KCE REPORTS 173S

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

HEPATITIS C: SCREENING AND PREVENTION

APPENDIX

KCE REPORTS 173S
HEALTH TECHNOLOGY ASSESSMENT

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HEPATITIS C: SCREENING AND PREVENTION

APPENDIX

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COLOPHON

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APPENDIX REPORT

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1. APPENDIX 1: HCV SCREENING

1.1. Effectiveness literature review

1.1.1. List of INAHTA members websites

Agency		Country
AETMIS	Agence d´Évaluation des Technologies et des Modes d´Intervention en Santé	Canada
AETS	Agencia de Evaluación de Tecnologias Sanitarias	Spain
AETSA	Andalusian Agency for Health Technology Assessment	Spain
AHRQ	Agency for Healthcare Research and Quality	USA
AHTA	Adelaide Health Technology Assessment	Australia
AHTAPol	Agency for Health Technology Assessment in Poland	Poland
ASERNIP-S	Australian Safety and Efficacy Register of New Interventional Procedures	Australia
AVALIA-T	Galician Agency for Health Technology Assessment	Spain
CADTH	Canadian Agency for Drugs and Technologies in Health	Canada
CAHTA	Catalan Agency for Health Technology Assessment and Research	Spain
CEDIT	Comité d'Évaluation et de Diffusion des Innovations Technologiques	France
CENETEC	Centro Nacional de Excelencia Tecnológica en Salud Reforma	Mexico
CMT	Centre for Medical Technology Assessment	Sweden
CRD	Centre for Reviews and Dissemination	UK
CVZ	College voor Zorgverzekeringen	Netherlands
DACEHTA	Danish Centre for Evaluation and Health Technology Assessment	Denmark
DAHTA @DIMDI	German Agency for HTA at the German Institute for Medical Documentation and Information	Germany
DECIT-CGATS	Secretaria de Ciência, Tecnologia e Insumos Estratégicos, Departamento de Ciência e Tecnologia	Brazil
DSI	Danish Institute for Health Services Research	Denmark
FinOHTA	Finnish Office for Health Care Technology Assessment	Finland
GR	Gezondheidsraad	Netherlands
HAS	Haute Autorité de Santé	France
HunHTA	Unit of Health Economics and Health Technology Assessment	Hungary
IAHS	Institute of Applied Health Sciences	UK
ICTAHC	Israel Centre for Technology Assessment in Health Care	Israel

Agency		Country
IECS	Institute for Clinical Effectiveness and Health Policy	Argentina
IHE	Institute of Health Economics	Canada
IMSS	Mexican Institute of Social Security	Mexico
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen	Germany
KCE	Belgian Federal Health Care Knowledge Centre	Belgium
LBI of HTA	Ludwig Boltzmann Institut für Health Technology Assessment	Austria
MAS	Medical Advisory Secretariat	Canada
MSAC	Medicare Services Advisory Committee	Australia
MTU-SFOPH	Medical Technology Unit - Swiss Federal Office of Public Health	Switzerland
NCCHTA	National Coordinating Centre for Health Technology Assessment	UK
NHS QIS	Quality Improvement Scotland	UK
NHSC	National Horizon Scanning Centre	UK
NOKC	Norwegian Knowledge Centre for Health Services	Norway
NZHTA	New Zealand Health Technology Assessment	New Zealand
OSTEBA	Basque Office for Health Technology Assessment	Spain
SBU	Swedish Council on Technology Assessment in Health Care	Sweden
UETS	Unidad de evaluacíon Technologias Santarias	Spain
VATAP	VA Technology Assessment Program	USA
VSMTVA	Health Statistics and Medical Technologies State Agency	Latvia
ZonMw	The Medical and Health Research Council of The Netherlands	Netherlands

1.1.2. Search strategy and flow chart

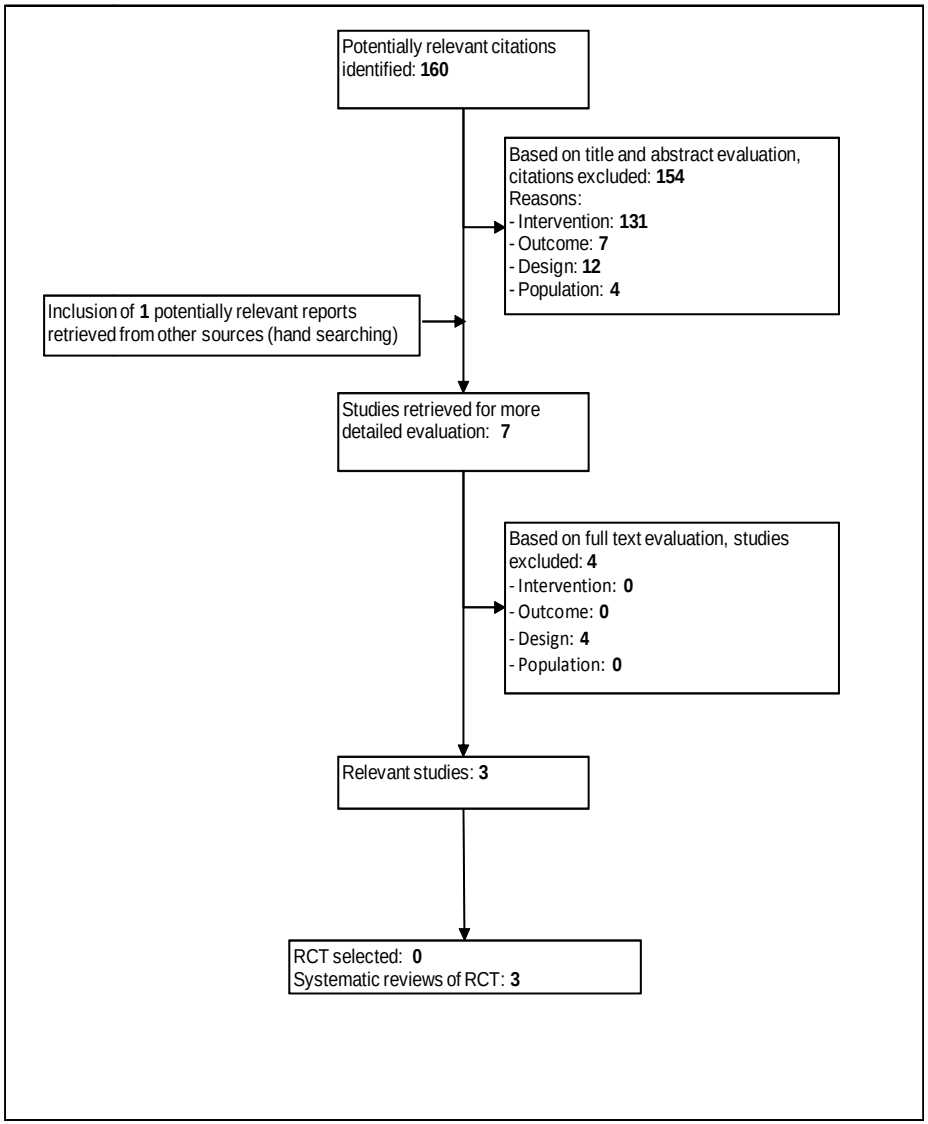
RCT

Date	July 4, 2011
Database (name + access)	Ovid MEDLINE®
Date covered	1948 to Present with Daily Update
Search Strategy	1 exp Hepatitis C/ (39425) 2 exp Hepatitis C Antibodies/ (4934) 3 exp Hepacivirus/ (19216) 4 hepatitis c.tw. (40382) 5 exp Mass Screening/ (86346) 6 screening.tw. (247976) 7 1 or 2 or 3 or 4 (51015) 8 5 or 6 (281257) 9 7 and 8 (3355) 10 limit 9 to (meta analysis or randomized controlled trial) (28) 11 (randomized clinical trial$ or randomized controlled trial$ or RCT or randomised clinical trial$ or randomised control led trial$).tw. (68714) 12 systematic review$.tw. (26027) 13 9 and 11 (11) 14 9 and 12 (12) 15 10 or 13 or 14 (45)
Note	

Date	July 4, 2011			
Database (name + access)	CINAHL			
Date covered	-	to present		
Search Strategy	#	Query	Limiters/Expanders	Results
	S12	s9 or s10 or s11	Search modes - Boolean/Phrase	9
	S11	s7 and s8	Search modes - Boolean/Phrase	4
	S10	s7	Limiters - Publication Type: Meta Analysis Search modes - Boolean/Phrase	0
	S9	s7	Limiters - Publication Type: Systematic Review Search modes - Boolean/Phrase	5
	S8	Randomized controlled or randomised controlled or Randomized clinical or Randomised clinical or rct	Search modes - Boolean/Phrase	34607
	S7	S3 and S6	Search modes - Boolean/Phrase	435
	S6	S4 or S5	Search modes - Boolean/Phrase	47358
	S5	screening	Search modes - Boolean/Phrase	47358
	S4	(MH "Health Screening")	Search modes - Boolean/Phrase	14048
	S3	S1 or S2	Search modes - Boolean/Phrase	5356
	S2	(MH "Hepatitis C, Chronic")	Search modes - Boolean/Phrase	472
	S1	hepatitis c	Search modes - Boolean/Phrase	5356
Note				

Date	July 4, 2011		
Database (name + access)	Embase		
Date covered	1974 to present		
Search Strategy	#21	#20 AND [embase]/lim	120
	#20	#18 NOT #19	137
	#19	editorial:it OR letter:it	1116098
	#18	#12 AND #17	139
	#17	#13 OR #14 OR #15 OR #16	415338
	#16	'randomized controlled':ab,ti OR 'randomised controlled':ab,ti OR 'randomized clinical':ab,ti OR 'randomised clinical':ab,ti OR 'rct':ab,ti OR 'systematic review':ab,ti OR 'systematic reviews':ab,ti OR 'meta analysis':ab,ti	155599
	#15	'randomized controlled trial'/exp	287320
	#14	'systematic review'/exp	42258
	#13	'meta analysis'/exp	55342
	#12	#8 AND #11	5963
	#11	#9 OR #10	510616
	#10	'screening':ab,ti	313063
	#9	'screening'/exp	351298
	#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	74036
	#7	'hepatitis virus non a non b':ab,ti OR 'hepatitis non a non b':ab,ti	272
	#6	'hepatitis c':ab,ti	52052
	#5	'hepatitis c antibody'/exp	6130
	#4	'hepatitis non a non b'/exp	2031
	#3	'hepatitis virus non a non b'/exp	465
	#2	'hepatitis c'/exp	54442
	#1	'hepatitis c virus'/exp	33470
Note			

	July 5, 2011		
Database (name + access)	Cochrane Library		
Date covered	- to present		
Search Strategy	#1	MeSH descriptor Hepacivirus explode all trees	772
	#2	MeSH descriptor Hepatitis C explode all trees	1835
	#3	MeSH descriptor Hepatitis C Antibodies explode all trees	102
	#4	(hepatitis c):ti,ab,kw	3770
	#5	(#1 OR #2 OR #3 OR #4)	3778
	#6	MeSH descriptor Mass Screening explode all trees	4434
	#7	(screening):ti,ab,kw	15008
	#8	(#6 OR #7)	15264
	#9	(#5 AND #8)	132
	#10	(randomized clinical trial):pt	214774
	#11	(meta analysis):pt	436
	#12	(randomized controlled) or (randomized clinical) or (randomised controlled) or (randomised clinical) or (RCT):ti,ab,kw	166087
	#13	(meta analysis) or (systematic review):ti,ab,kw	19720
	#14	(#10 OR #11 OR #12 OR #13)	320003
	#15	(#9 AND #14)	44
Note	**Cochrane Reviews [1] | Other Reviews [1] | Clinical Trials [40] | Methods Studies [0] | Technology Assessments [1] | Economic Ev aluations [1] | Cochrane Groups [0]**		


Potentially relevant citations identified: 160
Based on title and abstract evaluation, citations excluded: 154
Reasons:
- Intervention: 131
- Outcome: 7
- Design: 12
- Population: 4
Inclusion of 1 potentially relevant reports retrieved from other sources (hand searching)
Studies retrieved for more detailed evaluation: 7
Based on full text evaluation, studies excluded: 4
- Intervention: 0
- Outcome: 0
- Design: 4
- Population: 0
Relevant studies: 3
RCT selected: 0
Systematic reviews of RCT: 3

Modelling studies

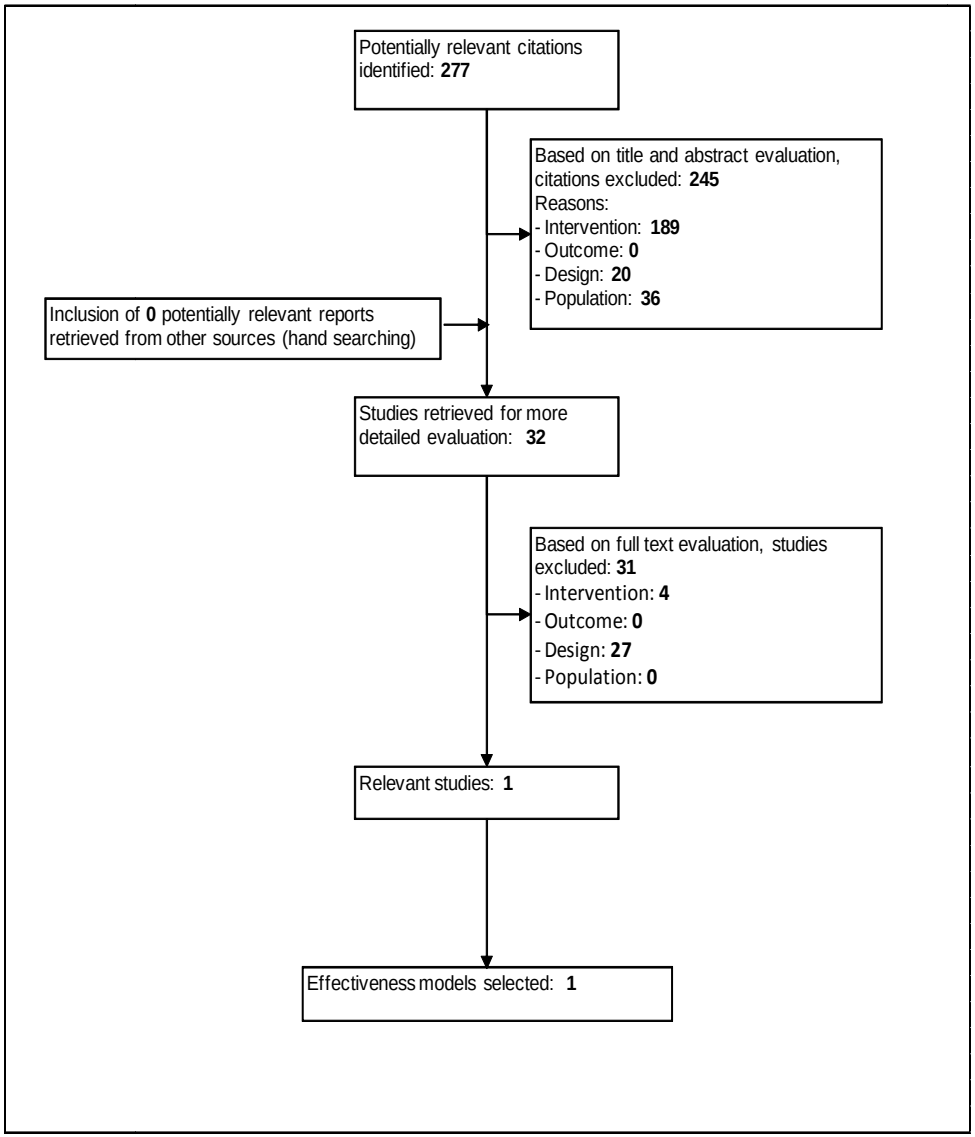
Date	June 24, 2011
Database (name + access)	Ovid MEDLINE®
Date covered	1950 to Present with Daily Update
Search Strategy	1 exp Hepatitis C/ (39382) 2 exp Hepatitis C Antibodies/ (4931) 3 exp Hepacivirus/ (19201) 4 hepatitis c.tw. (40337) 5 exp Mass Screening/ (86227) 6 screening.tw. (247557) 7 1 or 2 or 3 or 4 (50960) 8 5 or 6 (280802) 9 7 and 8 (3353) 10 exp Models, Theoretical/ (1026534) 11 exp Models, Statistical/ (199277) 12 exp Models, Economic/ (7998) 13 exp Models, Econometric/ (3431) 14 exp Logistic Models/ (64172) 15 exp Decision Making/ (98276) 16 exp Decision Making, Computer-Assisted/ (72228) 17 exp Decision Support Techniques/ (48471) 18 exp Computer Simulation/ (111054) 19 decision model$.tw. (1037) 20 decision analy$.tw. (3997) 21 mathematical model$.tw. (24082) 22 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (1239653) 23 9 and 22 (184)

Date	June 24, 2011
Database (name + access)	Econlit - Ovid
Date covered	1961 to May 2011
Search Strategy	1 hepatitis c.mp. [mp=heading words, abstract, title, country as subject] (5)

Date	June 24, 2011		
Database (name + access)	Embase		
Date covered	1974 to present		
Search Strategy	#24	#23 AND [embase]/lim	39
	#23	#12 AND #22	54
	#22	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21	285500
	#21	'decision model':ab,ti OR 'decision models':ab,ti OR 'mathematical model':ab,ti OR 'mathematical models':ab,ti	28542
	#20	'decision support system'/exp	8820
	#19	'statistical model'/exp	72603
	#18	'computer simulation'/exp	61434
	#17	'theoretical model'/exp	49478
	#16	'mathematical model'/exp	157628
	#15	'computer model'/exp	18965
	#14	'disease simulation'/exp	1676
	#12	#8 AND #11	5948
	#11	#9 OR #10	509371
	#10	'screening':ab,ti	312180
	#9	'screening'/exp	350409
	#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	73827
	#7	'hepatitis virus non a non b':ab,ti OR 'hepatitis non a non b':ab,ti	272
	#6	'hepatitis c':ab,ti	51904
	#5	'hepatitis c antibody'/exp	6124
	#4	'hepatitis non a non b'/exp	2031
	#3	'hepatitis virus non a non b'/exp	465
	#2	'hepatitis c'/exp	54262
	#1	'hepatitis c virus'/exp	33393
Note			

	June 24, 2011	
Database (name + access)	Cochrane Database of systematic reviews - Cochrane Library	
Date covered	1800 to present	
Search Strategy	#1 MeSH descriptor Hepacivirus explode all trees	2
	#2 MeSH descriptor Hepatitis C explode all trees	15
	#3 MeSH descriptor Hepatitis C Antibodies explode all trees	0
	#4 (hepatitis c):ti,ab,kw	33
	#5 MeSH descriptor Mass Screening explode all trees	21
	#6 (screening):ti,ab,kw	406
	#7 (#1 OR #2 OR #3 OR #4)	33
	#8 (#5 OR #6)	406
	#9 (#7 AND #8)	2
Note		

Date	June 24, 2011
Database (name + access)	CRD databases
Date covered	- to present
Search Strategy	1 MeSH DESCRIPTOR Hepacivirus EXPLODE ALL TREES 53 2 MeSH DESCRIPTOR Hepatitis C EXPLODE ALL TREES 279 3 MeSH DESCRIPTOR Hepatitis C Antibodies EXPLODE ALL TREES 11 4 "hepatitis c" 805 5 MeSH DESCRIPTOR Mass Screening EXPLODE ALL TREES 1704 6 screening 3761 7 #1 OR #2 OR #3 OR #4 805 8 #5 OR #6 3776 9 #7 AND #8 159 10 MeSH DESCRIPTOR Models, Statistical EXPLODE ALL TREES 1677 11 MeSH DESCRIPTOR Models, Theoretical EXPLODE ALL TREES 2056 12 MeSH DESCRIPTOR Models, Economic EXPLODE ALL TREES 1130 13 MeSH DESCRIPTOR Models, Econometric EXPLODE ALL TREES 314 14 MeSH DESCRIPTOR Logistic Models EXPLODE ALL TREES 138 15 MeSH DESCRIPTOR Decision Making EXPLODE ALL TREES 223 16 MeSH DESCRIPTOR Decision Making, Computer-Assisted EXPLODE ALL TREES 281 17 MeSH DESCRIPTOR Decision Support Techniques EXPLODE ALL TREES 1045 18 MeSH DESCRIPTOR Computer Simulation EXPLODE ALL TREES 277 19 decision model* 1152 20 decision analy* 1182 21 mathematical model* 101 22 #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 4565 23 #9 AND #22 79
Note	Dare: (0); NHS EED: (79); HTA (0)


Potentially relevant citations identified: 277
Based on title and abstract evaluation, citations excluded: 245
Reasons:
- Intervention: 189
- Outcome: 0
- Design: 20
- Population: 36
Inclusion of 0 potentially relevant reports retrieved from other sources (hand searching)
Studies retrieved for more detailed evaluation: 32
Based on full text evaluation, studies excluded: 31
- Intervention: 4
- Outcome: 0
- Design: 27
- Population: 0
Relevant studies: 1
Effectiveness models selected: 1

1.2. Cost-effectiveness literature review

1.2.1. Classification of economic studies

		Are both costs (inputs) and consequences (outputs) of the alternatives examined?		
		No		Yes
		Examines consequences only	**Examines costs only**	
Is there a comparison of at least two alternatives?	**No**	*Partial evaluation*		*Partial evaluation*
		Outcome description	Cost description	Cost-outcome description
	Yes	*Partial evaluation*		*Full economic evaluation*
		Efficacy or effectiveness evaluation	Cost comparison	Cost-minimisation analysis (CMA)
				Cost-effectiveness analysis (CEA)
				Cost-utility analysis (CUA)
				Cost-benefit analysis (CBA)

Adapted from Drummond et al.[1]

1.2.2. Search strategy

Date	September 23, 2010
Database (name + access)	Ovid MEDLINE®
Date covered	1950 to Present with Daily Update
Search Strategy	1 exp Hepatitis C/ (37841) 2 exp Hepatitis C Antibodies/ (4832) 3 exp Hepacivirus/ (18264) 4 hepatitis c.tw. (38606) 5 exp Mass Screening/ (83634) 6 screening.tw. (235874) 7 1 or 2 or 3 or 4 (48841) 8 5 or 6 (268215) 9 7 and 8 (3209) 10 Economics/ (25911) 11 exp "Costs and Cost Analysis"/ (152780) 12 "Value of Life"/ec [Economics] (200) 13 exp Economics, Hospital/ or exp Economics, Medical/ (29329) 14 Economics, Dental/ or Economics, Pharmaceutical/ or Economics, Nursing/ (7799) 15 (econom$ or cost$ or pric$).tw. (359563) 16 pharmaco?economic$.tw. (2127) 17 (expenditure$ not energy).tw. (13705) 18 budget$.tw. (13880) 19 (value adj1 money).tw. (16) 20 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 (471643) 21 9 and 20 (287) 22 letter.pt. (690812) 23 editorial.pt. (263228) 24 22 or 23 (953984) 25 21 not 24 (280)

Date	September 23, 2010
Database (name + access)	Econlit - Ovid
Date covered	<1969 to August 2010>
Search Strategy	1 hepatitis c.mp. [mp=heading words, abstract, title, country as subject] (5) 2 (screening).mp. (1327) 3 1 and 2 (0)

