relative to Australian norms.
*Gifford et al (2005) ¹⁴⁸	Australia	HCV ⁺ males (308)	HR-QoL (SF-12)	Reduced QoL in HCV, relative to Australian norms.
Gunasekera et al (2008) ¹⁴⁹	Australia	Rural clinic patients (80)	HR-QoL (SF-36)	Reduced QoL in HCV, lower in Drug & Alcohol clinics (same as city HCV patients).
Häuser et al (2004) ¹⁵⁰	Germany	Clinic patients (88)	HR-QoL (SF-36, CLDQ), mental health (HADS)	Reduced HRQoL in HCV, associated with mental health & comorbidities (not viral infection).
Helbling et al (2008) ¹⁵¹	Switzerland	Clinic patients (833)	HR-QoL (SF-36); Anxiety (HADS);	Reduced QoL in HCV, due to host & environment not viral factors.

Authors (year)	Country	Population (n)	Main QoL measures	Outcomes
Hickey et al (2008) ¹⁵²	Ireland	HCV ^{+/} females (236)	HR-QoL (SEIQoL-DW); Anxiety & depression (HADS); symptoms (IPQ)	More symptoms, anxiety & depression in medically acquired HCV – but no differences in QoL
Hussain et al (2001) ¹⁵³	US	Clinic patients (220)	HR-QoL (SF-36)	Reduced QoL in HCV, ALT or drug & alcohol not associated.
Kallman et al (2006) ¹⁵⁴	US	HCV ^{+/} (191)	HR-QoL (SF-36, CLDQ); fatigue (CFS)	Very reduced QoL in HCV, fatigue most important contributor to ↓ QoL.
*Kang et al (2005) ¹⁵⁵	Taiwan	HCV ^{+/} (560)	HR-QoL (SF-36)	Reduced QoL in HCV.
Kramer et al (2002) ¹⁵⁶	Austria	Clinic patients (100)	HR-QoL (SF-36); fatigue (FIS) & neuro-cognitive function	Significantly reduced QoL relative to population norms. Slight but significant neuro-cognitive impairment in HCV not associated with disease activity, fatigue or QoL
Kramer et al (2005) ¹⁵⁷	Austria	Clinic patients (120)	HR-QoL (SF-36); fatigue (FIS) & neuro-cognitive function	Significant fatigue in HCV independently associated with reduced QoL, but not with brain dysfunction
Kwan et al (2006) ¹⁵⁸	US	Male, HCV ^{+/} (3,023)	HR-QoL (SF-36)	Reduced QoL in HCV, independent of medical/psych. comorbidities.
Lim et al (2006) ¹⁵⁹	US	Male, HCV ^{+/} (3,023)	HR-QoL (SF-36)	Reduced QoL in HCV, predicted by depression & post-traumatic stress.
Mikocka-Walus et al (2008) ¹⁶⁰	Australia	HCV ^{+/} gastro. patients (139)	HR-QoL (SF-12); anxiety & depression (HADS); psychology (SCL090)	Reduced QoL in all patients, higher prevalence depression and comorbid psychological conditions in HCV
Miller et al (2001) ¹⁶¹	Australia	Clinic patients (95)	HR-QoL (SF-36); social support (SSM)	Reduced QoL in HCV, ALT & social support not related, social stigma common.
Moyer et al (2007) ¹⁶²	Canada	Clinic patients (123)	HR-QoL (SF-36); comorbidities (BSI)	Reduced QoL in HCV, lower in pessimistic persons.
Pojoga et al (2004) ¹⁶³	Italy	HCV ^{+/} (102)	HR-QoL (adapted SF-36)	Reduced QoL in HCV, ALT not related.
Rowan et al (2005) ¹⁶⁴	US	Clinic patients (62)	HR-QoL (SF-36, CLDQ); psychosocial (SCID-CV; BDI; BAI; abbreviated CM; SSM)	Reduced QoL in HCV, not related to clinical/viral/substance use/psych. disorder.
Schwarzinger et al (2004) ¹⁶⁵	Egypt	HCV ^{+/} (1,282)	HR-QoL (SF-12)	No difference in QoL or ALT – not aware of HCV status.
Teixeira et al (2006) ¹⁶⁶	Brazil	Blood donors (120)	HR-QoL (SF-12)	Reduced QoL in for all stages HCV, not related to lifestyle/demographic factor except female sex.
Teuber et al (2008) ¹⁶⁷	Germany	Clinic patients (123)	HR-QoL (SF-36);	Reduced QoL associated with