Date	September 23, 2010	
Database (name + access)	Cochrane Database of systematic reviews - Cochrane Library	
Date covered	1800 to present	
Search Strategy	#1 MeSH descriptor Hepacivirus explode all trees	1
	#2 MeSH descriptor Hepatitis C explode all trees	14
	#3 MeSH descriptor Hepatitis C Antibodies explode all trees	0
	#4 (hepatitis c):ti,ab,kw	32
	#5 MeSH descriptor Mass Screening explode all trees	20
	#6 (screening):ti,ab,kw	363
	#7 (#1 OR #2 OR #3 OR #4)	32
	#8 (#5 OR #6)	363
	#9 (#7 AND #8)	2
Note		

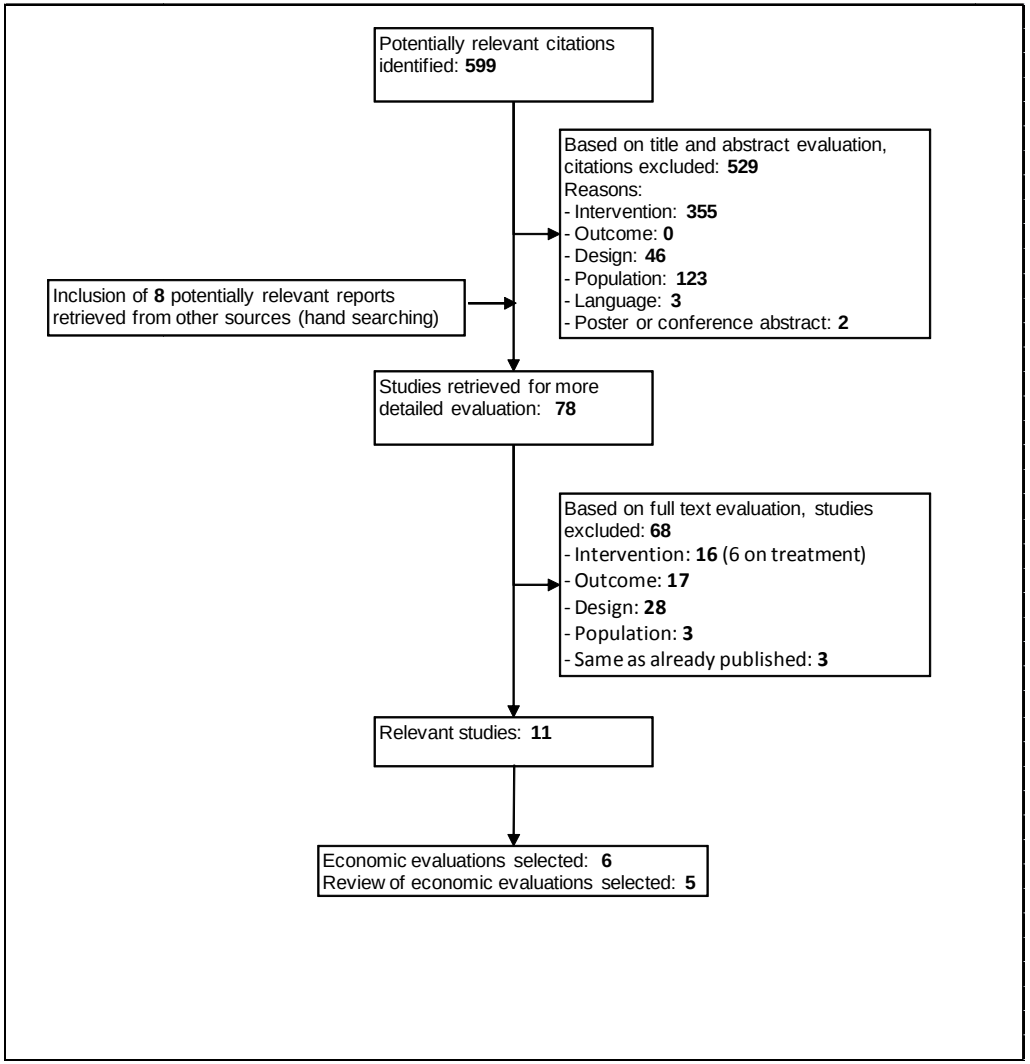
Date	September 23, 2010		
Database (name + access)	Embase		
Date covered	1974 to present		
Search Strategy	#25	#22 NOT #23 AND [embase]/lim	488
	#24	#22 NOT #23	572
	#23	editorial:it OR letter:it	1062357
	#22	#12 AND #21	619
	#21	#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20	978791
	#20	'value' NEAR/1 'money'	19
	#19	expenditure*:ab,ti NOT energy:ab,ti	17078
	#18	econom*:ab,ti OR cost*:ab,ti OR pric*:ab,ti OR pharmacoeconomic*:ab,ti OR budget*:ab,ti	474167
	#17	'financial management'/exp	228211
	#16	'cost'/exp	197252
	#15	'economics'/exp	187092
	#14	'health care cost'/exp	152816
	#13	'health economics'/exp	474794
	#12	#8 AND #11	5415
	#11	#9 OR #10	474139
	#10	'screening':ab,ti	286818
	#9	'screening'/exp	324726
	#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	67535
	#7	'hepatitis virus non a non b':ab,ti OR 'hepatitis non a non b':ab,ti	272
	#6	'hepatitis c':ab,ti	46988
	#5	'hepatitis c antibody'/exp	5839
	#4	'hepatitis non a non b'/exp	2029
	#3	'hepatitis virus non a non b'/exp	465
	#2	'hepatitis c'/exp	49462
	#1	'hepatitis c virus'/exp	30679
Note			

Date	September 23, 2010			
Database (name + access)	Database of Abstracts of Reviews of Effects (DARE) – CRD databases			
Date covered	1996 to present			
Search Strategy	#	1	MeSH Hepacivirus EXPLODE 1 2 3	18
	#	2	MeSH Hepatitis C EXPLODE 1 2 3	76
	#	3	MeSH Hepatitis C Antibodies EXPLODE 1 2 3	1
	#	4	"hepatitis c"	115
	#	5	MeSH Mass Screening EXPLODE 1 2 3 4 5 6 7	258
	#	6	screening	926
	#	7	# 1 or # 2 or # 3 or # 4	120
	#	8	# 5 or # 6	966
	#	9	# 7 and # 8	5
	#	10	MeSH Economics	1
	#	11	MeSH Costs and Cost Analysis EXPLODE 1	475
	#	12	MeSH Economics, Dental	0
	#	13	MeSH Economics, Nursing	1
	#	14	MeSH Economics, Pharmaceutical	4
	#	15	MeSH Economics, Hospital EXPLODE 1	15
	#	16	MeSH Economics, Medical EXPLODE 1	1
	#	17	(econom* OR cost* OR pric*)	2880
	#	18	pharmacoeconomic*	42
	#	19	"value for money"	8
	#	20	expenditure* NOT energy	40
	#	21	budget*	14
	#	22	#10 or # 11 or #12 or # 13 or # 14 or # 15 or # 16 or # 17 or # 18 or #19 or #20 or #21	3001
	#	23	# 9 and # 22	2
Note				

Date	September 23, 2010			
Database (name + access)	NHS Economic Evaluation Database (NHS EED) – CRD databases			
Date covered	1977 to present			
Search Strategy	#	1	MeSH Hepacivirus EXPLODE 1 2 3	41
	#	2	MeSH Hepatitis C EXPLODE 1 2 3	222
	#	3	MeSH Hepatitis C Antibodies EXPLODE 1 2 3	12
	#	4	"hepatitis c"	231
	#	5	MeSH Mass Screening EXPLODE 1 2 3 4 5 6 7	1501
	#	6	screening	2041
	#	7	# 1 or # 2 or # 3 or # 4	270
	#	8	# 5 or # 6	2350
	#	9	# 7 and # 8	75
	#	10	MeSH Economics	40
	#	11	MeSH Costs and Cost Analysis EXPLODE 1	24333
	#	12	MeSH Economics, Dental	6
	#	13	MeSH Economics, Nursing	22
	#	14	MeSH Economics, Pharmaceutical	645
	#	15	MeSH Economics, Hospital EXPLODE 1	2824
	#	16	MeSH Economics, Medical EXPLODE 1	237
	#	17	(econom* OR cost* OR pric*)	29250
	#	18	pharmacoeconomic*	1977
	#	19	"value for money"	139
	#	20	expenditure* NOT energy	635
	#	21	budget*	312
	#	22	#10 or # 11 or #12 or # 13 or # 14 or # 15 or # 16 or # 17 or # 18 or #19 or #20 or #21	29284
	#	23	# 9 and # 22	75
Note				

Date	September 23, 2010			
Database (name + access)	Health Technology Assessment Database (HTA) – CRD databases			
Date covered	1989 to present			
Search Strategy	#	1	MeSH Hepacivirus EXPLODE 1 2 3	3
	#	2	MeSH Hepatitis C EXPLODE 1 2 3	56
	#	3	MeSH Hepatitis C Antibodies EXPLODE 1 2 3	1
	#	4	"hepatitis c"	59
	#	5	MeSH Mass Screening EXPLODE 1 2 3 4 5 6 7	503
	#	6	screening	699
	#	7	# 1 or # 2 or # 3 or # 4	68
	#	8	# 5 or # 6	785
	#	9	# 7 and # 8	9
	#	10	MeSH Economics	9
	#	11	MeSH Costs and Cost Analysis EXPLODE 1	1042
	#	12	MeSH Economics, Dental	0
	#	13	MeSH Economics, Nursing	0
	#	14	MeSH Economics, Pharmaceutical	1
	#	15	MeSH Economics, Hospital EXPLODE 1	7
	#	16	MeSH Economics, Medical EXPLODE 1	6
	#	17	(econom* OR cost* OR pric*)	2471
	#	18	pharmacoeconomic*	9
	#	19	"value for money"	21
	#	20	expenditure* NOT energy	48
	#	21	budget*	106
	#	22	#10 or # 11 or #12 or # 13 or # 14 or # 15 or # 16 or # 17 or # 18 or #19 or #20 or #21	2559
	#	23	# 9 and # 22	5
Note				

1.2.3. Flow chart



1.2.4. Data extraction forms

Authors (Year)	Castelnuovo E, Thompson-Coon J, Pitt M, Cramp M, Siebert U, Price A, Stein K (2006)
Funding	NHS R&D HTA Programme Stein K: Grant from Schering Plough (UK) to carry out work on the cost-effectiveness of combination therapy for hepatitis C. Cramp M: Educational grants from Roche and Schering Plough to support research and development + NHS R&D grant Siebert U: HTA grant from the German Agency of HTA + grants from Essex Pharma GmbH Thompson-Coo J: Grant from The Hepatitis C Trust
Country	UK
Design	CEA-CUA
Model	For testing and diagnosis: Decision tree For long-term consequences: Markov state-transition model (developed in Excel): cycle length: 3 months
Perspective	National Health System
Time window	Lifetime
Interventions	**Groups:** 1) Systematic case-finding 2) Non-case-finding: spontaneous presentation for investigation **Settings explored:** 1) General case 2) General practice: target approach and population approach 3) Prisons: scenario 1 (During the induction program, a general lecture on blood-borne viruses was delivered) and scenario 2 (During the induction program, a lecture with a specific focus on IDU as risk factor for HCV was delivered) 4) Drug and alcohol services **Screening and diagnosis:** Initial test: ELISA; If positive: PCR at attendance in secondary care (with repeat ELISA); For genotype 1 or 4: offer of liver biopsy. **Treatment:** PegIFN α-2a or α-2b and ribavirin + reduction in alcohol consumption advised
Population	1) General case: Former IDUs 2) General practice: - Target approach: All patients with a history of injecting drug use (current and former IDUs) - Population approach: All patients aged 30-54 years attending for a non-urgent appointment 3) Prisons: All new prisoners entering a prison within the target age range of 25-39 years (24% prevalence of current and former IDUs) 4) Drug and alcohol services: All clients assessed for HBV vaccinations
Assumptions	Characteristics of baseline cohort Average age at presentation: 37-year old Severity of liver disease at presentation: Mild hepatitis: 75%; Moderate hepatitis: 13.7%; Severe hepatitis: 5.4% and cirrhos is: 5.9%. It was assumed that severity of liver disease at presentation was the same in the 2 groups. This severity is expected to be underestimated in the "non-case-finding" group and overestimated in the "case-finding group". Average length of infection (years) (SD): 20.8 (5.9) Genotype (for HCV infected people): Trent HCV Database: Genotype 2 or 3 : 51.6%; Genotypes 1, 4 or 5 = 48.4%.
	Screening parameters

Testing and diagnosis take place within a 3-month period (=Markov cycle length).

Setting	ELISA acceptance rate (%)	Proportion of positive results (%)
General case	49	49
Prison scenario 1	8.5	16
Prison scenario 2	12	42
General practice, targeted approach	49	49
General practice, population approach	10	12.5
Drug and alcohol services	49	68

Effectiveness of combination antiviral therapy for HCV using pegylated interferon and ribavirin
Sources: Shepherd 2004[2], adapted to take into account compliance to treatment
Important assumption: Treatment duration = 48 weeks for all patients receiving combination therapy; 12% of patients had absolute contra-indications to treatment and were therefore not treated; patients with genotypes 1 or 4 and mild disease were only treated if they progress to moderate hepatitis.
Treatment acceptance: 60.5% for genotypes 2 or 3 and 55% for genotypes 1 or 4.

SVR, Genotypes 1 or 4 (mild, moderate or severe hepatitis)	54
SVR, Genotypes 2 or 3 (mild, moderate or severe hepatitis)	94
SVR, Genotypes 1 or 4 (cirrhosis)	24
SVR, Genotypes 2 or 3 (cirrhosis)	48

Progression of HCV disease

1) Spontaneous clearance during the acute phase: Trent HCV Database: 18.6% (Best available UK estimate)
2) Progression between mild hepatitis, moderate hepatitis, severe hepatitis and cirrhosis

		Cumulative risk, tested individuals who also receive alcohol advice (%)		Cumulative risk, untested individuals, no alcohol advice (%)	
		20 years past infection	30 years past infection	20 years past infection	30 years past infection
Mild to moderate hepatitis	All	6.19	12.08	6.2	12.1
	Male	6.31	12.31	6.32	12.33
	Female	5.93	11.6	5.94	11.62
Moderate to severe hepatitis	All	7.52	14.59	7.54	14.62
	Male	7.67	14.87	7.68	14.89
	Female	7.22	14.03	7.23	14.05

Severe hepatitis to cirrhosis	All	8.75	16.87	8.77	16.9
	Male	8.92	17.18	8.94	17.21
	Female	8.4	16.22	8.42	16.25

3) Long-term consequences (progression rates)

Progression from cirrhosis to decompensated cirrhosis	5.8%/year
Incidence of HCC	2.5%/year
Probability of receiving a liver transplant	5%/year
Progression to decompensation following liver transplant	6.9%/year
Mortality from decompensated cirrhosis	49% at 5 years
Mortality from HCC	91%/year
Longer term mortality after liver transplant	31.2% at 10 years
Background mortality	Variable - by age and sex

Utilities

State	Non-symptomatic	Symptomatic	During treatment	Sustained response	Non-responder
Mild	0.79 (0.024)	0.75 (0.024)	0.65 (0.002)	0.82 (0.005)	0.76 (0.003)
Moderate	0.68 (0.03)	0.64 (0.030)	0.55 (0.003)	0.72 (0.007)	0.65 (0.0042)
Severe	0.60 (0.03)	0.56 (0.030)	0.50 (0.003)	0.66 (0.006)	0.61 (0.006)
Cirrhotic	0.55 (0.054)	0.51 (0.054)	0.46 (0.005)	0.61 (0.006)	0.55 (0.0038)
HCC	0.45 (0.056)	0.41 (0.056)			
Decompensated liver disease	0.45 (0.056)	0.45 (0.056)			
Waiting list for liver transplant	0.45 (0.056)				

Costs of testing and diagnosis:

Item	cost (£)	Standard error (£)	Source
Cost of ELISA test	17	6.7	Mild HCV Trial: Wright 2006[3]

Costs of communicating results, ELISA negative	2.7	0.27	Assuming one letter to patient and 5 minutes of nurse time to organise mail
Costs of counseling, communicating results, offer referral in ELISA positive individuals	30.7	3.7	One letter to patient + one GP visit to discuss results + cost of referral to specialist services (Curtis 2004)[4]
Cost PCR	130	10.17	Assuming one ELISA test (£17, SE £6.70), one PCR test (£56, SE £10.17) and one specialist consultation (£57, SE £5.70) (Curtis 2004)[4]
Cost of communicating result, PCR negative	2.7	0.27	Assuming one letter to patient and 5 minutes of nurse time to organise mail (Curtis 2004)[4]
Cost of genotyping	94	10.1	Cost of test only: Wright 2006[3]
Cost of offering liver biopsy to individuals who are genotype 1 or 4	57	5.7	Cost of one specialist consultation, counselling and referral (Curtis 2004)[4]
Cost of counseling and communicating PCR results to individuals who are not eligible for treatment	109.25	10.93	Cost of consultation, cost of counselling and referral to consultation with Drug and Alcohol Services (Curtis 2004)[4]
Cost of counseling and harm reduction advice	110.5	11.05	Consultation, cost of alcohol advice (Curtis 2004)[4]
Cost of liver biopsy	249	11.37	
Cost of communicating non-eligibility for treatment, counseling on harm reduction after liver biopsy	79	7.9	Specialist consultation, cost of alcohol advice (Curtis 2004)[4]
Cost of offering treatment (i.e. referral for treatment)	88.5	8.85	Consultation specialist and nurse appointment (Curtis 2004)[4]

Disease state costs and treatment costs: annual cost in £ (standard error)

Disease state		Combination therapy [a]	Sustained response	No response
Mild	138 (40)[b]	11 425[b]	259 (348)	118 (26)[b]

	Moderate	717 (76)[b]	11 529[b]	717 (76)	730 (64)[b]
	Severe	717 (76)	11 529[b]	717 (76)	717 (76)
	Cirrhotic	1 138 (224)	11 938[b]	1 138 (224)	1 138 (224)
	HCC	8 127 (1 910)			
	Decompensated liver disease	9 120 (1 519)			
	Waiting list for liver transplant	8 413 (930)			
	Liver transplant	27 330 (2 885)			
	Post-transplant decompensated	9 458 (2 548)[c]			
	(inflated by costs of further transplants)	9 538			
	Post-transplant healthy	1 385 (355)			

Source: Wright 2006[3];
[a] Total treatment costs included the cost of PegIFN (A 50:50 split was assumed in the use of the two preparations of PegIFN cur rently available in the UK) and ribavirin (where appropriate), outpatient visits, inpatient stays, investigations, procedures and other drugs. It was assumed that the duration of treatment was the same for mild to cirrhotic patients, that treatment duration with standard IFN and PegIFN w ere equal, and that resource consumption for all other types of health services when treated with PegIFN was equal to that when treated with stan dard IFN.
[b] Wright 2006 inflated with the cost of PegIFN from the British National Formulary;
[c] Liver transplant study of the Department of Health (reported in Wright 2006).

Data source for costs	See "assumptions"
Cost items included	£2004. Direct health care costs (see also assumptions)
Data source for outcomes	Systematic review of the literature. Prevalence: Bird et al. 2001 (pooled estimate): 49% 95%CI: 38-61%. Utilities: Wright et al 2006 and Ratcliffe 2002 (for LT), using EQ-5D.
Discounting	Costs: 6% (annual) Outcomes: 1.5% (annual)
Costs	Costs in £2004

Setting	Discount	Case-finding/1000	Non-case-finding/1000	Incremental/patient
General	Discounted	2 358 060	1 598 979	759
	Undiscounted	6 242 849	5 095 115	1 148
In prison: Scenario 1	Discounted	796 912	515 165	282
	Undiscounted	2 129 945	1 639 954	490

In prison Scenario 2	Discounted	1 965 836	1 355 167	611
	Undiscounted	5 451 764	4 313 040	1 139
In general practice: Target	Discounted	2 357 013	1 598 869	758
	Undiscounted	6 241 761	5 094 942	1 147
In general practice: Population	Discounted	570 446	400 193	170
	Undiscounted	1 607 480	1 276 695	331
In drug and alcohol services	Discounted	2 443 336	1 613 513	830
	Undiscounted	6 239 392	5 138 766	1 101

Outcomes

Life-year gained:

Setting	Discount	Case-finding/1000	Non-case-finding/1000	Incremental/patient
General	Discounted	30 008	29 971	0.038
	Undiscounted	41 016	40 958	0.058
In prison: Scenario 1	Discounted	30 258	30 250	0.008
	Undiscounted	41 392	41 379	0.013
In prison Scenario 2	Discounted	30 057	30 034	0.023
	Undiscounted	41 090	41 054	0.036
In general practice: Target (as reported)	Discounted	30 057	30 034	0.023
	Undiscounted	41 090	41 054	0.036
In general practice: Population	Discounted	30 285	30 278	0.007
	Undiscounted	41 433	41 422	0.01
In drug and alcohol services	Discounted	30 011	29 968	0.044
	Undiscounted	41 020	40 953	0.066

NB: results for general practice (target) were wrongly reported and should have been as followed:

Setting	Discount	Case-finding/1000	Non-case-finding/1000	Incremental/patient
In general practice: Target	Discounted	30 008	29 971	0.038

		Undiscounted	41 016	40 958	0.058

QALYs:

Setting	Discount	Case-finding/1000	Non-case-finding/1000	Incremental/patient
General	Discounted	9 050	9 004	0.046
	Undiscounted	12 357	12 286	0.071
In prison: Scenario 1	Discounted	2 906	2 892	0.014
	Undiscounted	3 969	3 947	0.022
In prison Scenario 2	Discounted	7 641	7 604	0.037
	Undiscounted	10 434	10 376	0.058
In general practice: Target	Discounted	9 050	9 004	0.046
	Undiscounted	12 357	12 286	0.071
In general practice: Population	Discounted	2 272	2 261	0.011
	Undiscounted	3 103	3 085	0.017
In drug and alcohol services	Discounted	9 119	9 071	0.047
	Undiscounted	12 451	12 378	0.072

Cost-effectiveness

CEA:

Setting	Discount	ICER (£/LYG)
General	Discounted	20 084
	Undiscounted	19 786
In prison: Scenario 1	Discounted	33 770
	Undiscounted	37 466
In prison Scenario 2	Discounted	26 773
	Undiscounted	31 931
In general practice: Target	Discounted	20 059
	Undiscounted	19 771
In general practice: Population	Discounted	25 665

	Undiscounted	31 847
In drug and alcohol services	Discounted	19 059
	Undiscounted	16 569

CUA:

Setting	Discount	ICER (£/QALY)
General	Discounted	16 514
	Undiscounted	16 190
In prison: Scenario 1	Discounted	20 083
	Undiscounted	22 153
In prison Scenario 2	Discounted	16 484
	Undiscounted	19 535
In general practice: Target	Discounted	16 493
	Undiscounted	16 177
In general practice: Population	Discounted	15 493
	Undiscounted	19 109
In drug and alcohol services	Discounted	17 515
	Undiscounted	15 207

Sensitivity analysis

One-way sensitivity analysis for the general case:
The one-way sensitivity analysis has shown that few parameters changes had an important impact on results. Parameters changes which g ave an ICER beyond £30 000/QALY were: 1) The SVR rate:

- <54.6% for patients with chronic hepatitis and genotypes 2 or 3
- <30.9% for patients with chronic hepatitis and genotypes 1 or 4
- <27.5% for patients with cirrhosis

2) The discount rate (tested: 1.5%, 3.5%, 6%):

- Outcomes: 3.5%; Costs: -1.5%
- Outcomes: 3.5%; Costs: 3.5% (= NHS guidelines!)
- Outcomes: 6.0%; Costs: -1.5%
- Outcomes: 6.0%; Costs: 3.5%
- Outcomes: 6.0%; Costs: 6.0%

3) The rate of spontaneous presentation and re-presentation (if maintained equal):

	- >5% for both 4) The following Quality of Life estimates had an important impact on results (details not reported): - Decrement in QoL at presentation - Decrement in QoL during treatment - Improvement in QoL following SVR in treated individuals - Improvement in QoL due to the avoidance of long-term consequences of HCV
	Probabilistic sensitivity analysis: This analysis shows uncertainty. In a limited number of cases, "case-finding" was dominated (i.e. less effective and more costly). Only figures such as a cost-effectiveness plane were reported but details such as the 95% CI of the ICER or the probability to be cost-effective at a threshold of £30 000 were not mentioned. They have to be deduced from the figures (the probability to be cost-effective at a threshold of £30 000 seems to vary between about 60% and about 80% according to the setting.
Conclusions	With an accepted willingness to pay of £30 000/QALY, case-finding for HCV is likely to be cost-effective but considerable uncertainty remains. Most of the uncertainty arises from the estimates of utility. The cost-effectiveness of case-finding is similar in all investigated settings. Moreover, case-finding is likely to be more cost-effective in older people than in those more recently infected.
Remarks (to be completed)	1) The choice of the discount rate was unfair and greatly influenced the results. 2) The genotypes distribution does not correspond to the Belgian setting 3) They assumed a treatment duration of 48 weeks for all patients without stopping rules. This does not reflect current clinical guidance: Ceasing treatment at 12 weeks if a viral load is not shown on quantitative PCR or treating patients with genotypes 2 or 3 only during 24 weeks. This assumption slightly overestimates treatment cost, which will bias against case-finding. 4) The possibility of relapse in injecting was not taken into account, which went in favor of the case-finding strategies. However, the size of the effect is not estimable. 5) Concerning the SVR rate, more information on the effectiveness of treatment in routing practice is needed. A poor compliance may lead to an ICER exceeding £30 000/QALY. 6) Spontaneous and re-presentation rates were difficult to model accurately and the spontaneous presentation rate assumed was probably overestimated. The size of this bias was not clear. 7) It was assumed that treatment eligibility and effectiveness was the same in all setting. Data specific for all setting are needed. 8) A more severe case-mix at presentation would tend to make the cost-effectiveness of case-finding more favorable. 9) The background mortality estimates came from the general population and were not specific to former IDU. We can expect that the risk of mortality would be higher in former IDU. This bias would be in favor of the case-finding strategy. 10) The estimation of the contribution of alcohol reduction to the cost-effectiveness of case-finding may be underestimated. Greater benefits may be seen in practice. 11) The impact of indirect productivity cost was not considered

Authors (Year)	Sutton AJ, Edmunds WJ, Sweeting MJ, Gill ON (2008)
Funding	Prison Health at the department of Health for England and Wales
Country	UK
Design	CUA
Model	For testing and diagnosis: Decision tree For long-term consequences: Markov state-transition model (developed in Excel), cycle length: 3 months
Perspective	National health care services (NHS)
Time window	80 years
Interventions	**Groups:** 3) Systematic case-finding offered on reception into prison + possibility of spontaneous presentation in a community location 4) Non-case-finding: spontaneous presentation in a community location **Screening and diagnosis:** Initial test: ELISA; If positive: PCR; if positive: genotyping. (Biopsy not necessary) **Treatment:** PegIFN and ribavirin during 24 weeks for genotypes 2 or 3 and 48 weeks for other genotypes [if no early virological response by 12

<table>
<tr><td></td><td>weeks, the therapy was stopped].</td></tr>
<tr><td>Population</td><td>All individuals who enter prison over a 3-month period, including non IDUs, current IDUs and former IDUs</td></tr>
<tr><td>Assumptions</td><td>HCV infections in non-IDUs are assumed not to occur
80% of infections are assumed to develop chronic HCV and those who do not develop chronic HCV may become re-infected but are 4x less likely to become chronically infected than those infected for the first time.</td></tr>
<tr><td></td><td>Characteristics of baseline cohort

Average age at presentation: Stratification per age:

- 15-24 years (average 20)
- 25-34 years (average 29)
- 35+ (average 44)
- Total (average 27)
Severity of liver disease for HCV infected person:
<table><tr><th>Age group</th><th>Mild (%)</th><th>Moderate (%)</th><th>Cirrhosis (%)</th></tr><tr><td>15–24</td><td>95.5</td><td>4.5</td><td>0.0</td></tr><tr><td>25–34</td><td>91.4</td><td>7.9</td><td>0.7</td></tr><tr><td>35+</td><td>82.9</td><td>15.1</td><td>2.0</td></tr><tr><td>Total</td><td>90.1</td><td>8.9</td><td>1.0</td></tr></table>
Average length of infection (years) (SD): Not reported

Genotype (for HCV infected people): Genotypes 2 or 3 : 51.6% and other genotypes: 48.4%

Proportion of individual with raised ALT:

- Mild chronic hepatitis: 0.57
- Moderate chronic hepatitis: 0.825</td></tr>
<tr><td></td><td>Screening parameters: Base case (Range)

All prisoners where undiagnosed on reception into prison.

In the case-finding group, only prisoners who responded in the positive to questions

regarding current or former injecting drug use were offered Elisa testing.

Testing and diagnosis took place during a 3 month period (= cycle length)

It was assumed that a biopsy was not necessary.

Rate of spontaneous presentation in a community setting:

- In the non case-finding group: 3.75% per year
- In the case-finding group: 7.5% per year
<table><tr><td>% IDUs that report IDU use (current or former)</td><td>75% (7.5%)</td></tr></table></td></tr>
</table>

% of those offered who accept ELISA testing in prison	10.25% (1.25%)
% of those offered who accept ELISA testing in community	49% (4.9%)
ELISA sensitivity	97.2% (0.01)
ELISA specificity	100%
% of those offered who accept PCR testing in prison	92% (0.035)
% Acceptance of PCR testing in the community	39% (0.026)

Source: Castelnuovo 2006, Skipper 2003, Sutton 2006, Horne 2004, Serfaty 1997, and Colin 2001

Effectiveness of combination antiviral therapy for HCV using pegylated interferon and ribavirin - %(Standard error)

Contraindications to treatment	12% (0.8%)
Acceptance of treatment	
Genotypes 1 or 4 in the community	55% (3.67%)
Genotypes 2 or 3 in the community	60.5% (4.03%)
All genotypes in a prison setting	50% (20.04%)
Treatment initiated in the community:	
24 weeks adherence	92% (9.2%)
48 weeks adherence	76% (7.6%)

Sources: Coon 2006, Skipper 2003, Hadziyannis 2004 and Castelnuovo 2006

EVR rate at 12 weeks	
Genotype 1 mild/mode	75% (SE 7.5%)
Genotype 1 cirrhosis	75% (SE 7.5%)
SVR rate at 24 weeks	
Genotypes 2 an 3 mild/moderate	87% (SE 8.7%)
Genotypes 2 and 3 cirrhosis	75% (SE 7.5%)
SVR rate at 48 weeks	
Genotypes 1 or 4 mild/moderate	57% (SE 5.7%)
Genotypes 1 or 4 cirrhosis	41% (SE 4.1%)

Source: NICE 2004 and Hadziyannis 2004

Progression of HCV disease: Base case (95% CI)

- It was assumed that current alcohol intake did not influenced the risk of progression
- Additional risk of death for current IDU (due to the risk of overdose): base case: 0%; sensitivity analysis: 0.77% per

year (for everybody?)
- HCV-RNA negatives individuals do not become infected in the future (sensitivity analysis: 0.05/person/year were infected)

Age group	Low ALT				High ALT			
	Mild to moderate hepatitis		Moderate to cirrhosis		Mild to moderate hepatitis		Moderate to cirrhosis	
0–29	0.007	(0.004)	0.007	(0.005)	0.021	(0.006)	0.022	(0.011)
30–39	0.004	(0.003)	0.007	(0.005)	0.013	(0.006)	0.022	(0.011)
40–49	0.007	(0.004)	0.007	(0.005)	0.02	(0.008)	0.022	(0.011)
>50	0.024	(0.011)	0.007	(0.005)	0.068	(0.0015)	0.022	(0.011)

Source: Sweeting 2006

Cirrhosis – decompensated cirrhosis	0.04 (0.004)
Cirrhosis or decompensated cirrhosis – HCC	0.025 (0.0025)
Decompensated cirrhosis – death	0.13 (0.013)
HCC – death	0.43 (0.043)
Decompensated cirrhosis/HCC – liver transplant	0.02 (0.0056)
Liver transplant – death (year 1)	0.15 (0.015)
Liver transplant – death (subsequent years)	0.03 (0.003)
All-cause death	Variable according to age
Additional overdose mortality rate	0.77% per year

Source: Castelnuovo 2006, Fattovich 1997, Siebert 2003, Wright 2006, Office for National statistics: London (death rate) 2005, and de Angelis 2004

Screening and diagnosis costs: (£2004)

Administer lecture/patient (Assume 10 patients per lecture)	5.40 (0.54)
Cost verbal test IDU status	10.98 (1.10)
Pre-ELISA test counsel	54.88 (5.49)
Total cost to administer an ELISA test	22.98 (2.30) (Including £12 cost of ELISA test virus)
Total cost to administer PCR test	67.98 (6.80)
Cost of communicating results	
ELISA/PCR negative	10.98 (1.10)

ELISA/PCR positive	54.88 (5.49)
Cost of genotyping	94 (10.10)
Cost of offering treatment (i.e. referral for treatment)	88.50 (8.85)

Source: Sutton 2006

Disease state costs and treatment costs:
Monitoring cost in a prison setting = monitoring cost in a community setting.

Treatment cost	£2004
Genotypes 2 and 3, pegylated interferon and ribavirin for 24 weeks	4827
Other genotypes pegylated interferon and ribavirin for 48 weeks	10 986
Cost of monitoring during first 24 weeks of treatment	714
Cost of monitoring during treatment weeks 24–48	235

NICE 2006, British national Formulary 2005 and Shepherd 2004

Disease state	£2004	SVR	Non-SVR
Mild (diagnosed)	138 (40)	259 (348)	118 (26)
Moderate (diagnosed)	717 (76)	717 (76)	730 (64)
Cirrhosis (diagnosed)	1 138 (224)	1138 (224)	1138 (224)
Mild (not diagnosed)	0		
Moderate (not diagnosed)	0		
Cirrhosis (not diagnosed)	0		
HCC	8 127 (1 910)		
Decompensated liver disease	9 120 (1 519)		
Liver transplant	29 670.38 (2 967)		
Liver transplant follow-up (0-12 months)	10 267.93 (1027)		
Liver transplant follow-up (12-24 months)	1503.60 (150)		

Source: Wright 2006

Utilities: Mean (standard error)

<table>
<tr><td></td><td>
<table>
<tr><th>State</th><th>Undiagnosed</th><th>Diagnosed</th><th>During treatment</th><th>Sustained response</th><th>Nonresponder</th></tr>
<tr><td>Mild</td><td>0.79 (0.024)</td><td>0.75 (0.024)</td><td>0.65 (0.002)</td><td>0.82 (0.005)</td><td>0.76 (0.003)</td></tr>
<tr><td>Moderate</td><td>0.64 (0.03)</td><td>0.60 (0.03)</td><td>0.525 (0.003)</td><td>0.69 (0.0065)</td><td>0.63 (0.0051)</td></tr>
<tr><td>Cirrhotic</td><td>0.55 (0.054)</td><td>0.51 (0.054)</td><td>0.46 (0.005)</td><td>0.61 (0.006)</td><td>0.55 (0.0038)</td></tr>
<tr><td>HCC</td><td></td><td>0.45 (0.056)</td><td></td><td></td><td></td></tr>
<tr><td>Decompensated cirrhosis</td><td></td><td>0.45 (0.056)</td><td></td><td></td><td></td></tr>
<tr><td>Post-liver transplant</td><td></td><td>0.67 (0.067)</td><td></td><td></td><td></td></tr>
</table>
Sources: Wright 2006 and Castelnuovo 2006 (using EQ-5D)
</td></tr>
<tr><td>Data source for costs</td><td>See above (no method or justification was given but is based on the study of Castelnuovo 2006 in which methods and justifications were given)</td></tr>
<tr><td>Cost items included</td><td>Direct health care costs in £2004</td></tr>
<tr><td>Data source for outcomes</td><td>See above (no method or justification was given but is based on the study of Castelnuovo 2006 in which methods and justifications were given)</td></tr>
<tr><td>Discounting</td><td>Costs: 3.5%
Benefits: 3.5%</td></tr>
<tr><td>Costs</td><td>NHS direct health care cost: £2004
<table>
<tr><th>Discounting</th><th>Case-finding/1000</th><th>Noncase-finding/1000</th><th>Incremental/patient</th></tr>
<tr><td>With
Without</td><td>1 012 509
2 368 963</td><td>737 798
1 963 344</td><td>275
406</td></tr>
</table>
</td></tr>
<tr><td>Outcomes</td><td>QALYs:
<table>
<tr><th>Discounting</th><th>Case-finding/1000</th><th>Noncase-finding/1000</th><th>Incremental/patient</th></tr>
<tr><td>With
Without</td><td>1650
3302</td><td>1644
3266</td><td>0.005
0.036</td></tr>
</table>
</td></tr>
<tr><td>Cost-effectiveness</td><td>With discounting:
<table>
<tr><th>Age group</th><th>£/QALY</th></tr>
<tr><td>15-24
25-34
35+</td><td>40 227
50 048
128 424</td></tr>
<tr><td>Total</td><td>54 852</td></tr>
</table>
Without discounting: £11 257/QALY (Total)</td></tr>
<tr><td>Sensitivity analysis</td><td>Univariate sensitivity analysis:
When the treatment adherence at 48 weeks, the representation rate in the case-finding group, the discount rate of outcomes and the Chronic HCV progression rates were varied, the case-finding strategy became a dominated strategy. The impact of utility estimates was not reported.</td></tr>
<tr><td></td><td>Probabilistic sensitivity analysis:
Results are uncertain and in some cases, the case-finding strategy was dominated by the non case-finding strategy. Case-finding strategy could only be considered as cost-effective at a willingness to pay threshold of £58 000/QALY.</td></tr>
<tr><td></td><td>Scenario analysis according to the discount rate:</td></tr>
</table>

	Discount rates / Incremental cost / Incremental effectiveness / ICER 3.5% costs - 3.5% benefits / £8 510 479 / 155.2 / £54 852/QALY 6% costs - 1.5% benefits / £6 864 272 / 511.9 / £13 408/QALY No discounting / £12 565 972 / 1116.2 / £11 257/QALY Scenario analysis according to the impact of HCV knowledge on QoL estimates Incremental cost / Incremental effectiveness / ICER Impact / £8 510 479 / 155.2 / £54 852/QALY No impact / £8 510 479 / 219.2 / £38 817/QALY
Conclusions	The screening of HCV is not likely to be a cost-effective strategy but results are uncertain. More data on the chronic HCV progression rate are needed.
Remarks	1) The impact of utility estimates was not reported but was expected to be important. 2) The distribution of genotypes does not correspond to the Belgian setting 3) The impact of indirect productivity cost was not considered

Authors (Year)	Plunkett BA, Grobman WA (2004)
Funding	Institute for Health Services Research and Policy studies at Northwestern University and National Research Service Award from the agency for Healthcare Research and Quality
Country	USA
Design	CUA
Model	For testing and diagnosis: Decision tree For long-term consequences: Markov state-transition model (developed in TreeAge): cycle length: 1 year
Perspective	Health care payer
Time window	Lifetime
Interventions	**Groups:** 1) No HCV screening in pregnancy 2) HCV screening in pregnancy and subsequent treatment for progressive disease 3) HCV screening in pregnancy, subsequent treatment for progressive disease and elective cesarean delivery to avert perinatal transmission **Screening and diagnosis:** Third-generation enzyme immunoassay test followed by a confirmatory PCR test (+ genotyping). **Treatment:** 1.5 µg/kg PegIFN α-2b + 800 mg Ribavirin during 48 weeks
Population	All asymptomatic, HIV-negative pregnant women without risk factors for HCV infection and their children
Assumptions	Characteristics of baseline cohort Average age at presentation: 30 years for the pregnant woman; and 20 years for the children Severity of liver disease at presentation: mild chronic hepatitis Average length of infection (years) (SD): Not reported Genotype (for HCV infected people): Not specified and no stratification by genotype

Screening parameters: Base case (Range)

Acceptance rate: 85% (85%-100%)

Prevalence of HCV infection: 1% (1%-10%)

Prevalence of chronic HCV disease: 74% (74%-85%)

Sensitivity of the third-generation enzyme immunoassay test: 98.6% (97.0%-99.9%)

Specificity of the third-generation enzyme immunoassay test: 99.3% (99.0%-99.9%)

Sensitivity of the PCR test: 100%

Specificity of the PCR test: 98% (97.0%-99.0%)

Effectiveness of combination antiviral therapy for HCV using pegylated interferon (%)
Patients were only treated when they reached the stage of moderate chronic hepatitis.
Proportion of treated patients at the stage of moderate chronic hepatitis: Screening : 70% (20%-100%); No-screening: 20%
SVR rate: 54%

Progression of HCV disease: Base case (95% CI)

Infected neonate remained in the mild hepatitis health state for a latency period

of 20 years.

Perinatal transmission to spontaneous clearance in first year of life	0.1 (0-0.2)
Mild hepatitis to remission	0.002 (0.001-0.004)
Mild chronic hepatitis to moderate chronic hepatitis: Mother:	
Moderate chronic hepatitis to compensated cirrhosis: Mother:	
Compensated cirrhosis to decompensated cirrhosis	0.039 (0.02-0.083)
Compensated cirrhosis to HCC	0.015 (0.005-0.02)
Decompensated cirrhosis to liver transplantation	0.031 (0.01-0.062)
Decompensated cirrhosis to HCC	0.015 (0.01-0.02)
Decompensated cirrhosis to death	0.129 (0.065-0.193)
HCC to death	0.427 (0.33-0.86)
Liver transplantation to death (initial year)	0.21 (0.06-0.42)
Liver transplantation to death (subsequent year)	0.057 (0.024-0.11)
Background mortality	

	Unknown or negative HCV status	Screened positive for HCV
Probability of elective cesarean delivery	0.123	0.843 (0.843-1)
Probability of emergent cesarean delivery	0.145	0.043
Probability of vaginal delivery	0.732	0.114 (0-0.114)

	Probability of perinatal transmission
Elective cesarean delivery	0 (0-0.077)
Emergent cesarean delivery	0.077 (0.059-0.12)
Vaginal delivery	0.077 (0.059-0.12)

Sources: Multiple sources given (22 references) without any justification.

Screening and diagnostic costs:

Infants born to women positive for HCV PCR received 3 serial HCV PCR tests over the first 18 months of life

Variable	2003 Base case ($)	Range ($)
Pretest counseling	34.50	14.70-34.50
Posttest counseling for negative test result	48.60	8.00-52.00
Posttest counseling for positive test result	121.40	23.30-121.40
Enzyme immunoassay, 3rd generation	47.80	28.40-67.70
PCR	127.70	99.50-156.00
Genotype	150.70	-

Sources: Grobman 1999 and Mauskopf 1996 (studies on the screening of HIV); Genotypes: Singer 2001 (screening of HCV)

Disease state costs and treatment costs:

Variable	2003 Base case ($)	Range ($)
Treatment cost (including office visits and laboratory services)	14 138.0	11 310-16 964
Delivery cost		
Elective cesarean delivery	6 523.0	5326-7788
Emergent cesarean delivery	8 155.0	6524-9786
Vaginal delivery	3 387.0	3387-5083
Infant testing	383.0	298-468
Disease state annual cost		
Mild hepatitis (known disease)	118.5	59-391
Mild hepatitis (not diagnosed)	0	not specified
Moderate hepatitis	118.5	59-391

Compensated cirrhosis	177.2	89-521
Decompensated cirrhosis	23 914.0	11 957-38 045
Hepatocellular cancer	17 609.0	10 870-29 349
Remission	0.0	0-109
Liver transplantation, initial year	118 483.0	89 134-32 9361
Liver transplantation, subsequent years	23 696.0	11 957-31 740

Sources:
Treatment cost: Manns 2001, Wong 2000 and Cohen 2002
Delivery cost: Singer 2001, Grobman 1999, Traynor 1998, and Rouse 1996
Disease states: Bennett 1997 and Wong 2000

Utilities:

Variable	Base case	Range
Remission	1	-
Mild hepatitis (known disease)	0.96	0.96-1.0
Mild hepatitis (not diagnosed)	1	-
Moderate hepatitis	0.92	0.82-0.98
Compensated cirrhosis	0.85	0.5-0.90
Decompensated cirrhosis	0.6	0.5-0.88
HCC	0.25	0.1-0.5
Liver transplantation, initial year	0.86	0.6-0.9
Liver transplantation, subsequent years	0.95	0.8-0.95
Treatment	0.88	0.82-0.91
Vaginal delivery[a]	-0.0027	(0.0037-0.0017)
Elective cesarean delivery[a]	-0.0035	(0.0045-0.0025)
Emergent cesarean delivery[a]	-0.0046	(0.0056-0.0036)

Sources: Sources: Multiple sources given (6 references) without any justification. [a] Utility values were determined by a panel of 5 experts using the time trade-off technique (6 weeks duration)

Data source for costs	Multiple sources given without any justification or method (see in the assumptions)
Cost items included	2003 US$: Direct health care costs
Data source for outcomes	Multiple sources given without any justification or method (see in the assumptions)
Discounting	Costs: 3% Outcomes: 3% Sensitivity analysis: 3% and 5%
Costs	2003 Direct health care costs in US$:

No screening (1)	Screening with treatment (2)	Addition of cesarean delivery (3)	Incremental cost (2) - (1)	Incremental Cost (3) - (1)
4552	4660	4669	108	117

Outcomes	QALY:

<table>
<tr><td></td><td>
<table>
<tr><td>No screening (1)</td><td>Screening with treatment (2)</td><td>Addition of cesarean delivery (3)</td><td>Incremental cost (2) - (1)</td><td>Incremental Cost (3) - (1)</td></tr>
<tr><td>54.48958</td><td>54.48947</td><td>54.48968</td><td>-0.00011</td><td>0.0001</td></tr>
</table>
</td></tr>
<tr><td>Cost-effectiveness</td><td>ICER:
<table>
<tr><td>Screening with treatment versus no screening</td><td>Dominated</td></tr>
<tr><td>Screening with treatment and cesarean delivery versus no screening</td><td>$1 170 000/QALY</td></tr>
</table>
</td></tr>
<tr><td>Sensitivity analysis</td><td>Univariate sensitivity analysis: No justifications on the ranges tested
No major impact on results (same conclusions)</td></tr>
<tr><td></td><td>Multivariate sensitivity analysis:
Variation of both the perinatal HCV transmission rates and the HCV prevalence.
Results: No major impact on results (same conclusions)</td></tr>
<tr><td></td><td>Probabilistic sensitivity analysis:
Not performed</td></tr>
<tr><td>Conclusions</td><td>The screening of asymptomatic pregnant women for HCV infection is not cost-effective</td></tr>
<tr><td>Remarks</td><td>1) Methods to determine the parameters of the model were not given and no justification of the choices was given.
2) The ranges of variables tested in the univariate sensitivity analysis were not justified. No probabilistic sensitivity analys is was performed
3) The impact of indirect productivity cost was not considered
4) The treatment does not correspond to the Belgian practice (48 weeks)</td></tr>
</table>