Authors (year)	Country	Population (n)	Main QoL measures	Outcomes
von Wagner et al (2009) ¹⁶⁸	Germany	HCV ⁺ / (165)	fatigue (FIS) HR-QoL (ELQ); psycho-emotional health (PMS)	fatigue and fibrosis. Reduced QoL in HCV, inc- reased anger & depression, not related to ALT.
<u>Former or current IDU:</u>				
Dalgard et al (2004) ¹⁶⁹	Norway	Current IDU (199)	HR-QoL (SF-36)	Reduced QoL associated with HCV status awareness, heroin use, female sex.
Gjeruldsen et al (2006) ¹⁷⁰	Norway	HCV ⁺ /non IDU-HCV ⁻ (68)	HR-QoL (SF-36)	Reduced QoL in HCV, relat- ed to drug use & marital status.
<u>Viral co-infections:</u>				
Baum et al (2008) ¹⁷¹	US	HIV mono- & co- infected drug users (192)	HR-QoL (SQLI)	Reduced QoL in HCV-HIV co-infection, related to dep- ression, ↑symptoms, ↑ health care utilisation, low HCV Tx access.
Braitstein (2005) ¹⁷²	Canada	HIV mono & co-infected (484)	HR-QoL (MOS-SF); mental health (CESD)	Reduced QoL in HCV-HIV most due to drug use & SE factors.
Fleming et al (2004) ¹⁷³	US	HIV & HCV mono- & co-infected (299)	HR-QoL (HQLQ)	Reduced QoL but similar across groups, predicted by IDU, psych illness,unemploy- ment.
Ozkan et al (2006) ¹⁷⁴	Turkey	HBV or HCV (107)	HR-QoL (SF-36); mental health (SCID-CV)	Reduced QoL in HCV & HBV, psych. morbidity associated.
Svrtlih et al (2008) ¹⁷⁵	Serbia	Inpatient HBV or HCV (227)	HR-QoL (SF-12)	Reduced QoL in HCV & HBV, cirrhosis associated.
Thein et al (2007) ¹⁷⁶	Australia	HIV & HCV mono- & co-/un-infected (94)	HR-QoL (HQLQ); mood (DASS); cognit- ive function (NART, TMT)	Little differences btwn HCV & HIV/HCV, but some in HIV/HCV vs controls.
Tsui et al (2007) ¹⁷⁷	US	HIV ⁺ homeless (216)	HR-QoL (SF-36)	Reduced QoL overall, lower physical health scores in HCV/HIV co-infection
<u>Various stages of disease progression:</u>				
Björnsson et al (2009) ¹⁷⁸	Sweden	HCV ⁺ / (472)	HR-QoL (SF-36, EQ _{index})	Impaired QoL in HCV, relat- ed to liver disease severity.
Chong et al (2003) ¹⁷⁹	Canada	HCV patients (193)	HR-QoL (SF-36, EQ _{index} , HUI)	Reduced QoL in HCV, small differences related to disease severity (ALT not related).
Córdoba et al (2003) ¹⁸⁰	Spain	HCV patients (120)	HR-QoL (SF-36); mental health (BDI,STAI) neuropsychology (AVL)	Reduced QoL unrelated to cognitive function, lower in severe disease (beta blockers, diuretics implicated).
Hsu et al (2009) ¹⁸¹	Canada	HCV patients (271)	HR-QoL (HQLQ, HUI, TTO)	Reduced QoL partially due to to disease severity, QoL ass- ociated with comorbidity & SE and marital status.

Authors (year)	Country	Population (n)	Main QoL measures	Outcomes
<u>Comorbidities:</u>				
Asfar et al (2009a) ¹⁸²	Turkey	HCV ⁺ / haemodialysis patients (165)	HR-QoL (SF-36); depression (BDI)	Reduced QoL in HCV ⁺ dialysis patients vs HCV ⁻
Asfar et al (2009b) ¹⁸³	Turkey	HCV ⁺ haemodialysis patients with HCV (32)	HR-QoL (SF-36); depression (BDI)	QoL not related to liver, but lower in depression, anaemia, malnutrition.
Posthouwer et al (2005) ¹⁸⁴	Netherlands	Haemophilia (602)	HR-QoL (SF-36)	Reduced QoL in HCV, independent of age, HIV, severity of haemophilia.
Marcellin et al (2007) ¹⁸⁵	France	115 HIV-HCV coinfect- ed patients	HR-QoL (WHOQOL- HIV Bref), depression (CES-D), fatigue (FIS)	Fatigue and depression account for the majority of variance in QoL scores noted. Fatigue associated with impaired physical QoL and social relationships, depression associated with lower environmental QoL (eg satisfaction with home, transport, health care access and quality, etc)

* study also included in other study category

Abbreviations: **ALT** – alanine aminotransferase; **AVL** – Auditory Verbal Learning; **BAI** – Beck Anxiety Inventory; **BDI** – Beck Depression Inventory; **BMSFI** – Brief Male Sexual Function Inventory; **BSI** – Brief Symptoms Index; **CESD** - Center for Epidemiological Studies Depression scale; **CFS** – Chronic Fatigue Screener; **CLDQ** – Chronic Liver Disease Questionnaire; **CM** – Cook Medley anger measure; **DASS** – Depression Anxiety Stress Scales; **EFQ** – Everyday Life Questionnaire (related to SF-36); **EQ_{index}** – European Quality of life index; **FIS** – Fatigue Impact Scale; **HADS** – Hospital Anxiety and Depression Scale; **HCV** – hepatitis C virus; **HQLQ** – Hepatitis Quality of Life Questionnaire (incorporating the SF-36); **HUI** – Health Utilities Index; **IDU** – injection drug use; **IPQ** – Illness Perception Questionnaire; **MINI-Plus** – Mini International Neuropsychiatric Interview; **MUIS** – Mishel Uncertainty in Illness Scale; **NART** – National Adult Reading Test; **PMS** – Profile of Mood States; **QoL** – quality of life; **SCAN** – Schedule for Assessment in Neuropsychiatry; **SCL-90** – Symptom Checklist-90-R; **SSM** – Medical Outcomes Study Social Support Measure; **SCID-CV** – Structured Clinical Interview for DSM-IV Axis I Disorders; **SEIQoL-DW** – Schedule for the Evaluation of Individual Quality of Life-Direct Weighting; **SQLI** – Spitzer Quality of Life Index; **STAI** – State Trait Anxiety Inventory; **TMT** – Trail Making Tests; **TTO** – Time Trade-Off instrument; **Tx** – treatment; **WHOQOL-HIV Bref** – World Health Organization Quality of Life –HIV Bref Questionnaire; **ZDS** – Zung Depression Scale

Table 7: Health related quality of life during and after treatment/transplant for hepatitis C infection.

Authors (year)	Country	Population (n)	Main QoL measures	Outcomes
<u>During antiviral treatment:</u>				
Batki et al (2009) ¹⁸⁶	Taiwan	On treatment (115)	HR-QoL (HQLQ); Social support (ISSB)	Low QoL, associated with finance, long Tx. duration & low social support.
Bianchi et al (2000) ¹⁸⁷	Italy	On treatment/not (126)	HR-QoL (SF-36, NHP); Depression (CESD); Psych. diagnoses (MINI-Plus)	Reduced QoL in HCV, further reduces by Tx.
Chang et al (2008) ¹⁸⁸	Taiwan	On treatment (115)	HR-QoL (HQLQ); social support (ISSB)	Reduced QoL associated with depression and anger during treatment.
*Bonkovsky et al (2007) ¹¹¹	US	On/end treatment (1,144) [all cirrhosis]	HR-QoL (SF-36)	Decreased QoL at baseline associated with histology severity & depression; improved post Tx if SVR.

Authors (year)	Country	Population (n)	Main QoL measures	Outcomes
*Dan et al (2006) ¹¹²	US	On/end treatment (271)	HR-QoL (SF-36)	Decreased SF-36 scores during Tx: associated with depression.
*Dan et al (2007) ¹¹³	US	On/end treatment (87)	HR-QoL (SF-36), anger (STAEI)	Increasing anger during Tx: associated with depression & ↓HR-QoL.
Fontana et al (2002) ¹⁸⁹	US	On treatment/not (126)	HR-QoL (SF-36), symptoms (BSI)	Reduced QoL associated with emotional distress, particularly in untreated & those expecting fatal outcome.
*Kang et al (2005) ¹⁵⁵	Taiwan	On treatment (47)	HR-QoL (SF-36)	Reduced QoL in Tx, lower by end Tx, no improvement in NVR (improved in SVR)
Hilsabeck et al (2005) ¹⁹⁰	US	Pre (30) & post treatment (11)	HR-QoL (SF-36) Depression/anxiety (BDI-II, BAI), cognitive function (SDMT &TMT)	Treatment associated with reduced cognitive abilities. QoL at baseline did not differ between Tx groups. QoL impact of Tx not reported.
*Hollander et al (2002) ¹¹⁶	Sweden	On/end treatment (147)	HR-QoL (SF-36), depression (CESD)	Baseline SF-36 reduced, reducing more in Tx, improving post Tx (best in SVR).
Hopwood & Treloar (2005) ¹⁹¹	Australia	Treatment experience (19)	In-depth semi-structured interviews[qualitative study]	All reported side-effects → ↓QoL; describes subjective negative responses and impact on social interaction; individual response & coping.
*McHutchison et al (2001) ¹¹⁷	US	On/end treatment (905)	HR-QoL (SF-36),	Baseline SF-36 reduced, improved in SVR (predicted by ALT, viral load, improved histology).
*Şahingöz et al (2009) ¹¹⁸	Turkey	On/end of treatment (36)	HR-QoL (WHOQOL-BREF), anxiety (HARS), depression (HDRS)	High incidence of depression during IFN, associated with anxiety & reduced QoL
Schäfer et al (2009) ¹⁹²	Germany	HCV ⁺ /ORT patients on treatment /not (2,414)	HR-QoL (WHO Euro-QOL EQ-5D), mental health (BSI)	Reduced QoL and sleep disturbance in HCV, but IFN not related to increased depression/reduced QoL/reduced ORT efficacy.
<u>After antiviral treatment:</u>				
Akyüz et al (2009) ¹⁹³	Turkey	Treated/untreated HCV ⁺ renal failure patients (95)	HR-QoL (SF-36), depression (BDI)	Low QoL with little differences between groups, IFN → reduced QoL further, general health perception improved in SVR.
*Falasca et al (2009) ¹¹⁵	Italy	End of treatment (18)	HR-QoL (SF-12), depression (BDI)	Improved subjective QoL, depression levels unchanged.
Fontana et al (2001) ¹⁹⁴	US	Unsuccessful Tx (107)	HR-QoL (HQLQ, HUI, TTO);	Reduced QoL, not related to ALT, alcohol, drugs or other demographic/viral factors. ↓QoL associated with comorbidities.
John-Baptiste et al (2009) ¹⁹⁵	Canada	SVR/NVR (235)	HR-QoL (HQLQ,	Reduced QoL in NVR, imp-