Authors (Year)	Kirkizlar E, Faissol DM, Griffin PM, Swann JL (2010)
Funding	AT&T Labs Fellowship Program, Nasa Harriet G. Jenkins Predoctoral Fellowship and National Science Foundation
Country	USA
Design	CUA
Model	Dynamic individual based model (Markov decision process); using MATLAB
Perspective	Health care payer perspective
Time window	Lifetime / Time horizon of the decision: between 15-35 years old (infection of HCV was assumed to be only possible between 15 and 35 years old)
Interventions	Screening (between 15 and 35 years old) versus no screening
Population	1) General population excluding heavy drinkers (= two or more drinks per day = 50g of alcohol) 2) General population including 4.9% of heavy drinkers (according to the 2001-2004 National Health and Nutrition Examination survey) 3) IDU population including 4.9% of heavy drinker
Assumptions	**Model:** Five health states: Healthy; Infected (unaware); Infected (aware); Decompensated cirrhosis including associated complications (HCC, Liver transplant); Death. Individuals were susceptible to HCV infection during the entire time horizon of ages 15-35.
	Characteristics of baseline cohort Age at presentation: 15 years old Genotype (for HCV infected people): Not reported (according to the source for the SVR rate:

Genotypes 2 or 3: 29% - Genotypes 1, 4, 5 or 6: 71%) (Manns 2001)

Severity of liver disease at presentation: Uninfected

Screening parameters:

Screening test not specified (seem to be only an ELISA test according to the source given for the cost)

Effectiveness of combination antiviral therapy for HCV using pegylated interferon and ribavirin - %

SVR rate for patients with chronic hepatitis C	54%	Manns 2001 (RCT)

Progression of HCV disease: Base case (95% CI)

The probability to infect other people is equal to the probability to be infected.
When heavy drinker are aware of their infection, their reduce their alcohol below the 50g/day, which also reduce the risk of infecting other people by 50% (tested in the sensitivity analysis: only 50% reduced their consumption)

Probability of infection for IDU population	0.014	Centers for disease control and prevention 2006 (hepatitis C)
Probability of infection for general population	0.0004	Centers for disease control and prevention 2006 (hepatitis surveillance n°61)
Probability of infection after age 33	0	Assumption
Progression to decompensated cirrhosis (with heavy alcohol consumption)	0.0115	Wiley 1998
Progression to decompensated cirrhosis (without heavy alcohol consumption)	0.0025	Wiley 1998
Death rate in decompensated cirrhosis	0.22	Fattovich 1997
Death rate due to other causes (ages 13–33)	0.0016	Centers for disease control and prevention: Deaths final data for 2003 (National vital statistic report 2006 n°54/13)
Death rate due to other causes (age > 33)	0.015	Centers for disease control and prevention: Deaths final data for 2003 (National vital statistic report 2006 n°54/13)

No justification or method reported

Screening and diagnosis costs:
Screening cost per patient: $24.42 (Stein 2003)

Disease state costs and treatment costs:

Decompensated cirrhosis	25 691	Sullivan 2004
Treatment	22 896	DMD America 2006 (Analy$ource online)

	Cost of infected others: 50 939 — Model calculation
	Utilities:

Infected aware	0.98	Singer 2001
Disease complications	0.48	Hornberger 2006

Data source for costs	Multiples sources were given without any justifications or methods (see in the assumptions).
Cost items included	Direct health care costs in US$ (year not reported).
Data source for outcomes	Multiples sources were given without any justifications or methods (see in the assumptions) .
Discounting	Costs: 3% Outcomes: 3%

Costs

	Overall population without heavy drinkers	Overall population with 4.9% of heavy drinkers	IDU without heavy drinkers	IDU with 4.9% of heavy drinkers
Mean incremental cost	0	$116.82	$3663.6	$3548.9

Outcomes

	Overall population without heavy drinkers	Overall population with 4.9% of heavy drinkers	IDU without heavy drinkers	IDU with 4.9% of heavy drinkers
Mean QALYs gained	0	0.0026	0.1401	0.1625

	Overall population without heavy drinkers	Overall population with 4.9% of heavy drinkers	IDU without heavy drinkers	IDU with 4.9% of heavy drinkers
Mean number of tests	0	1.983	17.591	17.591

Cost-effectiveness

	Overall population without heavy drinkers	Overall population with 4.9% of heavy drinkers	IDU without heavy drinkers	IDU with 4.9% of heavy drinkers
ICER (own calculation)	/	44 930.8	26 149.9	21 839.4

Sensitivity analysis

1) Acceptance rate of the screening test: 70% (100% in the base case)
2) When heavy drinker are aware of their infection, only 50% of them reduced their consumption (100% in the base case)

	Mean QALYs gained	Mean cost	Mean number of tests	ICER (own calculation)
With a screening test acceptance of 70%				
Overall population with 4.9% of heavy drinkers	0.0028	$119.39	1.970	42 639.3
IDU with 4.9% of heavy drinkers	0.1503	$3214.5	12.269	21 387.2

	With only 50% of heavy drinkers having reduced alcohol consumption of awareness of infection Overall population with 4.9% of heavy drinkers: not reported IDU with 4.9% of heavy drinkers: 0.1622 / $3551.1 / 17.591 / 21 893.3
Conclusions	The population who do not consume alcohol excessively (<50g/day) should not be screened. If 4.9% of the population was heavy drinker (>50g/day) and if 100% of heavy drinkers reduced their consumption after the diagnosis of hepatitis C, two tests should be performed (at 20 and 25 years old). If only 50% of heavy drinkers reduced their consumption after HCV diagnosis, no screening test sho uld be performed. A yearly screening of IDUs between 16 and 35 years old is cost-effective compared to no screening.
Remarks	1) Methods to estimate the model parameters were not reported 2) To model was a too simplistic representation of the reality (decompensated cirrhosis, liver transplant and hepatocellular carcinoma in one health state) 3) No probabilistic sensitivity analysis was performed 4) The impact of indirect productivity cost was not considered

Authors (Year)	Nakamura J, Terajima K, Aoyagi Y and Akazawa K (2008)
Funding	Not reported
Country	Japan
Design	CEA
Model	For testing and diagnosis: Decision tree For long-term consequences: Markov state-transition model (developed in TreeAge Pro 2006): cycle length: 1 year
Perspective	Health care payer (not reported)
Time window	30 years
Interventions	**Groups:** 1) Screening 2) No screening **Screening:** in 3 steps - every 5 years. 1) semi-quantitative HCV antibody test: If high titer => infected If moderate or low titer => 2) If negative => not infected 2) HCV core antigen test: If positive => infected If negative => 3) 3) HCV-PCR test: If positive => infected If negative => Not infected **Treatment:** 180 µg/week PegIFN α-2a and 800 mg/day ribavirin: 1) Genotype 1:

If HCV RNA negative at week 12 => treatment duration of 48 weeks; else
If HCV RNA negative at week 24 => treatment duration of 72 weeks; else
If HCV RNA positive at week 24 => treatment stop at 24 weeks
2) Genotypes 2 or 3: 24 weeks

Population

1) General population aged 40-70
2) High-risk group aged 40 years and over: having a high aminotransferase level, having undergone a major operation or having receive d a blood transfusion during childbirth

Assumptions

Characteristics of baseline cohort

Average age at presentation: results stratified by age group: 40-49; 50-59; 60-69; 70 and over.

Severity of liver disease at presentation: All patients were assumed to be detected at the state of chronic hepatitis without specification of the severity (mild, moderate or chronic).
Average length of infection (years) (SD): Not reported

Genotype (for HCV infected people): Genotypes 2 or 3 : 30%; Genotypes 1 = 70% (sources:

Tanaka 1995, Okamoto 1996; Ohno 1997)

Screening parameters:

Acceptance rate: Not taken into account => 100%

Proportion of positive results: Stratified by age:

Age group	Infection rate; % (95% CI)	
	General population	High-risk group
40-49	0.15 (0.08-0.22)	0.38 (0.21-0.55)
50-59	0.18 (0.12-0.23)	0.31 (0.20-'0.42)
60-69	0.36 (0.30-0.36)	0.66 (0.54-0.79)
70	0.61 (0.52-0.72)	1.60 (1.37-1.83)
Total	0.36 (0.32-0.40)	0.81 (0.73-0.90)

Effectiveness of combination antiviral therapy for HCV using pegylated interferon and ribavirin (%)
Important assumption:
Treatment duration = see the Intervention point
All detected patients received the combination therapy

SVR, Genotype 1 (chronic hepatitis)	50% (Source: Berg 2006)
SVR, Genotype 2 or 3 (chronic hepatitis)	71% (Source: Shiffman et al. 2007)

Progression of HCV disease: Base case (95% CI)

Progression from chronic hepatitis to compensated cirrhosis	0.065 (0.044-0.091)
Progression from chronic hepatitis to HCC	0.014 (0.007-0.020)
Progression from compensated cirrhosis to decompensated cirrhosis	0.029 (0.018-0.041)
Progression from compensated cirrhosis to HCC	0.073 (0.055-0.093)
Progression from decompensated cirrhosis to HCC	0.073 (0.055-0.093)
Progression from decompensated cirrhosis to death	0.153 (0.120-0.186)
Progression from HCC to death	0.194 (0.192-0.196)
Background mortality	Variable – age specific (abridged life table for Japan in 2004)

Sources: Multiple sources given (14 references) without any justification.

Screening costs: (sources: medical fees in Japan)
Semi-quantitative HCV antibody test: $10.2
HCV core antigen test: $20.4
HCV-PCR test: $30.6

Disease state costs and treatment costs:

	Inpatient cost	Outpatient cost	Total
Combination therapy:			
24 weeks of treatment	6 260.80	11 794.60	18 055.40
48 weeks of treatment	6 260.80	22 646.00	28 906.70
72 weeks of treatment (1st year)	6 260.80	24 435.00	30 695.70
72 weeks of treatment (2nd year)		9 932.90	9 932.90
Post SVR		690.2	690.2
Chronic hepatitis		1 581.80	1 581.90
Compensated cirrhosis		1 726.50	1 726.50
Decompensated cirrhosis	13 114.90	2 389.00	15 503.90
HCC	14 190.30	3 670.10	17 860.40

Sources: Inpatients costs: Niigata Medical and Dental University hospital. Outpatients costs were estimated by the simulated model (not clear).

Data source for costs	Medical fees in Japan (see also in the assumptions)
Cost items included	Direct health care costs (2007 US$)
Data source for outcomes	No systematic review, no justification (see the sources in the assumptions).

Discounting

Costs: 3%
Outcomes: 3%

Costs

1) General population:

	No-screening	Screening			Incremental
Age group	Total cost (screening cost = 0)	Health care costs	Screening cost	Total cost	Cost
40-49	57 409	52 728	6 929	59 657	2 248
50-59	51 995	49 751	5 779	55 530	3 535
60-69	42 948	44 849	2 883	47 732	4 784
70	37 622	41 914	1 725	43 640	6 018

2) High-risk group:

	No-screening	Screening			Incremental
Age group	Total cost (screening cost = 0)	Health care costs	Screening cost	Total cost	cost
40-49	57 409	52 728	2 697	55 425	-1 984
50-59	51 995	49 751	3 380	53 131	1 136
60-69	42 948	44 849	1 607	46 456	3 508

Outcomes

Incremental life-year gained:

1) General population

Age group	No-screening	Screening	Incremental LYG
40-49	14.74	17.39	2.65
50-59	13.75	15.92	2.17
60-69	12.02	13.55	1.53
70	10.89	12.13	1.24

2) High-risk group

Age group	No-screening	Screening	Incremental LYG
40-49	14.74	17.39	2.65
50-59	13.75	15.92	2.17

	60-69 | 12.02 | 13.55 | 1.53
Cost-effectiveness	1) General population: Age group | ICER ($/LYG) 40-49 \| 848 50-59 \| 1 627 60-69 \| 3 133 70 \| 4 825 2) High-risk group: Age group \| ICER ($/LYG) 40-49 | -749 (Dominant strategy) 50-59 | 523 60-69 | 2 297
Sensitivity analysis	One-way sensitivity analysis: SVR rate, transition probabilities and infection rate varied according to their 95% CI Treatment prices and screening cost: 1) -50%-+50%; 2) -50%-+100% All ICERs remained below $50 000/LYG (maximum = $11 812/LYG)
Sensitivity analysis	Probabilistic sensitivity analysis: Not performed
Conclusions	The screening strategy is cost-effective compared to no screening at a threshold of $50 000/LYG both for the general population and the high-risk group, especially for younger age group.
Remarks	1) The impact on the quality of life was not taken into account 2) The screening and treatment do not correspond to current practice in Belgium 3) No liver transplantation state 4) No acceptance rate for the screening and treatment was taken into account 5) Progression rate were expected to be the same between general population and high-risk group 6) Treatment at cirrhosis was not investigated 7) Probabilistic analysis was not performed 8) Methods to synthesize progression rates were not given nor justified 9) The impact of indirect productivity cost was not considered

Authors (Year)	Tramarin A, Gennaro N, Compostella FA, Gallo C, Wendelaar Bonga LJ, Postma MJ (2008)
Funding	Not specified
Country	Italy (Veneto region)
Design	CUA
Model	For testing and diagnosis: Decision tree For long-term consequences: Markov state-transition model
Perspective	Societal perspective according to the authors (but in fact, the health care payer perspective seems to be adopted)

<table>
<tr><td>Time window</td><td>Lifetime</td></tr>
<tr><td>Interventions</td><td>Groups:
1) Screening and early treatment of patients with acute hepatitis C
2) No screening and treatment of patients with chronic hepatitis C
Screening:
1) IDUs: HCV serology every 6 months (lifelong)
2) IWS: two tests of serology: at time 0 and at 6 months
Diagnostic: not included
Treatment: PegIFN + Ribavirin during 48 weeks for genotypes 1 or 4 and during 24 weeks for genotypes 2 or 3 .</td></tr>
<tr><td>Population</td><td>Injective drug users (IDUs) and individuals with surgery (IWSs)</td></tr>
<tr><td>Assumptions</td><td>Characteristics of baseline cohort
Age at presentation:
- IDUs: 32 years
- IWS: 42 years
Average length of infection (years) (SD): Not reported
Genotype (for HCV infected people): Genotypes 1 or 4: 67%, genotypes 2 or 3: 33% (Coppola 2000)
Severity of liver disease at presentation: Uninfected</td></tr>
<tr><td></td><td>Screening parameters: Not reported</td></tr>
<tr><td></td><td>Effectiveness of combination antiviral therapy for HCV using pegylated interferon and ribavirin- %
<table>
<tr><td>SVR rate for patients with acute hepatitis C</td><td>85%</td><td>Licata 2003</td></tr>
<tr><td>SVR rate for patients with chronic hepatitis C</td><td></td><td></td></tr>
<tr><td>Genotype 2 an 3</td><td>79%</td><td>Manns 2001 (RCT)</td></tr>
<tr><td>Genotype 1 or 4</td><td>42%</td><td>Manns 2001 (RCT)</td></tr>
</table>
Source: see above (no justifications or methods reported)</td></tr>
<tr><td></td><td>Progression of HCV disease: Base case (95% CI)
Probability to move from a healthy state to HCV infection (Fabris 2008):
- IDUs: 32%
- IWSs: 24%
Incidence of HCV per 100 000:
- IDUs: 2200 (Nomenclatore Tariffario Prestazioni Specialistiche Ambulatoriali 2006)
- IWSs: 50 (Kondili 2002)
Probability to be asymptomatic (for patients with acute hepatitis C): 84% (Manns 2001)
Proportion of spontaneous clearance of the virus (chronic hepatitis C): 30% (Mele 2001)
Proportion of patients evolving to chronic hepatitis C: 24% (Mele 2001)</td></tr>
</table>

<table>
<tr><td></td><td>Proportion of patients evolving to cirrhosis: 99% (Mele 2001)

Proportion of patients evolving to HCC: 2% (Mele 2001)

Annual transition rate were not reported.
Proportion of patients with liver transplantation: not reported.</td></tr>
<tr><td></td><td>Screening and diagnosis costs:
Screening cost per patient: 34.1 (serology cost + one clinical consultation) (Coppola 2000)</td></tr>
<tr><td></td><td>Disease state costs and treatment costs:
Annual cost of cirrhosis: 4255 (Coppola 2000)
Annual cost of transplantation in HCC: 81 482 (Coppola 2000)
Monthly cost of therapy (acute or chronic hepatitis): 1147 (Coppola 2000)</td></tr>
<tr><td></td><td>Utilities:
Not reported
Sources: Bonkokovsky 2007, Kallman 2007, Wong 2006</td></tr>
<tr><td>Data source for costs</td><td>Multiples sources were given without any justifications or methods (see in the assumptions).</td></tr>
<tr><td>Cost items included</td><td>Fees in euro (year not reported). Direct health care costs:
Screening: serology cost + one clinical consultation.
Health states: Admission costs, cost of orthotropic liver transplant, treatment cost (50% of market price). Outpatients' visits, laboratory tests and diagnostics interventions were not included.</td></tr>
<tr><td>Data source for outcomes</td><td>Multiples sources were given without any justifications or methods (see in the assumptions).</td></tr>
<tr><td>Discounting</td><td>Costs: 3%
Outcomes: 3%</td></tr>
<tr><td>Costs</td><td>In € (for all patients)
<table>
<tr><td></td><td>No screening</td><td>Screening</td><td>Incremental cost</td></tr>
<tr><td>IDUs</td><td></td><td></td><td></td></tr>
<tr><td>Genotypes 1 or 4</td><td>130 231 070</td><td>90 093 972</td><td>-40 13 098</td></tr>
<tr><td>Genotypes 2 or 3</td><td>22 934 277</td><td>34 767 017</td><td>11 832 740</td></tr>
<tr><td>Total</td><td>153 165 347</td><td>124 860 989</td><td>-28 304 358</td></tr>
<tr><td>IWSs</td><td></td><td></td><td></td></tr>
<tr><td>Genotypes 1 or 4</td><td>7 856 444</td><td>612 648 339</td><td>604 791 895</td></tr>
<tr><td>Genotypes 2 or 3</td><td>1 326 131</td><td>301 182 939</td><td>299 856 808</td></tr>
<tr><td>Total</td><td>9 182 575</td><td>913 831 278</td><td>904 648 703</td></tr>
</table></td></tr>
<tr><td>Outcomes</td><td>QALYs (for all patients):
<table>
<tr><td></td><td>No screening</td><td>Screening</td><td>Incremental effectiveness</td></tr>
<tr><td>IDUs</td><td></td><td></td><td></td></tr>
<tr><td>Genotypes 1 or 4</td><td>274 952</td><td>282 763</td><td>7 811</td></tr>
</table></td></tr>
</table>

	Genotypes 2 or 3	138 896	140 121	1 225
	Total	413 848	422 884	9 036
	IWSs			
	Genotypes 1 or 4	126 970 745	126 971 609	864
	Genotypes 2 or 3	62 538 216	62 538 345	129
	Total	189 508 961	189 509 954	993

Cost-effectiveness

ICER: Cost/QALYs

	ICER
IDUs	
Genotypes 1 or 4	-5 139 (Dominant)
Genotypes 2 or 3	9 659
Total	-3 132 (Dominant)
IWSs	
Genotypes 1 or 4	699 991
Genotypes 2 or 3	2 324 471
Total	911 026

Sensitivity analysis

Univariate sensitivity analysis: Only on the prevalence of genotypes 1 or 4:
Results were highly sensitive to the prevalence of genotypes 1 and 4 (67% in the base case):
- For IDUs: the ICER would become superior to €30 000/QALY from 10% or less of genotypes 1-4.
- For IWSs: the ICER is always superior to €30 000/QALY

Other variations were not reported

Sensitivity analysis

Probabilistic sensitivity analysis: Not performed.

Conclusions

Screening is a cost-effective strategy for IDUs but not for IWSs.

Remarks

1) Assumptions were not realistic (Healthy patients at presentation, then detected in the stage of acute hepatitis C thanks to a regular screening).
2) The screening strategy was not described (which test?) and seems to not correspond to the current practice in Belgium (no PCR test).
3) No acceptance rate was taken into account
4) The cost of diagnostic was not included.
5) Authors said that the societal perspective was adopted but only direct health care costs seems to be taken into account (=> health care payer perspective)
6) Most parameters of the models were not reported (utilities, annual transition rates, etc.)
7) The choice of the parameters was not justified and methods used to estimate them were not reported
8) Univariate sensitivity analysis was not reported for all uncertain parameters and no probabilistic sensitivity analysis was performed
9) The impact of indirect productivity cost was not considered

1.3. International comparison

1.3.1. France

Recommendations on HCV screening were performed in 2001 by the national agency for health accreditation and evaluation ("agence nationale d'accréditation et d'évaluation en santé (ANAES)); currently replaced by the French national authority for health ("haute autorité de santé" (HAS)). These recommendations were based on a review of the literature on clinical practice recommendations, consensus conferences, articles related to medical decisions, and other reviews of the literature. No cost-effectiveness studies were taken into account. According to their report, routine HCV screening in the general population is not recommended and only a targeted screening should be perform (see Figure 1.1).[5] In 2011, the HAS extended this report to HCV management and reported the same risk factors (based on the recommendations of the ANAES).[6]

Figure 1.1 : People who should be screened[5]

Recipients of stable blood products before 1988 or labile blood products before 1992
Recipients of tissue, cell or organ graft before 1992
People who might have received transfusion during a major medical or surgical treatment (major surgery (cardiac, etc.), period in intensive care, difficulties during labour, gastrointestinal bleeding, important neonatal or paediatric care such as for extremely premature babies, etc.)
Former IDUs
Current IDUs (regular screening)
Children born from HCV-seropositive mothers
Dialysis patients
People seropostive for HIV or HBV
Sexual partners and household members of HCV infected persons
Prisoners or former prisoners
People with tattoos and piercing and people who had been treated by mesotherapy or acupuncture if non disposable equipment was used
People with elevated alanine aminotransferase concentration with unknown origin
Immigrant people from countries with an expected high prevalence of HCV (South-east Asia, Middle East, Africa, South America)
People who received care in these countries

Concerning health professionals, they do not recommend a routine screening. They should only been screened if they had an accident involving exposure to blood.[5]

They also made recommendations on the ways of performing the screening (see Figure 1.2).

Figure 1.2 : Ways of performing screening[5]

No systematic lookback (systematic tracing and screening of transfused people)
Perform the screening by the treating doctor (GP, paediatrician, gynaecologist, anaesthetists) if risk factors are present
Inform the general population about risk factors in order that people with risk factors contact the doctor by themselves for a screening.
Focus on the information of drug users (e.g. messages on boxes used to collect needles or outreach work in place frequented by drug users or other marginalised people)

Moreover, three successive plans have been developed by the Ministry of health and sport to tackle hepatitis C, i.e. the 1999-2002 plan, the 2002-2005 plan, and the 2009-2012 plan. These plans also include actions for HBV but these actions are not reported in this report (out of scope). Methods to determine these actions were not clearly mentioned but they specified they were based on experts reports and working groups on this topics, on recommendations of the national health council and on recent epidemiological data. Only few economic considerations were taken into account.[7] Objectives and results of the two first plans are summarized in Table 1).