Authors (year)	Country	Population (n)	Main QoL measures	Outcomes
Taliani et al (2007) ¹⁹⁶	Italy	Untreated/relapsers/ non-responders (264)	HUI, TTO); comorbidities (ICED) HR-QoL (SF-36, CLDQ, WHOQOL-BREF)	roved QoL in SVR & benefit sustained over time. Reduced QoL in all groups, lowest in NR, associated with physical comorbidity.
<u>After liver transplantation:</u>				
Dudley et al (2007) ¹⁹⁷	UK	Post transplant (8)	Indepth interviews [qualitative study]	Transplant replaces one health state with other; feelings of stigma & future uncertainty may be worse in HCV transplants.
*Feurer et al (2002) ¹³⁵	US	HCV ⁺ / post transplant (75)	HR-QoL (SF-36), psychosocial (PAI)	HCV recurrence in 10%: associated with ↓functional performance → ↓ QoL.
Paterson et al (2000) ¹⁹⁸	US	Post transplant (87)	HR-QoL (SF-36), depression (BDI), adaption (BMICIS) psycho-emotional stress (POMS)	HCV recurrence in 62%: associated with ↓QoL and ↓functional performance (no difference in adaptive coping)

* study also included in other study category

Abbreviations: ALT – alanine aminotransferase; BAI – Beck Anxiety Inventory; BDI – Beck Depression Inventory; BMICIS – Billing and Moos Inventory of Coping with Illness Styles; BMSFI – Brief Male Sexual Function Inventory; BSI – Brief Symptoms Index; CESD - Center for Epidemiological Studies Depression scale; CLDQ – Chronic Liver Disease Questionnaire; HARS – Hamilton Anxiety Rating Scale; HCV – hepatitis C virus; HDRS – Hamilton Depression Rating Scale; HQLQ – Hepatitis Quality of Life Questionnaire (incorporating the SR-36); HR-QoL – health related quality of life; HUI – Health Utilities Index; ICED – Index of Co-Existent Disease; IFN – interferon; ISSB – Inventory of Socially Supportive Behaviours; MINI-Plus – Mini International Neuropsychiatric Interview; NHP – Nottingham Hill Profile; NR – non responders; ORT – opiate replacement therapy; PAI – Psychosocial Adjustment to Illness scale; POMS – Profile Of Mood States scale; QoL – quality of life; SDMT – Symbol Digit Modalities Test; SVR – sustained viral response; TMT – Trail Making Tests; TTO – Time Trade-Off instrument; Tx – treatment; WHOQOL-BREF – World Health Organisation Quality Of Life assessment.

Table 8: Psychosocial experience of living with hepatitis C infection.

Authors (year)	Country	Participants	Methodological approach	Outcomes and conclusions
<u>Social functioning:</u>				
Blasiolo et al (2006) ¹⁹⁹	US	352 HCV clinic patients	Primarily quantitative ; with semi-structured interviews.	Low social support, associated with living alone, unemployment, IDU history, anxiety & depression, and negative mood state
Carrier et al (2005) ²⁰⁰	Canada	36 HCV ⁺ / IDU	Qualitative study involving individual interviews and ethnographic observation	HCV given meaning by social interactions, media representations & person experiences. Social implications (↑stigma) → high anxiety.
Grundy & Beeching (2004) ²⁰¹	UK	8 female HCV clinic patients	Qualitative study involving semi-structured interviews	Fear of transmission impacts on family & sexual relationship → concerns about ability to fulfil gender roles.
Janke et al (2008) ²⁰²	US	40 HCV clinic patients	Qualitative study involving	Intense anger and ↓impulse

Authors (year)	Country	Participants	Methodological approach	Outcomes and conclusions
			ving focus groups	control; transmission fears → self-imposed isolation → ↓social support (even in Tx).
Sgorbini et al (2009) ²⁰³	Australia	5 HCV patients on Tx & their partners	Qualitative study involving individual semi-structured interviews	IFN substantial QoL impact; 4 themes – illness & Tx (↓ health, isolation), keeping a secret (disclosure, stigma), sharing experience (lending a hand, parenting in adversity), enduring struggle (finance, future etc).
Temple-Smith et al (2004) ²⁰⁴	Australia	32 HCV ⁺ people	Qualitative study involving in-depth interviews	Gender related differences in symptom recognition, health seeking behaviour and notions of social support (males likely to dismiss HCV impact & education + support needs.)
<u>Lifestyle:</u>				
Castera et al (2006b) ²⁰⁵	France	40 HCV clinic patients	Quantitative study, involving surveys, demographic & clinical data.	59% thought HCV always fatal; Sex-life changes in 58% (associated with males, perceived disease severity, anxiety) ; dietary changes in 48% (associated with age, anxiety).
Roy et al (2007) ²⁰⁶	Canada	39 HCV ⁺ IDU	Qualitative study involving in-depth interviews	HCV ‘trivial’ in context of other priorities, and in relation to HIV. But did aim to minimise transmission.
Scognamiglio et al (2007) ²⁰⁷	Italy	27 HCV clinic patients	Quantitative study, involving surveys, demographic & lifestyle data	75% drinkers modified alcohol intake; 21% smokers modified smoking; and 64% modified diet after diagnosis.
Sokyan et al (2005) ²⁰⁸	Turkey	46 HCV clinic patients	Quantitative study, involving surveys, demographic, clinical & lifestyle data	Sexual dysfunction in 35%: predicted by depression (and GGT levels).
Wright et al (2005) ²⁰⁹	UK	17 HCV ⁺ homeless IDU	Qualitative study involving in-depth interviews	Ongoing risk practices with some adoption of harm reduction (cleaning needles, washing spoons); modified diet, reduced drinking since diagnosis.
Zacks et al (2006) ²¹⁰	US	175 HCV clinic patients	Quantitative study, involving surveys, demographic, social functioning data	Less likely to share s towels, or drinking glass or prepare food. 20% less kissing, 27% less intercourse; majority reported financial difficulty, internalised shame, social rejection.

Authors (year)	Country	Participants	Methodological approach	Outcomes and conclusions
<u>Health and Wellbeing:</u>				
Bova et al (2008) ²¹¹	US	39 HIV-HCV coinfectd patients	Mixed method study: involving surveys incorporating HIV-SEI and MHI-5; semi-structured interviews	Average of 10 symptoms: pain fatigue GI problems most 'both-ersome'. 33% had poor mental well-being associated with greater symptom burden. Difficulty differentiating HCV and HIV symptoms. Symptom burden of coinfectd might not be greater than HIV alone.
Conrad et al (2006) ²¹²	Australia	32 HCV ⁺ people	Qualitative study involving semi-structured interviews	Debilitating "hep C attacks" associated with depression & views of HCV as fatal; fear of transmission & uncertainty common; universal anxiety about stigma & discrimination.
Copeland et al (2004) ²¹³	Scotland	16 HCV ⁺ ID	Qualitative study involving semi-structured interviews	Explored themes that explained circumstances leading to 'problem drug user' identity: problems growing up, ↑unemployment & ↓education, peer influence in IDU behaviour.
Dwight et al (2000) ²¹⁴	US	50 HCV patients	Quantitative study involving structured psychiatric interviews and validated questionnaires including MAF-FQ & SF-36	28% had depressive disorders not correlated with disease severity or demographics. Severity of depression correlated with fatigue level. Concludes disability and fatigue more related to depression than hepatic disease.
Forton et al (2002) ²¹⁵	UK	27 HCV-RNA ⁺ & 16 HCV-cleared patients	Quantitative study, involving cognitive assessment; QoL, fatigue & depression questionnaires	RNA+ impaired on more cognitive tasks. Impairment not accounted for by depression, fatigue, or IDU history. Suggests biological cause
Glacken et al (2001) ²¹⁶	Ireland	9 HCV ⁺ people	Qualitative study involving in-depth interviews	None experiencing health transition following diagnosis: impeded by uncertainty, ↓knowledge, 'contamination'; Facilitated by social support, information community participation, being positive.
Glacken et al (2003) ²¹⁷	Ireland	28 HCV ⁺ people	Qualitative study involving in-depth interviews particularly focusing on fatigue	Fatigue is multidimensional with 2 distinct types - chronic and idiopathic. Universally experienced as 'whole-body-sensation'. Suggests an HCV cause of fatigue that is perpetuated by secondary factors such as inactivity, pain and disability
Golden et al (2005) ²¹⁸	Ireland	90 HCV clinic patients	Quantitative study, involving structured psychiatric interviews and validated questionnaires	High prevalence of undiagnosed mood disorders. Depression associated with adverse experiences of illness (including

Authors (year)	Country	Participants	Methodological approach	Outcomes and conclusions
			including SCID-CV	stigma, poor adjustment & physical symptoms), anxiety not associated with any risk factor.
Goulding et al (2001) ²¹⁹	Ireland	77 HCV clinic patients	Quantitative study, involving structured clinical examination & history FIQ and HADS	Moderate increase in fibromyalgia in HCV with number of tender points associated with mode of acquisition. Anxiety & depression higher in HCV, possibly related to psychological factors.
Grassi et al (2002) ²²⁰	US	290 HCV ^{+/−} & HIV ^{+/−} IDU	Quantitative study, involving surveys, demographic, psychosocial data	Higher OCD, paranoid ideation, phobic anxiety in HCV (v HIV); lower 'fighting spirit', higher hopelessness & anxious disease preoccupation in HCV (v HIV).
Groessler et al (2008) ²²¹	US	8 male HCV clinic patients	Qualitative study involving semi-structured interviews	Pronounced social impact of diagnosis; greater impact in non-IDU; psychological issues prevalent; barriers to treatment and care common.
Hassoun et al (2002) ²²²	Canada	92 HCV patients	Quantitative study, involving demographic clinical data, assessing fatigue with the FIS	67% had fatigue – described as 'frequent and disabling'. Significantly increased compared to controls, fatigue severity not associated with disease activity or progress.
Hilsabeck et al (2002) ²²³	US	66 HCV ⁺ & 14 HCV [−] patients with liver disease	Quantitative study, involving assessment of four cognitive functions using validated cognitive tests	Significant cognitive difficulties for both patient groups. associated with liver fibrosis but still higher in HCV with and without cirrhosis.
Hilsabeck et al (2003) ²²⁴	US	21 HCV patients	Quantitative study, involving assessment of four cognitive functions using validated cognitive tests	Significant cognitive difficulties not related to psychiatric symptoms. Cognitive impairment level sufficient to impact on QoL.
Hogg et al (2003) ²²⁵	Canada	241 transfusion associated HCV patients & 222 HCV [−] patients	Quantitative study, involving surveys, demographic & clinical data	HCV more likely to have ≥ 2 symptoms, have worse health status than 10 years ago, and have higher illness intrusiveness rating.
Hopwood & Treloar (2008) ²²⁶	Australia	20 patients on/recently HCV treatment	Qualitative study involving semi-structured, in-depth interviews	Past experiences of marginalisation (disadvantage; other chronic illnesses, etc) → enhanced resilience in coping with HCV Tx.
Kinder (2009) ²²⁷	US	8 males, IFN treated	Qualitative study involving In depth, semi-structured Interviews	Confusion & surprise re diagnosis; anxiety re treatment decisions related to HCV seriousness & fear of side-effects; tx experience was negative with significant physical, emotional