Table 1: Objectives and results of the 1999-2002 and 2002-2005 plans[7]

Objective	Results
To detect 75% of patients with HCV	Screening has doubled on a 10-year period but only 54% of HCV infected patients were detected in 2004 (with only 26% among people with a risk factor other than the use of drugs or the fact to have received a transplantation before 1992)
To improve medical care and treatment access	Improvements were done but care are usually late and too much performed in hospitals. Centralization of care by the general practitioner and determination of a treatment algorithm to accelerate them are needed.
To monitor the epidemiology of HCV	An institute for health monitoring (Institut de veille sanitaire (InVS)) was settled.
To inform the general population but also people at risk and health professionals	Information was diffused by the national institute for health prevention and education ("Institut national de prévention et d'éducation à la santé" (INPES)) Consensus meeting, assessment of treatment and diffusion of assessment were organized by the French agency for the safety of health products ("Agence française de sécurité sanitaire des produits de santé" (AFSSAPS)). However, information on risked practices, on preventions means and on screening means should be improved.

Objectives and actions of the 2009-2012 plan are summarized in Table 2. Again, information and education of the general population and of the health professionals have a central place. Moreover, specific attentions on drug users and prisoners but also on the follow-up of HCV infected patients are present. Finally, the necessity to improve the knowledge on HCV (epidemiology, treatment, etc.) with a focus on cost-effectiveness considerations is highlighted.[7]

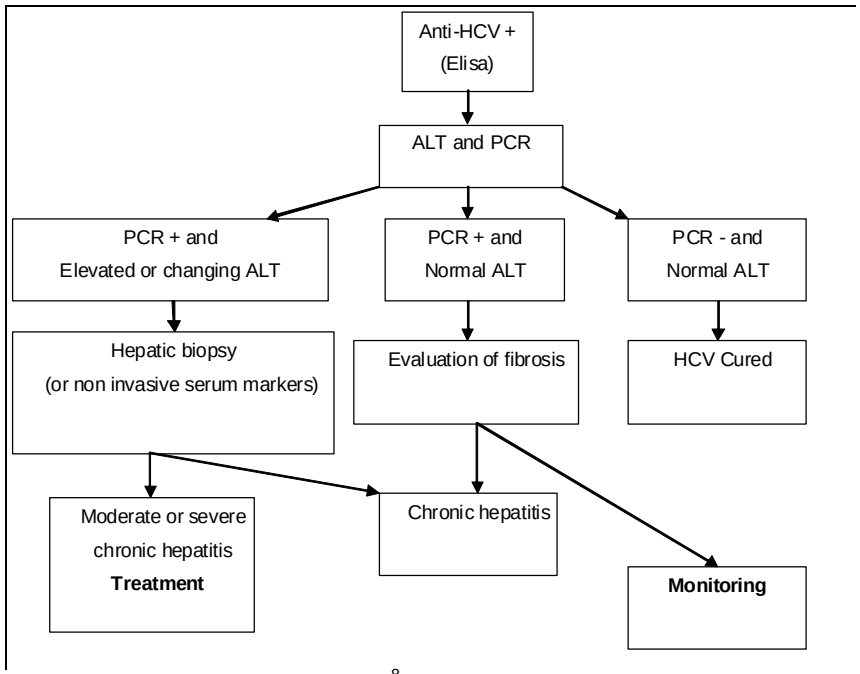
Table 2: Objectives and actions of the 2009-2012 plan[7]

Objectives	Actions
Reduction of HCV transmission	To improve **information and communication** about **prevention and treatment** possibilities. Especially for drug users, immigrants and health professionals
	To reduce transmission among **drug users** by health **education** on **hygiene** rules (reuse of needle) and on alcohol consumption. In parallel with the plan on prevention and care of addictions 2007-2011, a substitution treatment with methadone is available.
	To **train** people having a **profession involving an increased risk** of HCV transmission (nurses but also tattooist, chiropodists, etc.) about **hygiene** rules.

Objectives	Actions
To improve the screening coverage (to detect 80% of HCV infected patients)	To **inform health care professionals** in order that they systematically propose a test if a **risk factor** is detected
	To **inform the general population on risk factors** in order to incite people in the risk group to ask for a test by themselves. To modify the negative image linked to the secondary effects of the treatment. To focus on the information of people at risk.
	To analyse the **cost-effectiveness** of a targeted or even **systematic screening during anaesthesia consultations**
	To increase actions in the places frequented by **IDUs**, to repeat screening tests for this population (because of the persistence of the exposition to the risk), and to follow infected IDUs (adapted structure of care).
	To provide information about hepatitis in places dedicated to **immigrants**
	To determine **algorithm for hepatitis C screening and diagnostic** (validated by the HAS). This algorithm is described in the next paragraph.
	To **improve the follow-up** of infected people when diagnosed
To improve accessibility, quality of care and quality of life for HCV infected persons	To optimise medical practices and **care coordination**, with a **central role of the general practitioner**
	To promote the **therapeutic education of the patient**
	To **support** patients' and professionals' **associations**
	To improve the **training of health professionals**
To take special measures adapted to prisons	To invite to **screening at the entrance** and to **renew** the proposition regularly
	To **support infected patients** with the help of associations working in the prison
	To **study the prevalence** of infected patients
	To redact a **circular** on the prevention, education, and medical care **specific to prison life**
To improve the monitoring and epidemiological knowledge of HCV	To study the **prevalence** of HCV infected persons in **prisons and among IDUs**
	To reinforce the evaluations on HCV, especially via **cost-effectiveness evaluations and prospective researches**.
	To assess the 2009-2012 plan in 2014.

An algorithm on the diagnostic of hepatitis C was developed by a working group "Amélioration du dépistage des hepatise B et C".[7] Methods to develop this algorithm were however not developed in their report. This algorithm was then validated by the HAS and is described in the Figure 6.3.

Figure 1.3 : Algorithm on the diagnostic of hepatitis C (France)



Sources: Translated from Inpes 2007[8]

ALT = Alanine aminotransferase; HCV = Hepatitis C virus; PCR= Polymerase chain reaction

This algorithm was then validated by a working group of the HAS. They added the following recommendations:[6]

- KCE Bulleted example
- In case of negatives anti-HCV antibodies:
  - o If they suspect a recent infection, the dosage of anti-HCV antibodies should be repeated 4-6 weeks later
  - o If the person is very immunocompromised, they should search for HCV-RNA by PCR on the first blood sample.
- In case of positive anti-HCV antibodies:
  - o To monitor the serology by a new enzyme immunoassay test with a different reagent and a second sample and to simultaneously search for HCV-RNA by PCR on this second sample

These recommendations were based on a review of the literature (especially on recommendations in other countries) associated with experts opinions of the working group.

1.3.2. Germany

Germany has no national plan for HCV screening but has national medical guidelines stating who should be screened. Members of the German Society for Digestive and Metabolic Diseases (DGVS), the German Society for Pathology (DGP), the society for Virology (GfV), the Society for Pediatric Gastroenterology and Nutrition (GPGE) and the Competence Network for Viral Hepatitis (Hep-Net) has developed guidelines on prophylaxis, diagnosis and therapy of HCV Infection. According to these guidelines, HCV testing should be done in the risk groups reported in Figure 1.4.[9] These recommendations were based on the level of evidence 1c (all or none studies) according to the classification of the Oxford Centre for Evidence-based Medicine (http://www.cebm.net/).

Figure 1.4 : People who should be screened[9]

Persons with elevated serum aminotransferase levels and/or clinical signs of hepatitis or chronic liver disease
Recipients of blood or blood products (before 1992)
Recipients of organ transplants
Dialysis patients
Active and former IDUs
Prisoners
HIV- and/or HBV-infected persons
Household members or sexual partners of persons infected with HCV
Children of HCV-positive mothers
Immigrants from regions with increased prevalence of HCV
Health care workers
Blood and organ donors

Only the HCV screening of health care workers and blood/organ donors is mandatory in Germany.[10 9]

1.3.3. The Netherlands

In 1997, the Minister of Health, Welfare and Sport had raised the question of tracing and treating HCV infected people to the Health Council of the Netherlands. To respond to such a demand, a committee was set up. Concerning the screening, this committee had done the following recommendations:[11]

- To screen patients whose treatment involves an increased likelihood of HCV infection (see Figure 1.5) and to include this screening as part of their medical treatment.
- Do not systematically (e.g. based on databases) trace and test all people who received blood products before 1992 (= no general lookback) (recommendation based on experiences in France, Ireland and a sample of the Netherland population).
- Do not systematically screen the general population but inform it about hepatitis C, especially people at risk who are not under medical care (see Figure 1.6). With this information, people should be able to decide whether they need to contact a GP or a Municipal Health Services concerning a possible HCV infection.
- The screening of children having a positive HCV mother should exclusively be performed in the setting of a formal research protocol

Figure 1.5 : People under a medical treatment implying an increased likelihood of HCV infection and who should be screened[11]

Haemophiliacs
Dialysis patients
Polytransfusees
Patients who have had organ transplants
Patients with hypogammaglobulinaemia
People with puncture wounds

Figure 1.6 : People at risk who are not under medical care and for who information is especially needed[11]

Recipients of blood products before 1992
Recipients of tissue transplant
Current or former intravenous drug users
Immigrants
People with tattoos and other skin-penetrating interventions

To improve the quality of care and to limit the risk and impact of HCV infection, the committee had also done the following recommendations:[11]

- To improve the registration of the origin and use of blood products administered in hospitals in order to be enable to trace recipients.
- To encourage the training of GP and doctors on diagnostic and advising of patients at risk of HCV and to include hygiene rules in their educational training.
- To inform professions involving an increased risk of HCV transmission (hairdressers, chiropodists, etc.) about hygiene rules
- To advise HCV infected people to stop or minimize their alcohol consumption
- To perform epidemiological research to have an insight into the prevalence of HCV infection in the population groups.

The method used to obtain these recommendations was nevertheless not mentioned (expert opinion?) and only few references towards scientific literature were given.

With the improving of available treatments, a new report was performed in 2004. In this report, the same recommendations were done with a stress on the necessity to inform the general population and people at risk about the improved treatment possibilities.[12]

1.3.4. United Kingdom

According to the National Screening Committee, a systematic population screening program is not recommended. Antenatal screening for Hepatitis C should also not be offered.[13, 14] These recommendations are based on the criteria described in the section **Error! Reference source not found.** and include cost-effectiveness considerations.[15]

The department of health also published guidelines. According to these guidelines, screening should be performed in people listed in Figure 1.7, should be offered for people listed in Figure 1.8. and should not be performed for people listed in Figure 1.9.[16] However, the methodology to obtain these guidelines was not described.

Figure 1.7 : People who should be tested[16]

HIV infected people
Patients with renal failure on dialysis

Figure 1.8 : People for who a test should be offered[16]

People who have unexplained abnormal liver function tests or jaundice.
Current or former IDUs.
People who received transfused blood in the UK before 1991 or blood products before 1986

People who received organ or tissue transplants before 1992 or abroad in countries with a high HCV prevalence and where donors may not have been screened.

Babies born from HCV infected mother

Children of HCV infected mother

Regular sexual partners of HCV infected persons

Healthcare workers who have been accidentally exposed to blood where there is a risk of HCV transmission

People who have received medical or dental treatment in countries where hepatitis C is common and infection control may be poor (including people who have received blood transfusion products that have not been screened for hepatitis C)

People who have had tattoos, body piercing or other forms of skin piercing where infection control procedures are poor

Figure 1.9 : People who should not be tested[16]

Pregnant woman

Healthcare workers

Individuals with multiple sexual partners

Intranasal cocaine use

The royal college of general practitioners performed similar guidelines except that they consider that a test should also be offered to people who have or are snorting or smoking drugs such as cocaine, to HBV positive patients and to immigrants from countries where hepatitis C is endemic.[17] Again, the methodology to obtain these guidelines was not described.

The Scottish Intercollegiate Guidelines Network also published guidelines on the management of hepatitis C. They listed people for who a test should be done (see Figure 1.10) and those for who a test should be offered (see Figure 1.11). These recommendations are based on non-analytic studies (eg. case reports, case series), on expert opinion, or is extrapollated from well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal (=Grade D according to the SIGN methodology).[18, 19]

Figure 1.10 : People who should be tested[18]

Blood/tissue donors

Patients on haemodialysis

Healthcare workers who intend to pursue a career in a specialty that requires them to perform exposure prone procedures.

Figure 1.11 : People for who a test should be offered[18]

Patients with an otherwise unexplained persistently elevated alanine aminotransferase

People with a history of injecting drug use

People who are human immunodeficiency virus (HIV) positive

Recipients of blood clotting factor concentrates prior to 1987

Recipients of blood and blood components before September 1991 and organ/tissue transplants in the UK before 1992

Children whose mother is known to be infected with HCV

Healthcare workers following percutaneous or mucous membrane exposure to blood which is, or is suspected to be, infected with HCV

People who have received medical or dental treatment in countries where HCV is common and infection control may be poor

People who have had tattoos or body piercing in circumstances where infection control procedure is, or is suspected to be, suboptimal

People who have had a sexual partner/household contact who is HCV infected.

1.3.5. United States

The U.S. preventive service task force (USPSTF) assessed risk factors for hepatitis C by a review of the literature, including an analysis of the internal validity of the studies and the level of the evidence according to their

predefined criteria (classified in three categories: good, fair or poor).[20] They identified three independent risk factors for HCV infections with a good level of evidence (see Figure 1.12). Concerning other potential risks factors (tattoos, piercing, etc.), insufficient evidence was found.

Figure 1.12 : Independent risk factors with a good level of evidence[20]

Intravenous drug use
High-risk sexual behaviour
Transfusion before 1992

They also investigated HCV screening and concluded that adults who have no risk factors for HCV infection should not be screened (they found at least fair[a] evidence that the potential harms of HCV screening are likely to exceed the potential benefits). They also found no evidence to determine if adults at high risk should or should not be screened for HCV infection (no evidence that a screening of patient at high risk leads to improved long-term health outcomes).[21]

The Centers for disease control and prevention (CDC) also made recommendations on HCV screening. Their recommendations are based on expert opinions. They recommended to only screen people with risk factors listed in Figure 1.13.[22]

Figure 1.13 : People with risk factors who should be screened[22]

Former and current IDUs
People who received clotting factor concentrates produced before 1987
Dialysis patients
Haemophiliacs
People with persistently abnormal alanine aminotransferase levels
People who received blood transfusion or blood components before 1992
People who received an organ transplant before 1992
People who were notified that they received blood from a donor who later was tested positive for HCV infection
Healthcare, emergency medical and public safety worker after exposures (needle sticks, sharps or mucosal) to HCV-positive blood
Children born to HCV-positive woman

They also listed persons for whose routine testing was not recommended, except if they presented a risk factor (see Figure 6.14).

Figure 1.14 : People who should not be screened[22]

The general population
Healthcare, emergency medical and public safety workers
Pregnant woman
Household (nonsexual) contacts of HCV-positive persons

They also listed the situations for which the effectiveness of screening was not determined (see Figure 1.15).

Figure 1.15 : People for which no evidence on the effectiveness of the screening is available[22]

People who received transplanted tissue
Intranasal cocaine and other noninjecting illegal drug users
People with a history of tattoo or body piercing
People with a history of multiple sex partners or sexually transmitted diseases
Long-term steady sex partners of HCV-positive persons

[a] Fair = “Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes”[21]

As in other countries, they also insisted on the need to inform both the professionals and the population on hepatitis C (risk factors, treatment, hygiene rules, etc.), with a special focus on people who use illegal drugs or have high-risk sexual practices or occupations.[22]

2. APPENDIX 2: PRIMARY PREVENTION OF HCV AMONG IDUS

2.1. Effectiveness literature review

2.1.1. Search strategy and flow chart

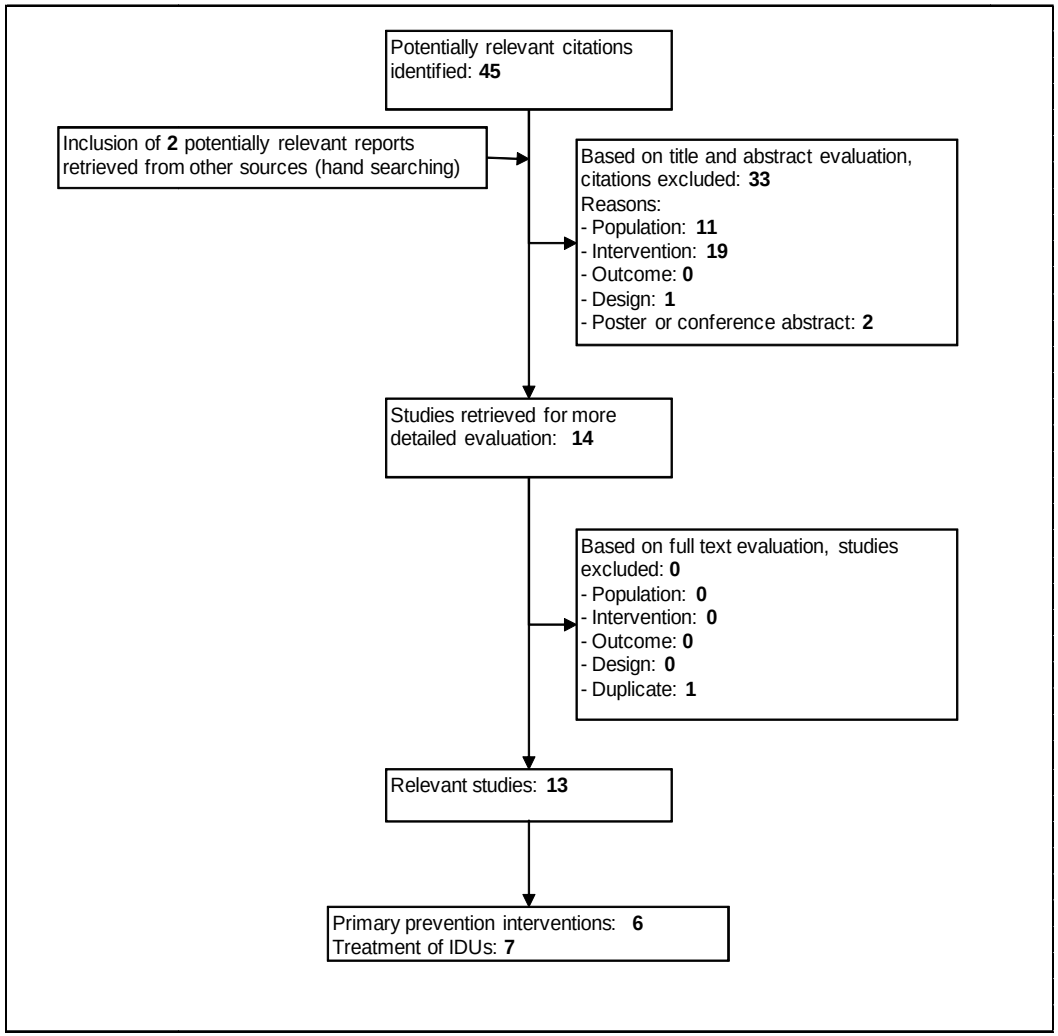
Systematic reviews, meta-analysis and HTA

Date	July 12, 2011
Database (name + access)	Ovid MEDLINE®
Date covered	1948 to Present with Daily Update
Search Strategy	1 exp Substance Abuse, Intravenous/ (10883) 2 exp Injections, Intravenous/ (73618) 3 exp Drug Users/ (543) 4 intravenous drug user$.tw. (2447) 5 IDU$.tw. (5437) 6 exp Primary Prevention/ (99294) 7 exp Preventive Health Services/ (368241) 8 exp Antiviral Agents/ (248166) 9 exp Drug Therapy/ (935953) 10 exp Treatment Outcome/ (499852) 11 (prevent$ or treatment$).tw. (2937839) 12 exp Hepatitis C/ (39533) 13 exp Hepacivirus/ (19301) 14 exp Hepatitis C Antibodies/ (4940) 15 hepatitis c.tw. (40541) 16 1 or 2 or 3 or 4 or 5 (88668) 17 6 or 7 or 8 or 9 or 10 or 11 (4125850) 18 12 or 13 or 14 or 15 (51186) 19 16 and 17 and 18 (1251) 20 limit 19 to meta analysis (11) 21 (systematic review$ or meta analysis or meta-analysis or HTA or health technology assessment).tw. (49396) 22 19 and 21 (16) 23 20 or 22 (19)

Date	July 13, 2011		
Database (name + access)	Embase		
Date covered	1974 to present		
Search Strategy	#26	#21 AND #25	37
	#25	#22 OR #23 OR #24	104477
	#24	'systematic review':ab,ti OR 'systematic reviews':ab,ti OR 'meta analysis':ab,ti OR 'meta-analysis':ab,ti OR 'hta':ab,ti OR 'health technology assessment':ab,ti	64945
	#23	'systematic review'/exp	42484
	#22	'meta analysis'/exp	55475
	#21	#18 AND #19 AND #20	1741
	#20	#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17	74181
	#19	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	5172766
	#18	#1 OR #2 OR #3	20242
	#17	'hepatitis virus non a non b':ab,ti OR 'hepatitis non a non b':ab,ti	272
	#16	'hepatitis c':ab,ti	52156
	#15	'hepatitis c antibody'/exp	6139
	#14	'hepatitis non a non b'/exp	2031
	#13	'hepatitis virus non a non b'/exp	465
	#12	'hepatitis c'/exp	54551
	#11	'hepatitis c virus'/exp	33538
	#10	treatment*:ab,ti	3116728
	#9	prevent*:ab,ti	922381
	#8	'treatment outcome'/exp	737382
	#7	'drug therapy'/exp	1391719
	#6	'antivirus agent'/exp	504972
	#5	'preventive health service'/exp	17580
	#4	'primary prevention'/exp	21877
	#3	idu*:ab,ti	6693
	#2	'drug user':ab,ti OR 'drug users':ab,ti	13122
	#1	'intravenous drug abuse'/exp	6558
Note			

Date	July 12, 2011		
Database (name + access)	Database of Abstracts of Reviews of Effects (DARE) - Cochrane Library		
Date covered	1996 to present		
Search Strategy	#1	MeSH descriptor Substance Abuse, Intravenous explode all trees	14
	#2	MeSH descriptor Injections, Intravenous explode all trees	44
	#3	MeSH descriptor Drug Users explode all trees	1
	#4	(intravenous drug user):ti,ab,kw or (intravenous drug users):ti,ab,kw or (IDU):ti,ab,kw or (IDUs):ti,ab,kw	2
	#5	MeSH descriptor Primary Prevention explode all trees	119
	#6	MeSH descriptor Preventive Health Services explode all trees	981
	#7	MeSH descriptor Antiviral Agents explode all trees	299
	#8	MeSH descriptor Drug Therapy explode all trees	2210
	#9	MeSH descriptor Treatment Outcome explode all trees	4225
	#10	(prevent):ti,ab,kw or (prevents):ti,ab,kw or (prevention):ti,ab,kw or (preventions):ti,ab,kw or (treatment):ti,ab,kw	7913
	#11	MeSH descriptor Hepatitis C explode all trees	87
	#12	MeSH descriptor Hepacivirus explode all trees	20
	#13	MeSH descriptor Hepatitis C Antibodies explode all trees	1
	#14	(hepatitis c):ti,ab,kw	90
	#15	(#1 OR #2 OR #3 OR #4)	58
	#16	(#5 OR #6 OR #7 OR #8 OR #9 OR #10)	9231
	#17	(#11 OR #12 OR #13 OR #14)	90
	#18	(#15 AND #16 AND #17)	5
Note			