Authors (year)	Country	Participants	Methodological approach	Outcomes and conclusions
Kozanoglu et al (2003) ²²⁸	Turkey	95 HCV ⁺ patients & 95 HCV-	Quantitative study of demographic, clinical data, information on fibromyalgia	side-effects and concern re paradox of injecting IFN. Higher prevalence of fibromyalgia syndrome (FS) in HCV with more tender spots with higher pain intensity compared to controls with FS
Kraus et al (2000) ²²⁹	Germany	Post transplant (87)	Quantitative study, involving surveys, demographic & clinical data	Depression in 22%, anxiety 15%; associated with age, advice not to seek Tx, recent diagnosis. Emotional state or coping style not associated with infection mode or liver damage
Lang et al (2006) ²³⁰	Australia	Phase 1- 73 people with HCV; Phase 2- 188 people with HCV	Phase 1 – focus groups & individual interviews Phase 2 – quantitative surveys and serology	Tiredness, irritability, depression, mental tiredness & abdominal pain most prevalent symptoms. 4 symptom ‘clusters’: neuropsychiatric; gastro-intestinal; algescic (e.g. joint & muscle pain); and dysthetic (eg noise/light sensitivity, skin problems)
Lehman et al (2002) ²³¹	US	120 veterans with HCV	Quantitative study, involving surveys, demographic & clinical data	Depression in 44%, anxiety in 38%, post traumatic stress disorder 21%; alcohol-related problems 27%. All outcomes positively correlated with each other.
McAndrews et al (2005) ²³²	Canada	37 HCV patients & 46 HCV- controls	Quantitative study involving radiographic, clinical and neuropsychologic assessment	Marginally reduced learning efficiency in HCV not associated with increased fatigue and depression in this group. HCV group had changes in brain metabolites, not associated with liver histology and not explanatory of ‘brain fog’ reported by people with HCV
McDonald et al (2002) ²³³	Australia	115 HCV clinic patients	Quantitative study, involving surveys, demographic & clinical data fatigue (FIS) symptoms (modified SCL-90-R)	Fatigue in 83%, all the time in 31%, psychopathology in 50% Fatigue weakly correlated with liver histology but strongly correlated with all psychological domains, particularly depression
McKenna et al (2009) ²³⁴	Ireland	290 people with iatrogenically acquired HCV	Quantitative survey of sociodemographic and clinical characteristics	After mean 26 years infection 62% hepatic & 99% extra-hepatic symptoms. Fatigue in 88% and pain in 96%. 89% reported diagnosed co-morbid diseases. Reported symptoms associated with age, female sex, and co-morbidities
Nagano et al (2004) ²³⁵	Japan	69 HCV patients	Quantitative study involving clinical and demographic data,	All stress inventory scales related to the ‘type 1’ personality (low sense of control, objective

Authors (year)	Country	Participants	Methodological approach	Outcomes and conclusions
			‘stress inventory’	dependence of loss, unfulfilled need for acceptance, altruism) associated with severity of disease (according to ALT and liver cirrhosis). Chronic stress related to type 1 personalities might influence HCV progression
Obhrai, et al (2001)	US	149 HCV+/- patients with/without alcohol problems and/or liver disease	Quantitative study, involving surveys, demographic & clinical data	Fatigue higher in HCV cf other groups (not statistical) but did not improve with rest as effectively. Fatigue and psychological symptoms more common, severe and less responsive to remedies in HCV
Piche et al (2002) ²³⁶	France	78 HCV patients, 22 HCV- controls, 13 billiary cirrhosis patients	Quantitative study, involving surveys (FIS), demographic & clinical data	Fatigue higher in HCV and more in females. Correlated with leptin (as in billiary cirrhosis) but not age, liver function, or viral load
Poynard et al (2002) ²³⁷	France	1614 HCV patients	Quantitative study, retrospective analysis of demographic, clinical, virologic, immunologic and other data	Fatigue in 53%, severe enough to impair activity in 17%, independently associated with female sex, age > 50 years, cirrhosis, depression and purpura
Silberbogen et al (2007) ²³⁸	US	29 veterans with HCV (32% on Tx)	Quantitative study, involving data on pain (MPQ-SF; WHYMPI; NRS) & depression (CES-D)	Pain reported in 83%, most in upper limb, hip, lower limb & lower back. Alcohol and smoking associated with pain and depression in HCV.
Weissenborn et al (2004) ²³⁹	Germany	30 HCV patients with fatigue, 15 HCV- controls	Quantitative study, involving neurological & neuropsychological assessment, EEG, MRI & MRS	Some cognitive impairment, higher anxiety and depression (none had cirrhosis or fibrosis) Evidence of central nervous system involvement (per MRI), associated with higher severity of fatigue
Yovtcheva et al (2001) ²⁴⁰	US	306 veterans with HCV	Quantitative study, retrospective analysis of past & present DSM-IV based psychiatric disorders recorded in clinical database	Mood disorders in 38%, personality disorders in 30%, post traumatic stress disorder in 19% and other in 17%. 86% diagnosed with alcohol disorders & 28% with IDU history (noted high prevalence of psychiatric disorders exist in veterans)

* study also included in other study category

Abbreviations: **BDI-II** – Becks Depression Inventory-II; **BAI** – Becks Anxiety Inventory; **CES-D** – Center for Epidemiologic Studies Depression Scale; **EEG** – electroencephalography; **FIQ** – Fibromyalgia Impact Questionnaire; **FIS** – Fatigue Impact Scale; **FSS** – Fatigue Severity Scale; **HADS** – Hospital Anxiety and Depression Score; **HCV** – hepatitis C virus; **HIV-SEI** – HIV Symptom Experience inventory; **IDU** – injection drug user; **MAF-FQ** – MAF Fatigue Questionnaire; **MHI-5** – Mental Health Index-5; **MPQ-SF** – McGill Pain Questionnaire-Short Form; **MRI** – magnetic resonance imaging; **MRS** – magnetic resonance spectroscopy; **NRS** – Numeric Rating Scale; **SCID-CV** – Structured Clinical Interview for DSM-IV Axis I Disorders: Clinician Version; **SCL-90-R** – Symptom Checklist, 90 item; **SF-36** – Short Form 36; **QoL** – quality of life; **Tx** – treatment; **WHYMPI** – West Haven-Yale Multidimensional Pain Inventory

Table 9: Diagnosis, management and treatment of chronic hepatitis C infection.

Authors (year)	Country	Participants	Methodological approach	Outcomes and conclusions
<u>Diagnosis impact</u>				
Castera et al (2006a) ²⁴¹	France	185 HCV clinic patients	Quantitative study, involving surveys, demographic & clinical data	Diagnosis a major stressful event: < death of loved one or divorce, but > home removal or job loss. Associated with perceived disease severity.
Craine et al (2004) ²⁴²	UK	43 HCV ⁺ / IDU	Qualitative study involving semi-structured interviews and focus groups	Lower risk behaviour in HCV variable risk behaviour after HCV diagnosis (availability) of clean injecting equipment greater influence).
Gill et al (2005) ²⁴³	Pakistan	90 recently diagnosed HCV patients	Quantitative study, involving surveys, demographic, anxiety & clinical	Diagnosis related stress associated with perceived disease severity: > divorce, loss of income source, or moving to another city.
Harris et al (2009) ²⁴⁴	Australia & New Zealand	40 HCV ⁺ people	Qualitative study involving semi-structured interviews	HCV diagnosis: ‘no big deal’ 50%, ‘shocking’ ‘devastating’ 50%. Meaning of HCV varied with social context; ‘calculable risk’ – better than HIV. HCV more stigmatising than HIV in co-infected; other competing life issues a higher priority.
Sutton & Treloar (2007) ²⁴⁵	Australia	36 HCV ⁺ people	Qualitative study involving semi-structured interviews	HCV shifted in priority when competing with other pressures - weighed against dynamic social and health circumstance.
Tomkins et al (2005) ²⁴⁶	UK	17 HCV ⁺ homeless IDU	Qualitative study involving in-depth interviews	Diagnosis → shock, anger, devastation + long-lasting emotional psychosocial physical effects. Stigma and unpredictable effects of disclosure. (↑info→ ↓negative diagnosis impact.
<u>Stigma and discrimination:</u>				
Crockett et al (2004) ²⁴⁷	Australia	17 HCV ⁺ IDU	Qualitative study involving semi-structured interviews	Social exclusion & marginalisation; profound impact of stigma (feeling ‘unclean’ etc) related to transmission fears; perceived discrimination in health care; child-bearing decisions affected by transmission fears.
Fraser & Treloar (2006) ²⁴⁸	Australia	6 HCV ⁺ people	Qualitative study involving semi-structured interviews	Stigmatising responses, sense of contamination, inevitability of disclosure. Despair→ belief infection with other BBV not important.