Date	July 12, 2011		
Database (name + access)	Health Technology Assessment Database (HTA) - Cochrane Library		
Date covered	1989 to present		
Search Strategy	#1	MeSH descriptor Substance Abuse, Intravenous explode all trees	3
	#2	MeSH descriptor Injections, Intravenous explode all trees	9
	#3	MeSH descriptor Drug Users explode all trees	0
	#4	(intravenous drug user):ti,ab,kw or (intravenous drug users):ti,ab,kw or (IDU):ti,ab,kw or (IDUs):ti,ab,kw	1
	#5	MeSH descriptor Primary Prevention explode all trees	60
	#6	MeSH descriptor Preventive Health Services explode all trees	704
	#7	MeSH descriptor Antiviral Agents explode all trees	109
	#8	MeSH descriptor Drug Therapy explode all trees	517
	#9	MeSH descriptor Treatment Outcome explode all trees	248
	#10	(prevent):ti,ab,kw or (prevents):ti,ab,kw or (prevention):ti,ab,kw or (preventions):ti,ab,kw or (treatment):ti,ab,kw	2251
	#11	MeSH descriptor Hepatitis C explode all trees	59
	#12	MeSH descriptor Hepacivirus explode all trees	3
	#13	MeSH descriptor Hepatitis C Antibodies explode all trees	1
	#14	(hepatitis c):ti,ab,kw	61
	#15	(#1 OR #2 OR #3 OR #4)	12
	#16	(#5 OR #6 OR #7 OR #8 OR #9 OR #10)	3173
	#17	(#11 OR #12 OR #13 OR #14)	61
	#18	(#15 AND #16 AND #17)	2
Note			


Potentially relevant citations identified: 45
Inclusion of 2 potentially relevant reports retrieved from other sources (hand searching)
Based on title and abstract evaluation, citations excluded: 33
Reasons:
- Population: 11
- Intervention: 19
- Outcome: 0
- Design: 1
- Poster or conference abstract: 2
Studies retrieved for more detailed evaluation: 14
Based on full text evaluation, studies excluded: 0
- Population: 0
- Intervention: 0
- Outcome: 0
- Design: 0
- Duplicate: 1
Relevant studies: 13
Primary prevention interventions: 6
Treatment of IDUs: 7

Modelling studies

Date	July 12, 2011
Database (name + access)	Ovid MEDLINE®
Date covered	1948 to Present with Daily Update
Search Strategy	1 exp Substance Abuse, Intravenous/ (10883) 2 exp Injections, Intravenous/ (73618) 3 exp Drug Users/ (543) 4 intravenous drug user$.tw. (2447) 5 IDU$.tw. (5437) 6 exp Primary Prevention/ (99294) 7 exp Preventive Health Services/ (368241) 8 exp Antiviral Agents/ (248166) 9 exp Drug Therapy/ (935953) 10 exp Treatment Outcome/ (499852) 11 (prevent$ or treatment$).tw. (2937839) 12 exp Hepatitis C/ (39533) 13 exp Hepacivirus/ (19301) 14 exp Hepatitis C Antibodies/ (4940) 15 hepatitis c.tw. (40541) 16 1 or 2 or 3 or 4 or 5 (88668) 17 6 or 7 or 8 or 9 or 10 or 11 (4125850) 18 12 or 13 or 14 or 15 (51186) 19 16 and 17 and 18 (1251) 20 exp Models, Theoretical/ (1034440) 21 exp Models, Statistical/ (201254) 22 exp Models, Economic/ (8047) 23 exp Models, Econometric/ (3444) 24 exp Logistic Models/ (64879) 25 exp Decision Making/ (98782) 26 exp Decision Making, Computer-Assisted/ (72694) 27 exp Decision Support Techniques/ (48803) 28 exp Computer Simulation/ (112010) 29 decision model$.tw. (1049) 30 decision analy$.tw. (4020) 31 mathematical model$.tw. (24226) 32 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 (1248822) 33 19 and 32 (101) 34 letter.pt. (719642) 35 editorial.pt. (278830) 36 34 or 35 (998411) 37 33 not 36 (100)

Date	June 24, 2011
Database (name + access)	Econlit - Ovid
Date covered	1961 to May 2011
Search Strategy	1 hepatitis c.mp. [mp=heading words, abstract, title, country as subject] (5)

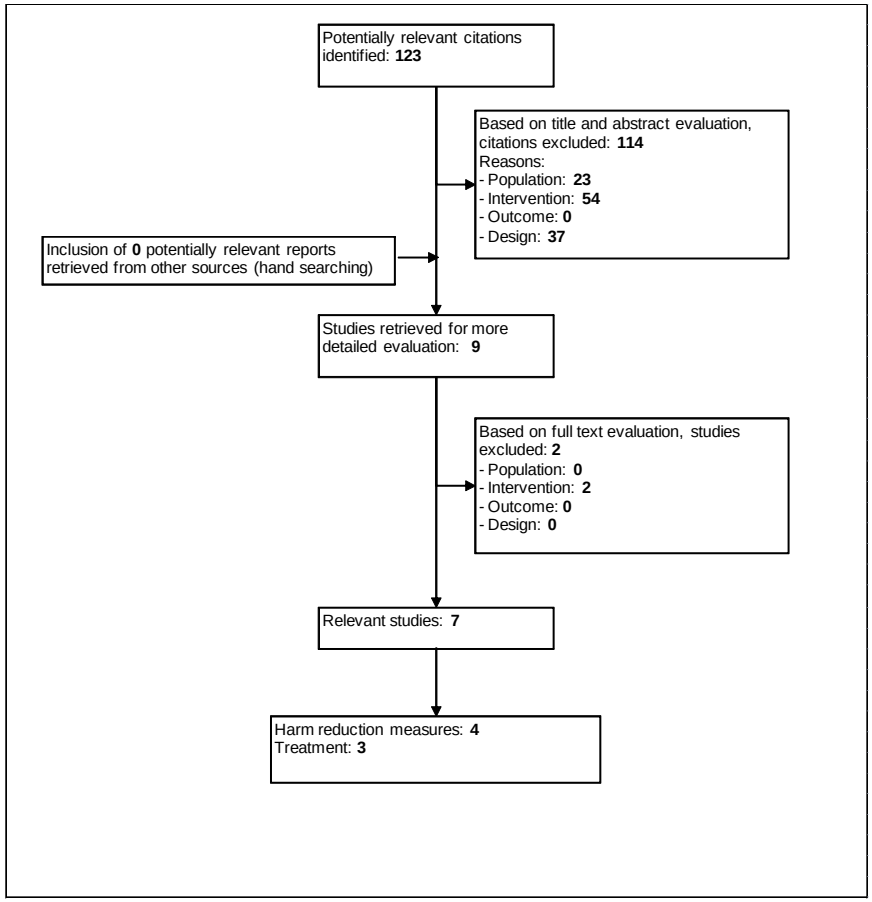
Date	July 13, 2011		
Database (name + access)	Embase		
Date covered	1974 to present		
Search Strategy	#30	#21 AND #29	33
	#29	#22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28	276904
	#28	'decision support system'/exp	8866
	#27	'statistical model'/exp	72942
	#26	'computer simulation'/exp	61657
	#25	'theoretical model'/exp	49624
	#24	'mathematical model'/exp	158227
	#23	'computer model'/exp	19101
	#22	'disease simulation'/exp	1683
	#21	#18 AND #19 AND #20	1741
	#20	#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17	74181
	#19	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	5172766
	#18	#1 OR #2 OR #3	20242
	#17	'hepatitis virus non a non b':ab,ti OR 'hepatitis non a non b':ab,ti	272
	#16	'hepatitis c':ab,ti	52156
	#15	'hepatitis c antibody'/exp	6139
	#14	'hepatitis non a non b'/exp	2031
	#13	'hepatitis virus non a non b'/exp	465
	#12	'hepatitis c'/exp	54551
	#11	'hepatitis c virus'/exp	33538

	#10	treatment*:ab,ti	3116728
	#9	prevent*:ab,ti	922381
	#8	'treatment outcome'/exp	737382
	#7	'drug therapy'/exp	1391719
	#6	'antivirus agent'/exp	504972
	#5	'preventive health service'/exp	17580
	#4	'primary prevention'/exp	21877
	#3	idu*:ab,ti	6693
	#2	'drug user':ab,ti OR 'drug users':ab,ti	13122
	#1	'intravenous drug abuse'/exp	6558
Note			

Date	July 12, 2011		
Database (name + access)	NHS Economic Evaluation Database (NHS EED) - Cochrane Library		
Date covered	1977 to present		
Search Strategy	#1	MeSH descriptor Substance Abuse, Intravenous explode all trees	35
	#2	MeSH descriptor Injections, Intravenous explode all trees	87
	#3	MeSH descriptor Drug Users explode all trees	0
	#4	(intravenous drug user):ti,ab,kw or (intravenous drug users):ti,ab,kw or (IDU):ti,ab,kw or (IDUs):ti,ab,kw	3
	#5	MeSH descriptor Primary Prevention explode all trees	291
	#6	MeSH descriptor Preventive Health Services explode all trees	1581
	#7	MeSH descriptor Antiviral Agents explode all trees	424
	#8	MeSH descriptor Drug Therapy explode all trees	1751
	#9	MeSH descriptor Treatment Outcome explode all trees	2443
	#10	(prevent):ti,ab,kw or (prevents):ti,ab,kw or (prevention):ti,ab,kw or (preventions):ti,ab,kw or (treatment):ti,ab,kw	5875
	#11	MeSH descriptor Hepatitis C explode all trees	129
	#12	MeSH descriptor Hepacivirus explode all trees	30
	#13	MeSH descriptor Hepatitis C Antibodies explode all trees	8
	#14	(hepatitis c):ti,ab,kw	131

#15	(#1 OR #2 OR #3 OR #4)	121
#16	(#5 OR #6 OR #7 OR #8 OR #9 OR #10)	7214
#17	(#11 OR #12 OR #13 OR #14)	131
#18	(#15 AND #16 AND #17)	12

Note



2.1.2. Data extraction forms

Harm reduction measures

Authors (Year)	Hutchinson SJ, Bird SM, Taylor A, Goldberg DJ (2006)
Funding	Medical Research Council and the Department of Health
Country	UK
Model	Stochastic modelling
Time window	1960-2000 (period of harm reduction = 1988-2000)
Intervention	Harm reduction measures performed in UK during 1988-2000 (not described) compared to no measure.
Population	IDUs
Assumptions	***Incidence and cessation of injecting drug use:*** Delphi approach which combined expert opinion with capture–recapture prevalence data (Hutchinson, Bird, Taylor, & Goldberg, 2006).
	Mortality rate: 1–2% per annum (Frischer, Goldberg, Rahman, & Berney, 1997)
	IDUs were randomly selected with equal probability to leave the pool
	Behavioral factors (from multi-site, community-wide surveys): Frequency of injecting: three times per day for 48 weeks per year (4 weeks' abstinence from injecting; increased to 12 weeks during 1995–2000) Percentage of IDUs who had shared a needle/syringe: Generated by sampling from a uniform distribution, where limits were varied in epochs: 1960–1976: 50–89% 1977–1985: 70–89% 1986–1990: Linear reduction 1991–1997: 35-49% 1998-2000: 40-54% Assignment of needle/syringe sharing partners to each IDU (mean number): 1960–1976: 2 1977–1985: 8 1986–1990: Linear reduction 1991–1997: 2 1998-2000: 3 (geometric distribution) Frequency of needle/syringe sharing: Individuals were randomly assigned a frequency of sharing according to the number of partners they had.
	Viral factors: Transmissions through other routes, such as sexual intercourse were not considered in the model. **Transmissibility:** Probability of becoming acutely infected after exposure: mean of 2–3% (range: 0–10%). Beta distribution (mean 0.03, variance 0.0001). Individuals became infectious 2 weeks post-infection. Infectivity constraint: 10-fold higher infectivity to newly HCV infected IDUs during the short period of high viraemia following seroconversion. **Carriage:** Viral clearance: beta distribution (mean 0.25, variance 0.001) Intervals from infection to recovery: geometric distribution (parameter 1/290 days) Individuals who recover from their acute HCV infection reentered the susceptible population, but were half as likely to develop new viraemia following re-exposure and were twelve times less likely to develop chronic infection following acute status.

Data source for outcomes	Multi-site, community-wide survey in Glasgow and in Edinburgh For HCV parameters: the literature: CDC 1997; Gerberding 1995; Simmonds 1998; Longini 1989; Vickerman 2002; Marcellin 1999; A lter 2000; Jauncey 2003, Farci 1992).
Outcomes	Median cumulative number of newly HCV infected IDUs during 1988–2000: Without harm reduction measures: 13 420 (80%CI: 11 370–16 290) With harm reduction measures: 8910 (80%CI: 7720-10 340) ⇨ HCV infections prevented: 4500 (80%CI: 2400-7700) HCV prevalence without harm reduction measures: 83-90%
Sensitivity analysis	1) The percentage of IDUs who had shared per year was reduced to: - 1-10% - 11-20% - 21-30% Before: 1988-1990: 45-79%; 1991-1997: 35-49%; 1998-2000: 40-54% ⇨ The median cumulative number of newly HCV-infected IDUs during 1988–2000 would have been 1310, 3700 and 5860, respectively (instead of 8910). For 11-20%: HCV infection prevented: 5200 (80%CI:4200-6600). ⇨ HCV prevalence: median of 18%, 33% and 46%. ⇨ HCV incidence: median of 1, 7 and 14 infections per 100 susceptible injector-years. 2) The mean number of needle/syringe sharing partners per annum was reduced to: 1 and 1.5 (before: 1988-1990: 3-6; 1991-1997: 2; 1998-2000: 3). ⇨ The median cumulative number of newly HCV-infected IDUs during 1988–2000 would have been 3650 and 6360, respectively (instead of 8910). For 1 partner: HCV infection prevented: 5300 (80%CI:4100-6700). ⇨ HCV prevalence: median of 33% and 48%. ⇨ HCV incidence: median of 5 and 13 infections per 100 susceptible injector-years. 3) The percentage of injecting episodes shared was reduced to below 10% (from that illustrated in Fig. 4). ⇨ The median cumulative number of newly HCV-infected IDUs during 1988–2000 would have been 6280 (instead of 8910). ⇨ HCV prevalence: median of 48%. ⇨ HCV incidence: median of 14 infections per 100 susceptible injector-years.
Conclusions	Around 4500 HCV infection (80%CI: 2400-7700) were prevented during 1988-2000 as a result of harm reduction interventions. HCV incidence can yet be reduced by other measures (e.g. To reduce the number of partners to 1 person or to reduce the proportion of IDUs who share syringes to 11-20%).
Remarks	- Harm reduction measures (mostly dedicated to reduce HIV transmission) were not described - Uncertainty of parameters. Biases may exist as a result of IDUs' under- or over-reporting risk behaviour. More data on the incidence and cessation of injecting drug use are needed. - Heterogeneity in the behaviour of IDUs was not taken into account. Future modelling needs to consider differences in risk behaviour in the

	initial versus subsequent years following onset of injecting drug use. - Infections through means other than needle/syringe sharing were not considered in this model. - Virological studies are needed to attest this assumption of higher infectivity during the primary phase of HCV infection

Authors (Year)	Vickerman P, Hickman M, Judd A (2007).
Funding	DTI Foresight Programme; NHS Career Scientist grant; DFID funded AIDS Knowledge Programme.
Country	UK
Model	Mathematical model of HCV transmission
Time window	/
Intervention	Decrease of syringe sharing
Population	IDUs (London)
Assumptions	The model was fit in a staged process to HCV prevalence data from London in 2002-2003. Because of uncertainty of the parameters, several models gave equally good fits to the observed data. Key differences centred on how they simulated the rapid spread of HCV infection amongst new IDUs (by assuming large sub-group of high-frequency syringe sharing IDUs, increased syringe sharing among new IDUs, or higher transmission during the acute infection phase). All IDUs are susceptible to be infected.

IDUs behavioural parameters:

Rate of leaving	10%/year
Percentage of IDUs reporting syringe sharing	33% in last month, 66% at least once
Average frequency of syringe injecting	700 per year
Number of syringes distributed to each IDU	140 per year
Mean frequency of syringe re-use before disposal	3.5 times
Estimated frequency of syringe sharing	16 per month
Percentage of IDUs in higher frequency syringe-sharing sub-group	0–50% of those that share
Factor increase in sharing rate amongst high-frequency syringe sharing IDUs	1–10
Percentage of IDUs at the start of their injecting career that share with older IDUs	0–100%
Factor increase in syringe sharing frequency amongst IDUs at the start of their injecting career	1–10

HCV related parameters:

Patients with chronic hepatitis C remain anti-HCV positive until death (no treatment).

Transmission probability per syringe-sharing act in chronic infection phase	0.84–10%
Ratio of initial peak of viraemia to viraemia in chronic phase	1–10
Ratio of initial viraemia peak to viraemia in chronic phase for those that resolve their infection	0.1–1
Duration of acute phase	6–24 weeks
Proportion of infecteds that resolve their infection	18–50%

	Duration till sero-convert after infection: 2–14 weeks Duration till lose antibody response after resolve infection: 7–15 years for serum test. Less for oral tests. HCV seroprevalence: >50% HCV seroincidence: >30%
Data source for outcomes	From the literature.
Outcomes and conclusions	Modest reductions in syringe sharing frequency (<25%) will reduce HCV seroprevalence in newly initiated IDUs (<4 years) but m uch larger and sustained reductions (>25%) are required to reduce HCV prevalence in long-term IDUs (>8 years). The frequency of syringe sharing has to decrease to 1 or 2 times per month to reduce HCV seroprevalence to < 10%. Large reductions in HCV seroprevalence will be achieved only if interventions target all IDUs, reach IDUs within 12 months of injecting (= reach new injectors) and are sustained for many years.
Remarks	- Heterogeneity in the behaviour of IDUs was not taken into account. - Uncertainty of parameters. More accurate data on IDUs behavioral (e.g. sharing frequency) and HCV parameters (% of IDUs that clear infection) are needed. - Infections through means other than needle/syringe sharing were not considered in this model.

Authors (Year)	Murray J, Law MG, Gao Z, Kaldor JM (2003).
Funding	/
Country	Australia
Model	Mathematical model of HIV and HCV transmission.
Time window	1960-2000 (Introduction of needle exchange programs in about 1985)
Interventions	Needle exchange programs and harm reduction measures.
Population	IDUs
Assumptions	Total number of IDUs increased at an annual rate of 7% until 1997 and 5% after. Homogeneous group Parameters (HIV parameters not reported in this report):

Definition	Value	Bounds
Risk of HCV per injection	0.04	[0.012, 0.1]
Fraction of needles cleaned before use in 1980, 1988, 1994	0;0.2;0.5	+/- 50%
Cleaning effectiveness against HCV relative to HIV	0.25	[0.1, 0.75]
Number of injections per year	60	+/- 50%
Average number of people using equipment per injecting episode in 1985 and 1994	1.2, 1.1	1+ [0.5(x– 1), 1.5(x– 1)]
Rate at which IDU with HCV infection leave the IDU population	0.05	[0.03, 0.07]
Annual number of new HCV infections from non-needle sharing in 1990	300	+/- 50%

Data source for outcomes	Literature
Outcomes	HCV prevalence in 2005: 32.7% and will stay above 25% in the long term. HCV incidence in 2005: 13 400 On average, every IDU would need to share with 5.7 others over a year before HCV prevalence started to rise to significant le vels in the entire IDUs community. Critical sharing level for infected numbers is below 3. Because the cu rrent sharing estimates is 6, more significant decrease is thus required for absolute numbers of HCV-infected IDU to fall.

Sensitivity analysis	Harm reduction measure:
	If 20% of infected IDUs know they are infected and use equipment last, then
	HCV prevalence in 2005: 31.3% (-1.4%)
	HCV incidence in 2005: 11 600 (-1800)
	If 50% of infected IDUs know they are infected and use equipment last, then
	HCV prevalence in 2005: 28.7% (-4%)
	HCV incidence in 2005: 8300 (-5100)

Conclusions	Needle exchange programs are effective at limiting the spread of HIV among IDU in Australia but ineffective at avoiding or markedly reducing HCV. Halving of sharing through harm reduction interventions is needed for HCV prevalence to fall significantly (current l evel= 6; critical level = 3 IDUs partners per years.
Remarks	- The needle exchange program was not described. - Heterogeneity in the behaviour of IDUs was not taken into account. - Uncertainty of parameters.

Authors (Year)	Kwon JA, Iversen J, Maher L, Law M, Wilson DP (2009).
Funding	Australian Research Council and Australian Government Department of Health and Ageing.
Country	Australia.
Model	Mathematical model of HIV and HCV transmission in a single year (static).
Interventions	Needle and syringe programs (NSP) (introduced in 1980 and active on HCV prevention since 1990).
Population	Active IDUs
Assumptions	Uniform distribution for each parameter.

Biological transmission parameters			
β	Transmission probability per injection with a contaminated syringe	HIV	0.001–0.005
		HCV	0.025–0.05
Epidemiology and NSP parameters			
p0	Prevalence among IDUs in Australia	HIV	0.5%–1.5%
		HCV	50%–70%
N	Population size of IDUs in Australia		215,000
P	Total number of no. syringes distributed per year		29,873,802
v	Percentage of syringes distributed that are not used		0.5%–1%
Behavioral parameters			

	m	Average size of a sharing group		2
	Pd	Proportion of IDUs who inject every day		45%–55%
	f	No. injections per day for IDUs that inject every day		1–2
	t	Average no. days between injections for IDUs that inject less frequently than daily		7–21 d
	n	Average frequency of injecting per IDU per year		n = 365 [Pd f + (1 — Pd) 1/t]
		(weighted average of daily and nondaily injectors)		(ranges 170–430)
	s	Proportion of IDUs who share syringes		15%–20%
	q	Proportion of injections that are shared for IDUs that share syringes		13%–17%
	dS	Average no. times each shared syringe is used before disposal		2.6–2.8
	dP	Average no. times each nonshared syringe is used before disposal		median 2.1
	Syringe cleaning parameters			
	pc	Proportion of syringes used multiple times by multiple people that are cleaned before reuse		0%–1%
	ec	Effectiveness of syringe cleaning	HIV	70%–80%
			HCV	30%–40%

Data source for outcomes	Literature. Data were based on non random samples or case notifications.
Outcomes	Threshold duration of injecting postseroconversion required to sustain an epidemic is 11.6 (IQR 7.0-22.4) years for HIV and 2.3 (IQR 1.8-3.2) years for HCV.
Sensitivity analysis	The number of times each syringe is used before disposal is the most sensitive behavioral factor, followed by the percentage of injections that are shared.