Authors (year)	Country	Participants	Methodological approach	Outcomes and conclusions
Golden et al (2006) ²⁴⁹	Ireland	87 HCV clinic patients	Quantitative study, involving surveys, demographic, psychiatric, stigma & clinic data	Fear of disclosure; social isolation & social rejection; stigma associated with depression & ↓SE status; stigma associated with ↓illness acceptance, social adjustment and ↑symptoms.
Hopwood et al (2006) ²⁵⁰	Australia	504 HCV ⁺ people	Quantitative study, involving surveys, demographic, social & risk factor data	Health care discrimination in 65%; negative health impact of discrimination in 45%; discrimination associated with pessimism re future health, ↓social interaction, HCV fatigue, knowing ↑people with HCV.
Zickmund et al (2003) ²⁵¹	US	257 HCV clinic patients	Mixed methods involving surveys and semi-structured interviews	HCV stigma in 57%: associated with females; loss of control; anxiety & depression; ↓QoL (no other demographic factor); Stigmatised reported problems in healthcare, work, families.
<u>Health service access:</u>				
Banwell et al (2005) ²⁵²	Australia	462 HCV ⁺ females	Quantitative study, involving surveys, demographic, psychosocial data	Lesbians more dissatisfied with GP; heterosexuals more likely to be referred to specialist; lesbians more likely to use alternative health services. HCV experience of health services differs per sexual identity.
Bratstein et al (2006) ²⁵³	Canada	707 HCV ⁺ - HIV ^{+/-} IDU	Quantitative study, involving surveys, demographic, clinical & management history data	HCV-mono reported highest rate HCV symptoms, but HCV-HIV coinfecting had more HCV health care utilisation
Butt et al (2008) ²⁵⁴	Canada	26 HCV clinic patients	Qualitative study involving open interviews & daily participant recordings.	All described stigma in many settings: associated with fear of transmission & IDU association. Stigma = barrier to health care access (reports of refusal of care).
*Gifford et al (2003) ¹⁴⁷	Australia	462 HCV ⁺ females	Quantitative study, involving survey (SF-12) & social & clinical data	52% referred to specialist but Tx only in 17%; low health status and 50% report symptoms; 48% report less favourable treatment from health professionals. (high need but low specialist service access, particularly in IDU)
*Gifford et al (2005) ¹⁴⁸	Australia	308 HCV ⁺ males	Quantitative study, involving survey (SF-12) & social & clinical data	30% referred to specialist but Tx only in 20%; low health status and 58% report symptoms; 40% report less favourable treatment from health professionals. (high need but low specialist service access).
Harris et al (2005) ²⁵⁵	New Zealand	20 HCV clinic patients	Qualitative study involving individual	Frustration with reduced info from doctors; dissatisfied with

Authors (year)	Country	Participants	Methodological approach	Outcomes and conclusions
			interviews	liver focus (only IFN on offer); many told diagnosis on phone; common reports withdrawal/refusal health treatment (→ reluctance to disclose but feeling obligation to disclose).
Paterson et al (2006) ²⁵⁶	Canada	33 HCV clinic patients	Qualitative study involving individual interviews	Frustration with model of care with dominance in acute rather than chronic care; >50% used CAM to assume control & not need doctors (who they felt delegitimised their knowledge & experience of HCV).
Schackman et al (2008) ²⁵⁷	US	93 HCV patients & 23 treating health professionals	Quantitative study, involving surveys, demographic & clinical data	Low QoL in HCV; anticipated Tx side effects rated worse by patients than providers; 1-yr of side effects rated equal to 4 yrs of mild HCV symptoms if returned to current health status post Tx, and 2 yrs if return to population norms. 73% willing to risk life on 'certain cure' (standard gamble).
Taylor-Young & Heldebrandt (2009) ²⁵⁸	US	One person undergoing HCV treatment	Qualitative study involving series of in-depth interviews	Four themes: transition or change; maintaining control of one's life; social support & communication; side effects.
Zickmund et al (2004) ²⁵⁹	US	322 HCV clinic patients	Mixed methods, involving surveys, demographic & clinical data, & semi-structured interviews	Poor communication with doctors in 40% (re ↓doctor skill, poor doctor HCV management; feelings of misdiagnosis, misleading advice or abandoned, stigmatisation by doctor). Patient psychosocial problems predicted by communication difficulties.
<u>Treatment decisions:</u>				
Khokhar & Lewis (2007) ²⁶⁰	US	280 patients declining treatment	Quantitative study involving interrogation of a clinical database	Reasons for declining Tx: 44% asymptomatic; 22% side effect concerns; 20% comorbid conditions; 10% ↓social/financial support; 4% efficacy doubts. 79% confirmed ongoing satisfaction with decision 12 months later.
McNally et al (2006) ²⁶¹	Australia	224 HCV ⁺ people	Quantitative study involving surveys on Tx & diagnosis experience, health service access & demographic data	46% reported health 'fair to poor' & HCV symptoms in 63% (only 47% seeing GP); side effects most important in declining & adhering to Tx; efficacy most important in deciding to try Tx; diagnosed <5 years most likely to try Tx.
Ogawa and Bova (2009) ²⁶²	US	31 HCV-HIV co-infected	Qualitative study invol-	HCV Tx not a priority; a topic

Authors (year)	Country	Participants	Methodological approach	Outcomes and conclusions
		IDU	ving semi-structured interviews	of fear (might reintroduce injecting) and misinformation (unaware of role of alcohol); others recommended to other IDU to 'get clean & try it'. Fragile nature of 'recovery' from substance use.
Rowan et al (2007) ²⁶³	US	12 male HCV veterans - Tx after delay due to alcohol or depression.	Qualitative study involving focus groups.	Decision making in 4 categories; health care processes; education re Tx contraindications; communication; health behaviours. Most satisfied with Tx decision making process & made changes →Tx start.
Treloar & Hopwood (2008) ²⁶⁴	Australia	20 HCV patients on Tx & 6 health care workers	Qualitative study involving semi-structured interviews	'Unrealistic optimism' in both patients & health care workers; patients didn't think pre-Tx info was relevant to them & would not experience side effects → delays in treatment for mental health problems.

* study also included in other study category

Abbreviations: HCV – hepatitis C virus; IDU – injection drug user; QoL – quality of life; Tx – treatment;

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