Parameter	Estimate	Expected annual HIV incidence	Expected annual HCV incidence
Number of times each shared syringe is used before disposal	2.7	34	10268
	1.5 (-44%)	19 (-44%)	5704 (-44%)
Proportion of injections that are shared	15%	34	10268
	10% (-33%)	23 (-33%)	6845 (-33%)
Distribution of syringes	30000000	34	10268

		10000000 (*1/3)	100 (*3)	31000 (*3)
		20000000 (*2/3)	51 (*1.5)	15000 (*1.5)
		60000000 (*2)	17 (1/2)	5100 (1/2)
Conclusions	HIV is effectively controlled through NSP distribution of sterile syringe. In contrast, HCV incidence is expected to remain h igh and its control is not feasible in the foreseeable future. Doubling syringe coverage could results in significant reductions in viral transmission among IDUs but thousand of people will continue to be HCV infected. Other feasible and effective interventions that reduce HCV incidence are required.			
Remarks	- The description of the needle exchange program was limited to the number of syringe distributed per year. - Heterogeneity in the behaviour of IDUs was not taken into account. - Infections through means other than needle/syringe sharing were not considered in this model. - Static model based on the current level of IDUs and not a dynamic model showing how epidemics may evolve over time. Parameters such as mortality, immigration and cessation of drug injection were therefore not included in this model..			

Treatment

Authors (Year)	Zeiler I, Langlands T, Murray JM, Ritter A (2010)
Funding	Colonial Foundation Trust; UNSW Goldstar Grant; NHMRC Career Development Award
Country	Australia
Design	Theoretical mathematical model
Model	Deterministic system of ordinary differential equations
Time window	Long-term steady-state
Intervention	Antiviral treatment
Population	Active injecting drug users (all IDUs or those on/off methadone maintenance programs)
Model compartments	Susceptible, acute HCV infected, chronic HCV infected, treated, immune
Assumptions	Model assumptions Resolution of acute infection via spontaneous clearance, or successful treatment of chronic infection leads to immunity. Only chronic infected can undergo antiviral treatment. Those undergoing treatment are not infectious. Those who succeed treatment initially enter an immune stage and cannot be reinfected unless re-enter susceptible stage upon waning immunity. All reinfections or treatment failures can be retreated.
	Characteristics of baseline scenario Single group model (all IDUs): Baseline epidemic at steady state Baseline acute+chronic HCV prevalence among IDUs: 60% (National Centre in HIV Epidemiology and Clinical Research, 2007, 2008) New IDUs per year: 4500 (Chalmers et al., 2009).

	Total population of IDUs: 54,217 Probability of clearing acute infection: 0.25 (Micallef et al 2006) Duration of acute infection: 0.5 years Spontaneous recovery rate per year: 0.5 Rate of progression to chronic state: 1.5 per year Rate of infection due to sharing: 1/3 per year per contact with an infected individual Rate of individuals leaving the immune state: 0.25 per year Percentage of individuals on HCV treatment: 1% per year (Matthews et al 2005) Exit rate per year: 0.083 (fit to prevalence)
	Two-group model (IDUs on/off MMT): As above, with: Sharing rate for those not in MMT: 8-fold higher than in MMT (Mattick et al., 2001; Moore et al., 2007; Teesson et al., 2006). Rate of infection of IDUs (not in MMT) due to sharing: 0.503 per year per contact with an infected individual Rate of infection of IDUs (in MMT) due to sharing: 0.060 per year per contact with an infected individual Number of HCV-infected IDUs entering treatment not in MMT: `1% per year Number of HCV-infected IDUs entering treatment in MMT: 1% per year Duration in MMT: 8 months (Chalmers et al., 2009) Rate of leaving MMT per year: 3/2 Rate of entering MMT: 1 per year (Chalmers et al., 2009)
	Duration and effectiveness of combination antiviral therapy for HCV: Rate of leaving HCV treatment when failing: 52/18 per year (Novick and Kreek 2008) Rate of leaving HCV treatment when succeeding: 52/36 per year (Novick and Kreek 2008) Probability of success of HCV treatment: 50% (Novick and Kreek 2008)
Outcomes	Single group model: Annual treatment rate required to eradicate HCV at long-term steady state: 56.5% Time to halve chronic prevalence at 56.5% annual treatment rate: 3.3 years Time to halve acute prevalence at 56.5% annual treatment rate: 11.1 years
	Two-group model: At current treatment levels (1% annually), all therapy should be targeted at those not in MMT. Assuming equal treatment adherence for both groups, with an annual treatment level of 60%, optimal allocation of treatment is 15% to those in MMT

	and 85% to those not in MMT. If treatment adherence in the non-MMT group is below 44.3% that of the MMT group, then more testing and treatment should be allocated to those in MMT.
Sensitivity analysis	A sensitivity analysis on predicted steady state HCV prevalence was performed. The methodology described was insufficient. It appears the authors varied each parameter univariately by +/-10% and determined the resulting impact on steady state HCV prevalence.
Conclusions	Increasing HCV treatment can lead to a relatively large decrease in chronically HCV-infected IDU. Reinfection significantly impacts the success of HCV treatment as a prevention intervention. Majority of therapy should be allocated to those actively injecting and not in MMT, due to reinfection and high turnover in MMT.
Remarks	The use of differential exit rates for those who do and do not attain SVR means any cohort of IDUs on treatment will experience treatment failure at a faster rate than success, resulting in a net 33% treatment SVR, instead of the 50% reported (Vickerman et al 2010). Insufficient description and analysis of the two-group model and inconsistent results in this section brings these results into question. It is not clear whether the finding results from less IDUs being treated when MMT is targeted, possibly because of fewer IDUs being on MMT, or whether less impact is achieved per IDU treated in the MMT population (Vickerman et al 2010). Attempts to replicate this result have failed (Martin NK, unpublished work) SVR rates were assumed to be comparable to the former or non-injector population. Data specific for current injectors are needed. No genotype distribution was noted, which limits its applicability to the Belgian setting They assumed a treatment duration of 36 weeks for genotype 1 without stopping rules. This does not reflect current clinical guidance of ceasing treatment at 12 weeks if a viral load is not shown on quantitative PCR. The presence and duration of immunity was difficult to model accurately due to a lack of data. It assumed that treatment eligibility was the same for all groups. Data specific for those enrolled and not enrolled in opiate substitution therapy is needed. The model did not explore the impact of a policy where nonresponders are not retreated. Lack of incorporation of heterogeneity with respect to HCV risk and treatment accessibility across the population (genotype distribution, age, high/low risk injectors) as well as across an injecting career (times in/out prison or homeless).

Authors (Year)	Martin NK, Vickerman P, Hickman M (2011)
Funding	Scottish Government Hepatitis C Action Plan, NCCRCD/NIHR CRDHB, MRC New Investigator Award
Country	UK
Design	Theoretical mathematical model
Model	Deterministic system of ordinary differential equations
Time window	Long-term steady-state and 0-100 years
Intervention	Antiviral treatment
Population	Active injecting drug users

Model compartments	Susceptible, chronic HCV infected, treated, immune
Assumptions	Model assumptions Resolution of acute infection via spontaneous clearance, or successful treatment of chronic infection can lead to sterilising immunity. Only chronic infected can undergo antiviral treatment. Those undergoing treatment are not infectious. Those who succeed treatment can immediately become reinfected. All those who exit treatment can be retreated.
	Characteristics of baseline scenario Baseline epidemic at steady state Baseline chronic HCV prevalence among IDUs: 20%, 40%, and 60% Proportion of acute infections which spontaneously clear: 0.26 (Micallef et al 2006) Proportion of spontaneous clearance or treatment success which lead to immunity: 0.25 (conservative estimation, Mehta et al., 2002) New injectors: 85 per year (fit to 1000 total injectors) Total population: 1000 IDUs Exit rate due to death or cessation: 0.085 per year (Sweeting et al. 2009, Hickman et al. 2007, Nordt and Stohler 2006 and Hi ckman et al. 2009) Genotype distribution: 50% genotype 1, 50% genotype 2/3 (NICE, 2006) Number of individuals on treatment at baseline: 0
	Duration and effectiveness of combination antiviral therapy for HCV: Probability of success of HCV treatment: 62.5% (weighted average of 45% genotype `1, 80% genotype 2/3) (NICE, 2006) Exit rate from treatment: 1.992 per year (weighted average of duration of treatment: 12 weeks genotype 1 nonresponders, 48 we eks genotype 2/3 responders, 24 weeks genotype 2/3) (NICE, 2006)
Outcomes	Fixed treatment term (treating a fixed number of IDUs per year): At 20% baseline chronic prevalence, eventual eradication could be achieved by treating 2 per 1000 IDUs annually. At 40% baseline chronic prevalence, eventual eradication could be achieved by treating 9 per 1000 IDUs annually. Treating 16 per 1000 IDU annually can result in eradication within 60 years. At 60% chronic prevalence, eventual eradication could be achieved treating 29 per 1000 IDUs annually. Proportional treatment term (treating a fixed percentage of chronically infected IDUs per year): Settings with prevalence below 50% require treating less than 20% of chronic infections annually to eradicate the disease. At 20%, 40%, and 60% baseline chronic prevalence, annually treating 4%, 10%, or 25% respectively could result in eventual era dication. At a baseline prevalence of 40%, treating 2%, 4%, or 6% annually could reduce prevalence within 20 years by over 15%, 33%, or 50%, respectively.
Sensitivity analysis	Univariate sensitivity analysis: A one-way sensitivity analysis of the threshold treatment level needed for eradication was performed through the calculation of a s ensitivity coefficient, describing the factor relative change in the target variable relative to a factor change in a paramet er. At all prevalence levels the threshold treatment level is most sensitive to the infection rate, and higher prevalences are more sensitive to the exit rate and the fraction of infected progressing to chronic infection.
Conclusions	Low levels of antiviral treatment could act as a prevention measure for the wider IDU community by reducing prevalence by large amounts across a wide range of prevalence settings.
Remarks	SVR rates were assumed to be comparable to the former or non-injector population. Data specific for current injectors are needed. A mixed genotype distribution of 50% genotype 1 and 50% genotype 2/3 was modelled, which may not be applicable to the Belgian setting The presence and duration of immunity was difficult to model accurately due t o a lack of data. Model did not include an acute HCV stage. It assumed that treatment eligibility was the same for IDUs. The model did not explore the impact of a policy where nonresponders are not retreated.

	Lack of incorporation of heterogeneity with respect to HCV risk and treatment accessibility across the population (genotype distribution, age, high/low risk injectors) as well as across an injecting career (times in/out prison or homeless).

Authors (Year)	Martin NK, Vickerman P, Foster GR, Hutchinson SJ, Goldberg DJ, Hickman M (2011)
Funding	Scottish Government Hepatitis C Action Plan, NCCRCD/NIHR CRDHB, MRC New Investigator Award
Country	UK
Design	Theoretical mathematical model
Model	Deterministic system of ordinary differential equations
Time window	5, 10, 20 years
Intervention	Antiviral treatment
Population	Active injecting drug users
Model compartments	Susceptible, chronic HCV infected, treated, immune
Assumptions	Model assumptions No immunity Only chronic infected can undergo antiviral treatment. Those undergoing treatment are not infectious. Those who succeed treatment can be immediately reinfected. Treatment is administered to a fixed number of IDUs per year. Those who fail treatment cannot be retreated.
	Characteristics of baseline scenario Baseline epidemic at steady-state Baseline chronic HCV prevalence among IDUs: 20%, 40%, and 60% Proportion of acute infections which spontaneously clear: 0.26 (Micallef et al 2006) Proportion of spontaneous clearance or treatment success which lead to immunity: 0 New injectors: 85 per year (fit to 1000 total IDUs) Total population: 1000 IDUs Exit rate due to death or cessation: 0.085 per year (Sweeting et al. 2009, Hickman et al. 2007, Nordt and Stohler 2006 and Hi ckman et al. 2009) Genotype distribution: 50% genotype 1, 50% genotype 2/3 (NICE, 2006) Number of individuals on treatment at baseline: 0
	Duration and effectiveness of combination antiviral therapy for HCV: Probability of success of HCV treatment: 62.5% (weighted average of 45% genotype `1, 80% genotype 2/3) (NICE, 2006)

	Exit rate from treatment: 1.992 per year (weighted average of duration of treatment: 12 weeks genotype 1 nonresponders, 48 we eks genotype 2/3 responders, 24 weeks genotype 2/3) (NICE, 2006)
Outcomes	For an IDU population with 20% chronic prevalence, treating 5, 10, 20, or 40 per 1000 IDU annually results in a 15%, 30%, 62 %, or 72% reduction in prevalence, respectively, after 10 years. Annually treating 10 per 1000 IDU results in a 16%, 30%, and 57% reduction in prevalence within 5, 10, and 20 years, respectively. For an IDU population of 40%, expected prevalence reductions are at most halved as compared to the 20% scenario, and quartere d for 60% prevalence. At 40% prevalence, treating 10 per 1000 IDUs annually reduces prevalence by 8% after 5 years, and 22% after 20 years. At 60% prevalence, treating 10 per 1000 annually reduces prevalence by 9% after 20 years. For baseline prevalences less than 60%, treatment of IDUs results in more HCV free life years gained per person treated than for treating ex/non-IDUs given equal treatment success rates.
Sensitivity analysis	Probabilistic multivariate sensitivity analysis: A multivariate uncertainty analysis of the impact of treatment on HCV prevalence was performed by performing latin hypercube sampling from distributions of all the parameters. Overall model uncertainty increases as time progresses (+/- 50% after 20 years) and for higher treatment rates. Uncertainty surrounding the proportion of spontaneous clearance or successful treatment leading to immunity (0 -50%) has little impact on projections. Uncertainty in infection rate, exit rate, and treatment success rate accou nt for the majority of uncertainty in the treatment impact projections.
	Univariate sensitivity analysis: Alterative scenarios explored increasing/decreasing average treatment success rates and retreatment of nonresponders. Varying treatment success rates (0.3-0.45 for genotype 1, 0.65-0.8 for genotype 2/3) can alter projections by +/- 27% over 20 years with an annual treatment rate of 10-20 per 1000 IDU. Allowing retreatment of nonresponders does not change short-term (5 year) projections.
Conclusions	Achievable rates of antiviral treatment may be an effective prevention tool for substantially reducing HCV prevalence, across a wide range of prevalence settings and despite the risk of reinfection.
Remarks	SVR rates were assumed to be comparable to the former or non-injector population. Data specific for current injectors are needed. A mixed genotype distribution of 50% genotype 1 and 50% genotype 2/3 was modelled, which may not be applicable to the Belgian setting The presence and duration of immunity was difficult to model accurately due to a lack of data. Model did not include an acute HCV stage. It assumed that treatment eligibility was the same for IDUs. Lack of incorporation of heterogeneity with respect to HCV risk and treatment accessibility across the population (genotype distribution, age, high/low risk injectors) as well as across an injecting career (times in/out prison or homeless).

2.2. Cost-effectiveness Literature review

2.2.1. Search strategy and flow chart

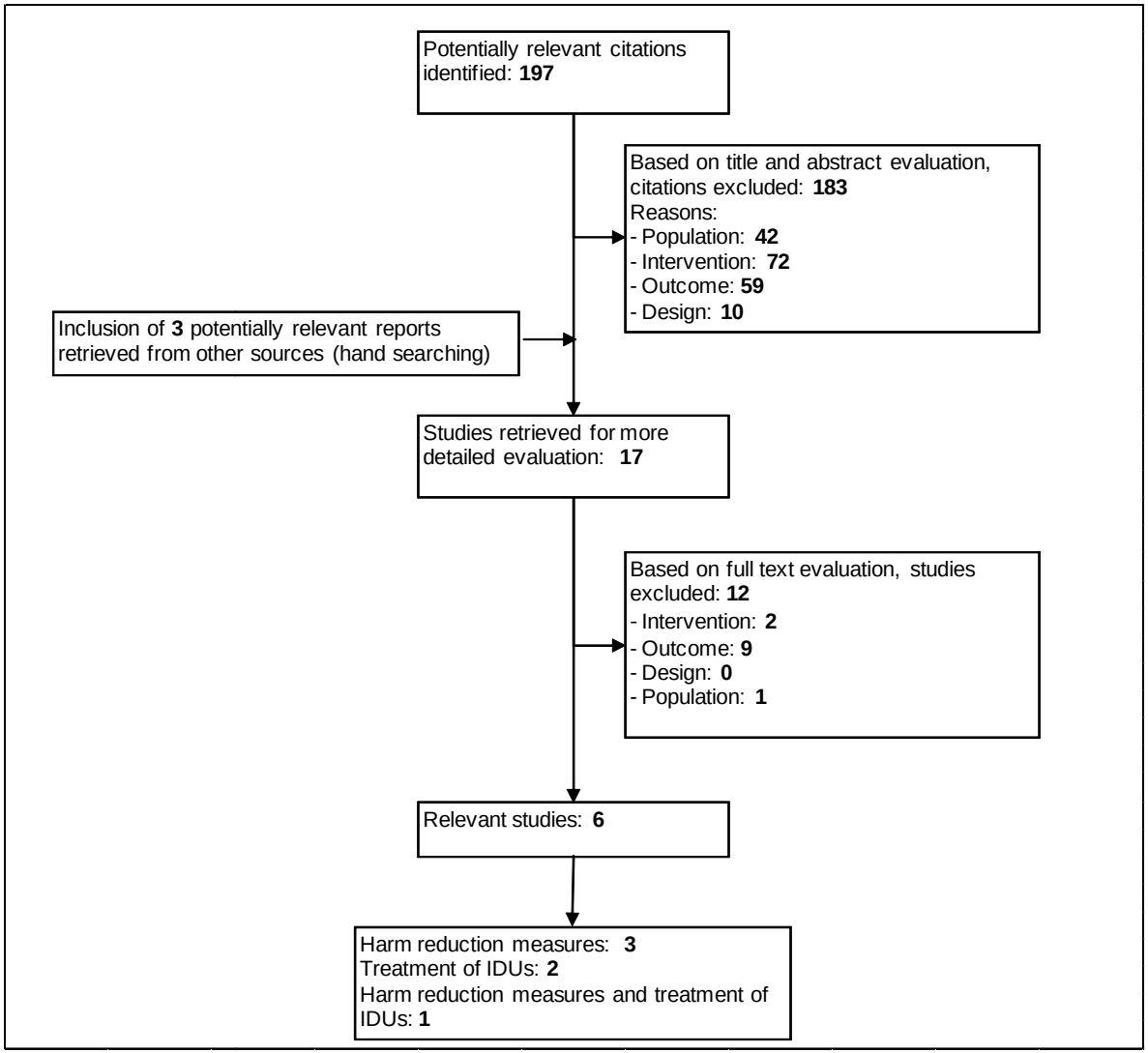
Date	July 12, 2011
Database (name + access)	Ovid MEDLINE®
Date covered	1948 to Present with Daily Update
Search Strategy	1 exp Substance Abuse, Intravenous/ (10883) 2 exp Injections, Intravenous/ (73618) 3 exp Drug Users/ (543) 4 intravenous drug user$.tw. (2447) 5 IDU$.tw. (5437) 6 exp Primary Prevention/ (99294) 7 exp Preventive Health Services/ (368241) 8 exp Antiviral Agents/ (248166) 9 exp Drug Therapy/ (935953) 10 exp Treatment Outcome/ (499852) 11 (prevent$ or treatment$).tw. (2937839) 12 exp Hepatitis C/ (39533) 13 exp Hepacivirus/ (19301) 14 exp Hepatitis C Antibodies/ (4940) 15 hepatitis c.tw. (40541) 16 1 or 2 or 3 or 4 or 5 (88668) 17 6 or 7 or 8 or 9 or 10 or 11 (4125850) 18 12 or 13 or 14 or 15 (51186) 19 16 and 17 and 18 (1251) 20 Economics/ (26083) 21 exp "Costs and Cost Analysis"/ (157763) 22 "Value of Life"/ec [Economics] (209) 23 exp Economics, Hospital/ or exp Economics, Medical/ (29939) 24 Economics, Dental/ or Economics, Pharmaceutical/ or Economics, Nursing/ (7922) 25 (econom$ or cost$ or pric$).tw. (380089) 26 pharmaco?economic$.tw. (2310) 27 (expenditure$ not energy).tw. (14336) 28 budget$.tw. (14528) 29 (value adj1 money).tw. (20) 30 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 (494870) 31 19 and 30 (64) 32 letter.pt. (719642) 33 editorial.pt. (278830) 34 32 or 33 (998411) 35 31 not 34 (63)

Date	June 24, 2011
Database (name + access)	Econlit - Ovid
Date covered	1961 to May 2011
Search Strategy	1 hepatitis c.mp. [mp=heading words, abstract, title, country as subject] (5)

Date	July 13, 2011		
Database (name + access)	Embase		
Date covered	1974 to present		
Search Strategy	#33	#31 NOT #32	176
	#32	editorial:it OR letter:it	1117198
	#31	#21 AND #30	191
	#30	#22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29	1042398
	#29	'value' NEAR/1 'money'	20
	#28	expenditure*:ab,ti NOT energy:ab,ti	18209
	#27	econom*:ab,ti OR cost*:ab,ti OR pric*:ab,ti OR pharmacoeconomic*:ab,ti OR budget*:ab,ti	511673
	#26	'financial management'/exp	241111
	#25	'cost'/exp	208466
	#24	'economics'/exp	194576
	#23	'health care cost'/exp	162858
	#22	'health economics'/exp	502076
	#21	#18 AND #19 AND #20	1741
	#20	#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17	74181
	#19	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	5172766
	#18	#1 OR #2 OR #3	20242
	#17	'hepatitis virus non a non b':ab,ti OR 'hepatitis non a non b':ab,ti	272
	#16	'hepatitis c':ab,ti	52156
	#15	'hepatitis c antibody'/exp	6139

	#14	'hepatitis non a non b'/exp	2031
	#13	'hepatitis virus non a non b'/exp	465
	#12	'hepatitis c'/exp	54551
	#11	'hepatitis c virus'/exp	33538
	#10	treatment*:ab,ti	3116728
	#9	prevent*:ab,ti	922381
	#8	'treatment outcome'/exp	737382
	#7	'drug therapy'/exp	1391719
	#6	'antivirus agent'/exp	504972
	#5	'preventive health service'/exp	17580
	#4	'primary prevention'/exp	21877
	#3	idu*:ab,ti	6693
	#2	'drug user':ab,ti OR 'drug users':ab,ti	13122
	#1	'intravenous drug abuse'/exp	6558
Note			

Date	July 12, 2011		
Database (name + access)	NHS Economic Evaluation Database (NHS EED) - Cochrane Library		
Date covered	1977 to present		
Search Strategy	#1	MeSH descriptor Substance Abuse, Intravenous explode all trees	35
	#2	MeSH descriptor Injections, Intravenous explode all trees	87
	#3	MeSH descriptor Drug Users explode all trees	0
	#4	(intravenous drug user):ti,ab,kw or (intravenous drug users):ti,ab,kw or (IDU):ti,ab,kw or (IDUs):ti,ab,kw	3
	#5	MeSH descriptor Primary Prevention explode all trees	291
	#6	MeSH descriptor Preventive Health Services explode all trees	1581
	#7	MeSH descriptor Antiviral Agents explode all trees	424
	#8	MeSH descriptor Drug Therapy explode all trees	1751
	#9	MeSH descriptor Treatment Outcome explode all trees	2443
	#10	(prevent):ti,ab,kw or (prevents):ti,ab,kw or (prevention):ti,ab,kw or (preventions):ti,ab,kw or (treatment):ti,ab,kw	5875
	#11	MeSH descriptor Hepatitis C explode all trees	129
	#12	MeSH descriptor Hepacivirus explode all trees	30
	#13	MeSH descriptor Hepatitis C Antibodies explode all trees	8
	#14	(hepatitis c):ti,ab,kw	131
	#15	(#1 OR #2 OR #3 OR #4)	121
	#16	(#5 OR #6 OR #7 OR #8 OR #9 OR #10)	7214
	#17	(#11 OR #12 OR #13 OR #14)	131
	#18	(#15 AND #16 AND #17)	12
Note			


Potentially relevant citations identified: 197
Based on title and abstract evaluation, citations excluded: 183
Reasons:
- Population: 42
- Intervention: 72
- Outcome: 59
- Design: 10
Inclusion of 3 potentially relevant reports retrieved from other sources (hand searching)
Studies retrieved for more detailed evaluation: 17
Based on full text evaluation, studies excluded: 12
- Intervention: 2
- Outcome: 9
- Design: 0
- Population: 1
Relevant studies: 6
Harm reduction measures: 3
Treatment of IDUs: 2
Harm reduction measures and treatment of IDUs: 1

2.2.2. Data extraction forms

Authors (Year)	Martin NK, Vickerman P, Miners A, Graham RF, Hutchinson SJ, Goldberg DJ, Hickman M 2011
Funding	Scottish government hepatitis C action plan
Country	UK
Design	CUA
Model	Open dynamic HCV transmission model (cycle length = 6 months)
Perspective	Health care provider
Time window	10 years of treatment and 50 years of follow-up (10+40).
Interventions	Treatment of IDUs (10 treatments per 1000 IDU annually for 10 years) compared to treating ex- or non- IDUs (10 treatment annually for 10 years) or compared to no treatment.
Population	IDUs
Assumptions	Prevalence of chronic hepatitis C in the IDUs population: 3 scenarios: 20%, 40% and 60% Genotype distribution: genotype 1: 50% and genotype 2/3: 50%.

Progression of HCV disease:

Parameter	Mean value [95% interval]	Distribution
Mild to Moderate transition probability	0.025[0.018-0.033]	Beta(38.086, 1485.3516)
Moderate to Cirrhosis	0.037[0.025-0.052]	Beta(26.905,700.2582)
Cirrhosis to decompensated cirrhosis	0.039 [0.030-0.083]	Beta(14.617,260.1732)
Cirrhosis/decompensated cirrhosis to HCC	0.014 [0.002-0.039]	Beta(1.9326,136.1074)
Decompensated cirrhosis/HCC to transplant	0.03[0.012-0.056]	Beta(6.5256,210.9945)
Transplant to death	0.21 [0.127-0.307]	Beta(16.276,61.2294)
Post transplant to death	0.057 [0.037-0.082]	Beta(22.902,378.8825)
Decompensated cirrhosis to death	0.13 [0.111-0.150]	Beta(147.03, 983.97)
HCC to death	0.43 [0.372-0.489]	Beta(117.1, 155.23)

SVR rate:

Parameter	Mean value	Distribution
SVR Genotype 1	0.45	Uniform(0.40,0.50)
SVR Genotype 2/3	0.8	Uniform(0.75,0.80)

Parameters related to IDUs:

Parameter	Mean value	Distribution
Average lifespan (age 20 in 2010)	76 [75.9-76.1]	Normal(76,0.06)
Average injecting duration[b]	11 [6.25-15.75]	Uniform(6,16)
Average excess IDU death rate (excluding HCV related death)	0.01	Poisson
Rate IDUs enter the IDU population	Fit to total population of 1000 injectors	-
Infection rate	Fit to give prevalence considered	-

Utility values:

Parameter- utility values	Mean yearly value [95% interval]	Distribution
Uninfected		
Ex/non-IDU	1	N/A
IDU	0.85	Uniform [0.8-0.9]
HCV		
Mild	0.77 [0.74-0.80]	Beta(521.238,155.6943)
Moderate	0.66 [0.60-0.72]	Beta(168.246,86.6723)
Cirrhosis	0.55 [0.44-0.65]	Beta(47.1021,38.5381)
Decompensated cirrhosis	0.45 [0.39-0.51]	Beta(123.75,151.25)
HCC	0.45 [0.39-0.51]	Beta(123.75,151.25)
Liver transplant	0.45 [0.39-0.51]	Beta(123.75,151.25)
Post transplant	0.67 [0.53-0.79]	Beta(32,16)
On treatment		
Mild	0.66 [0.59-0.73]	Beta(115.706,59.6063)
Moderate	0.55 [0.44-0.65]	Beta(47.1021,38.5381)
SVR		
Mild	0.82 [0.73-0.90]	Beta(65.8678, 14.4588)
Moderate	0.72 [0.62-0.81]	Beta(58.0608, 22.5792)

HCV infection related costs:

Parameter- costs	Mean 2003-2004 value*	Distribution	Units
Mild HCV	138	Gamma(25.7,5.3698)	£ per year
Moderate HCV	717	Gamma(88.85,8.0698)	£ per year
Cirrhosis	1138	Gamma(24.234,46.984)	£ per year
HCC	8127	Gamma(18.108,448.8045)	£ per year

	Decompensated cirrhosis	9120	Gamma(36.0249,253.1582)	£ per year
	Liver transplant	27330	Gamma(89.7536,304.5004)	£ per transplant
	Hospital costs year of transplant	9458	Gamma(13.7788,686.4168)	£ per year
	Post transplant	1385	Gamma(15.2189,91.0053)	£ per year
	Mild SVR	259	Gamma(28.8141, 8.9887)	£ per year
	Moderate SVR	717	Gamma(89.004,8.0557)	£ per year
	Cirrhosis SVR	1138	Gamma(25.81,44.091)	£ per year

Antiviral treatment delivery costs:
Cost per item can be found in the publication and include staff time and test costs required for undertaking treatment (distribution: +/-20%).

Treating IDUs accrues additional treatment delivery costs (2 psychiatric sessions prior to treatment, double the number of bas ic assessments during treatment, and 50% additional nursing time at each hospital visit

Antiviral treatment cost (=drug cost):
Mean cost £5,406 for 24 weeks, sampled uniformly between £4,806 -£6,418, and halved/doubled for treatment durations of 12/48 weeks

Follow-up cost:
Includes inpatient/outpatient services, investigations, procedures, and blood te sts

Data source for costs	HCV infection related cost and treatment delivery cost: hospital community health services pay and prices index Treatment cost: British National Formulary Treatment delivery cost: Shepherd et al
Cost items included	2010 UK £ Direct health care costs.
Data source for outcomes	Literature
Discounting	3.5% for both costs and outcomes
Costs	

Scenario	Mean total costs (95% CI)
20% prevalence	
No treatment	20 010 000 (12 654 000-32 344 000)
Treat IDUs	20 163 000 (12 986 000-32 246 000)
Treat ex/non-IDUs	20 552 000 (13 243 000-32 788 000)
40% prevalence	
No treatment	40 774 000 (26 053 000-65 483 000)

	Treat IDUs: 41 119 000 (26 536 000-65 873 000) Treat ex/non-IDUs: 41 316 000 (26 610 000-66 035 000) 60% prevalence No treatment: 61 475 000 (39 424 000-98 863 000) Treat IDUs: 62 066 000 (40 048 000-99 456 000) Treat ex/non-IDUs: 62 017 000 (39 969 000-99 413 000)
Outcomes	QALYs gained:

Scenario	Mean total QALYs (95% CI)
20% prevalence	
No treatment	137 066 (96 704-206 932)
Treat IDUs	137 360 (96 916-207 307)
Treat ex/non-IDUs	137 146 (96 762-207 057)
40% prevalence	
No treatment	123 053 (87 031-185 394)
Treat IDUs	123 217 (87 191-185 618)
Treat ex/non-IDUs	123 133 (87 129-185 488)
60% prevalence	
No treatment	109 084 (76 883-163 857)
Treat IDUs	109 161 (76 978-163 961)
Treat ex/non-IDUs	109 163 (76 979-163 972)

Cost-effectiveness

Scenario	Mean ICER (£/QALY)

		(95%CI)
	20% prevalence Treat IDUs	521 (Dominant - 1839)
	Treat ex/non-IDUs	Dominated
	40% prevalence Treat IDUs	2539 (1262-4822)
	Treat ex/non-IDUs	Dominated
	60% prevalence	
	Treat ex/non-IDUs	6803 (Dominant-38 570)
	Treat IDUs	Dominated

Sensitivity analysis

Probabilistic analysis (see the CI95%)
Linear regression ANCOVA analysis: % variability in the ICER at 40% prevalence results from:

- Health care costs of the different HCV progression states (55%)
- Mild SVR utility value (6%)
- Transition probabilities from mild to moderate (6%), moderate to cirrhosis (12%), cirrhosis to decompensated cirrhosis (5%), and IDU death (7%).
- Uninfected IDU utility value and costs related to antiviral treatment contributes little to the variablity in projections.

Univariate sensitivity analysis: No change in conclusion. Performed on:

- IDU SVR rate (1/2 or 3/4 of non/ex-IDU SVR)
- Genotype (all genotype 1 or all genotype 2/3)
- Time horizon (100 or 200 years),
- Discount rate (0% for outcomes)
- Treatment number (5 or 20 treatments per year),
- Treatment duration (5 or 20 years)
- Treatment delivery costs for IDU (equal or double the mean cost for an ex/non- IDU).
- Ex-IDU uninfected utility values are reduced (from 1 to 0.9)
- Average lifespan for both IDU and ex-IDU is reduced by 7 years

	• Treatment at a moderate stage instead of a mild stage.
Conclusions	Providing antiviral treatment to IDUs is the most cost-effective policy option in chronic prevalence scenarios of 20% and 40%. In chronic prevalence scenarios of 60%, providing antiviral treatment to ex/non-IDUs is slightly more cost-effective than treating IDUs.
Remarks	A prevalence of 60% is the more realistic scenario. At this level, the probability that treating IDUs was the most cost-effective option is inferior to 50% for every threshold values and this strategy is dominated compared to treating ex/non IDUs (slightly more costly and sli ghtly less effective). Confidence for this latest result would have been interesting. Limits: Important uncertainty around several parameters (SVR rate for active IDUs in the community; data related to IDUs and ex-IDUs utility values and lifespan) Heterogeneity in infection risk and treatment acceptability was not taken into account. Lack of age-structure in the model (e.g. no age-specific death rates)

Authors (Year)	Vickerman P, Miners A, Williams J (2008)
Funding	Not specified (NHS?)
Country	UK
Design	CUA
Model	Dynamic model
Perspective	societal perspective (NHS costs + costs of IDUs associated crimes)
Time window	20-year period
Interventions	1) In syringe distribution coverage (longer opening hours, etc.) 2) Increase (++13.5%, +26.9%, +53.8% and +100%) the recruitment of IDUs on to opiate substitution therapy (OST) and 3) Impact of treating for HCV (5% and 10% of HCV infected IDUs per year)
Population	IDUs (Homeless IDUs and those in prison were excluded) 2 groups: people who have just started injecting (<= 3 years) and those that have been injecting for longer (> 3 years). 3 subgroups: people who do not share syringes, people who share syringe with a low frequency (1-4 times in last 4 weeks) and people who share syringes with a high frequency (> 4 times in last 4 weeks).
Assumptions	Costs and benefits of preventing HBV infection were excluded (low prevalence among IDUs).
	Related to drug consumption, the following assumptions were done (value not detailed, see the report): Duration of inject drugs % of those that cease injecting % of those who die due to overdose % of IDUs that share equipment (1-4 x / 4 weeks and > 4 x/ 4 weeks) Frequency of syringe sharing % people that started injecting % people that have been injecting for longer
	Assumption related to HCV:

Ratio of HCV transmission to HIV transmission probability	7.5-15

Duration of acute phase of infection in months	3-24 months
Proportion of HCV infecteds that resolve infection	26% (20-50%)
Proportion of resolved/treated infecteds that become immune	50-100%
Percentage of HCV chronic infected IDUs that have had HCV treatment	<4.8%
Proportion of HCV positive IDUs that enter treatment	1.6-9% of those newly tested
Duration of treatment	9 months
Proportion of IDUs that have been tested for HCV	79% in Bristol and 50% in Teesside
Proportion of IDUs that have received a HCV test per year	27% in Bristol and 10% in Teesside
Percentage of treated infections cured (includes compliance)	52%

Resource item	Value	Source
Intervention		
One off total intervention cost for a 2 hour consultation	2 x £30**	Assumption
Transport to initial consultation	£15	Assumption
HIV associated costs		
Symptomatic HIV infection	£11,677	Miners 2001
Asymptomatic HIV infection	£12,818	Miners 2001
AIDS	£25,563	Miners 2001
Cost of HAART	£3,201	Miners 2001
HCV associated costs		
HCV acute infection	£0	Assumption
HCV chronic infection	£629	Weighted average calculated from Shepherd 2007
HCV antiviral therapy (37.8 weeks treatment for mild HCV infection)	£8,269	Weight average calculated from Shepherd 2007
OST and IDU associated costs		
Health care costs of OST	£1,482	Dijkgraaf 2005
Health care costs of successful OST	£1,455	Godfrey 2004 (NTROS study)
Health care costs of unsuccessful OST	£1,285	Godfrey 2004 (NTROS study)

	CJS and victim costs of successful OST	£18,327	Godfrey 2004 (NTROS study) and Adi 2007
	CJS and victim costs of unsuccessful OST	£40,136	Godfrey 2004 (NTROS study) and Adi 2007

Health state	Value	Source
IDU no viral infection*	0.85	Assumption
asymptomatic HIV* and HCV	0.5	Assumption
symptomatic HIV* and HCV	0.5	Assumption
AIDS* and HCV*	0.5	Assumption
HCV acute infection*	0.7	Shepherd 2007
HCV chronic infection*	0.66	Weighted average calculated from Shepherd 2007
No viral infection and successful OST[$]	0.95	Assumption, based on Stein 2004

*values for these health states were multiplied by 0.9 for IDUs $No allowance is made for the length of time on successful OS T

Data source for costs	See the assumptions
Cost items included	Direct health care costs and costs of crime IDU-associated (no productivity costs); cost in £2007
Data source for outcomes	Systematic review of Jones 2008: the only one study of quality identified = the RCT of Strathdee et al. Epidemiological and behavioral data : cross sectional survey form Bristol (high HCV prevalence: 64.9%) and Teesside (low HCV prevalence: 26.8%) + fitting algorithm
Discounting	3.5% for both costs and outcomes.
Costs	Total cost in the societal perspective (£2007)

	Bristol	
	Total cost	Incremental cost
Current NSP	481 129 096	
Intervention to increase recruitment to high syringe coverage (% increase in 100% coverage recruitment rate: +12.5%)	481 248 303	119 207
Intervention to increase recruitment to high syringe coverage (% increase in 100% coverage recruitment rate: +100%)	481 318 473	189 377
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -12.5%)	481 245 327	116 231
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -75%)	481 224 069	94 973
Intervention to increase recruitment in OST (% increase in OST recruit rate: +13.5%)	473 111 950	-8 017 146
Intervention to increase recruitment in OST (% increase in OST recruit rate: +107.8%)	432 846 008	-48 283 088
	Total cost	Incremental cost

Current NSP (base case: 0%)	481 161 632	
Intervention to increase recruitment to HCV antiretroviral treatment (5%)	482 353 143	1 191 511
Intervention to increase recruitment to HCV antiretroviral treatment (10%)	483 396 578	2 234 946

	Teesside	
	Total cost	Incremental cost
Current NSP	375 057 269	
Intervention to increase recruitment to high syringe coverage (% increase in 100% coverage recruitment rate: +12.5%)	375 114 253	56 984
Intervention to increase recruitment to high syringe coverage (% increase in 100% coverage recruitment rate: +100%)	375 074 979	17 710
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -12.5%)	375 106 936	49 667
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -75%)	375 049 718	-7 551
Intervention to increase recruitment in OST (% increase in OST recruit rate: +13.5%)	368 578 145	-6 479 124
Intervention to increase recruitment in OST (% increase in OST recruit rate: +107.8%)	342 234 596	-32 822 673
	Total cost	Incremental cost
Current NSP (base case: 0%)	374 820 539	
Intervention to increase recruitment to HCV antiretroviral treatment (5%)	375 454 450	633 911
Intervention to increase recruitment to HCV antiretroviral treatment (10%)	375 300 508	479 969

Outcomes

	Bristol	
	Total QALYs	Incremental effectiveness
Current NSP	10 563	
Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +12.5%)	10 566	3
Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +1000%)	10 583	20
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -12.5%)	10 565	2
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -75%)	10 586	23
Intervention to increase recruitment in OST (% increase in OST recruit rate: +13.5%)	10 612	49
Intervention to increase recruitment in OST (% increase in OST recruit rate: +107.8%)	10 861	298
	Total QALYs	Incremental effectiveness
Current NSP (base case: 0%)	10 266	
Intervention to increase recruitment to HCV antiretroviral treatment (5%)	10 380	114
Intervention to increase recruitment to HCV antiretroviral treatment (10%)	10 488	222

	Teesside	
	Total QALYs	Incremental effectiveness
Current NSP	10 998	
Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +12.5%)	11 000	2
Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +1000%)	11 010	12
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -12.5%)	11 000	2
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -75%)	11 013	15
Intervention to increase recruitment in OST (% increase in OST recruit rate: +13.5%)	11 038	40
Intervention to increase recruitment in OST (% increase in OST recruit rate: +107.8%)	11 201	203
	Total QALYs	Incremental cost
Current NSP (base case: 0%)	10 898	
Intervention to increase recruitment to HCV antiretroviral treatment (5%)	10 958	60
Intervention to increase recruitment to HCV antiretroviral treatment (10%)	11 012	114

Cost-effectiveness

	Bristol		
	ICER	£20 000 Threshold	£30 000 Threshold
Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +12.5%)	38 679	Not cost-effective	Not cost-effective
Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +1000%)	4 359	321	526
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -12.5%)	45 821	Not cost-effective	Not cost-effective
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -75%)	4 088	370	602
Intervention to increase recruitment in OST (% increase in OST recruit rate: +13.5%)	Dominant		
Intervention to increase recruitment in OST (% increase in OST recruit rate: +107.8%)	Dominant		
	ICER	£20 000 Threshold	£30 000 Threshold
Intervention to increase recruitment to HCV antiretroviral treatment (5%)	10 500	1 078	2213
Intervention to increase recruitment to HCV antiretroviral treatment (10%)	1 062	2 208	4429

	Teesside

		ICER	£20 000 Threshold	£30 000 Threshold
	Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +12.5%)	29 309	Not cost-effective	1
	Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +1000%)	1 483	221	341
	Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -12.5%)	31 106	Not cost-effective	Not cost-effective
	Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -75%)	Dominant	295	438
	Intervention to increase recruitment in OST (% increase in OST recruit rate: +13.5%)	Dominant		
	Intervention to increase recruitment in OST (% increase in OST recruit rate: +107.8%)	Dominant		
		ICER	£20 000 Threshold	£30 000 Threshold
	Intervention to increase recruitment to HCV antiretroviral treatment (5%)	10 623	560	1156
	Intervention to increase recruitment to HCV antiretroviral treatment (10%)	4 232	1 788	2923
Sensitivity analysis	One-way sensitivity analysis showed that for OST interventions, most of the cost and utility variables did not influenced greatly the ICER.			
Conclusion	The scope for these NSP-related interventions to be cost-effective was high. However, quality of effectiveness data used was poor and more data from RCT are needed.			
Remarks	1) Result was mostly due to the impact on HIV infection 2) Quality of effectiveness data used was poor and more data from RCT are needed 3) Univariate sensitivity was limited and no probabilistic sensitivity analysis was performed. 4) Results are not generalisable to the Belgium setting (e.g. different HCV prevalence)			

Authors (Year)	Vickerman P, Miners A, Williams J (2008)
Funding	Not specified (NHS?)
Country	UK
Design	CUA
Model	Dynamic model
Perspective	societal perspective (NHS costs + costs of IDUs associated crimes)
Time window	20-year period
Interventions	2) In syringe distribution coverage (longer opening hours, etc.) 2) Increase (++13.5%, +26.9%, +53.8% and +100%) the recruitment of IDUs on to opiate substitution therapy (OST) and 3) Impact of treating for HCV (5% and 10% of HCV infected IDUs per year)
Population	IDUs (Homeless IDUs and those in prison were excluded) 2 groups: people who have just started injecting (<= 3 years) and those that have been injecting for longer (> 3 years). 3 subgroups: people who do not share syringes, people who share syringe with a low frequency (1-4 times in last 4 weeks) and people who share syringes with a high frequency (> 4 times in last 4 weeks).
Assumptions	Costs and benefits of preventing HBV infection were excluded (low prevalence among IDUs).
	Related to drug consumption, the following assumptions were done (value not detailed, see the report):

Duration of inject drugs
% of those that cease injecting
% of those who die due to overdose
% of IDUs that share equipment (1-4 x / 4 weeks and > 4 x/ 4 weeks)
Frequency of syringe sharing
% people that started injecting
% people that have been injecting for longer

Assumption related to HCV:

Ratio of HCV transmission to HIV transmission probability	7.5-15
Duration of acute phase of infection in months	3-24 months
Proportion of HCV infecteds that resolve infection	26% (20-50%)
Proportion of resolved/treated infecteds that become immune	50-100%
Percentage of HCV chronic infected IDUs that have had HCV treatment	<4.8%
Proportion of HCV positive IDUs that enter treatment	1.6-9% of those newly tested
Duration of treatment	9 months
Proportion of IDUs that have been tested for HCV	79% in Bristol and 50% in Teesside
Proportion of IDUs that have received a HCV test per year	27% in Bristol and 10% in Teesside
Percentage of treated infections cured (includes compliance)	52%

Resource item	Value	Source
Intervention		
One off total intervention cost for a 2 hour consultation	2 x £30**	Assumption
Transport to initial consultation	£15	Assumption
HIV associated costs		
Symptomatic HIV infection	£11,677	Miners 2001
Asymptomatic HIV infection	£12,818	Miners 2001
AIDS	£25,563	Miners 2001
Cost of HAART	£3,201	Miners 2001
HCV associated costs		

	HCV acute infection: £0 (Assumption) HCV chronic infection: £629 (Weighted average calculated from Shepherd 2007) HCV antiviral therapy (37.8 weeks treatment for mild HCV infection): £8,269 (Weight average calculated from Shepherd 2007) OST and IDU associated costs Health care costs of OST: £1,482 (Dijkgraaf 2005) Health care costs of successful OST: £1,455 (Godfrey 2004 (NTROS study)) Health care costs of unsuccessful OST: £1,285 (Godfrey 2004 (NTROS study)) CJS and victim costs of successful OST: £18,327 (Godfrey 2004 (NTROS study) and Adi 2007) CJS and victim costs of unsuccessful OST: £40,136 (Godfrey 2004 (NTROS study) and Adi 2007)
	Health state / Value / Source: IDU no viral infection*: 0.85 (Assumption) asymptomatic HIV* and HCV: 0.5 (Assumption) symptomatic HIV* and HCV: 0.5 (Assumption) AIDS* and HCV*: 0.5 (Assumption) HCV acute infection*: 0.7 (Shepherd 2007) HCV chronic infection*: 0.66 (Weighted average calculated from Shepherd 2007) No viral infection and successful OST$: 0.95 (Assumption, based on Stein 2004) *values for these health states were multiplied by 0.9 for IDUs $No allowance is made for the length of time on successful OS T
Data source for costs	See the assumptions
Cost items included	Direct health care costs and costs of crime IDU-associated (no productivity costs); cost in £2007
Data source for outcomes	Systematic review of Jones 2008: the only one study of quality identified = the RCT of Strathdee et al. Epidemiological and behavioral data : cross sectional survey form Bristol (high HCV prevalence: 64.9%) and Teesside (low HCV prevalence: 26.8%) + fitting algorithm
Discounting	3.5% for both costs and outcomes.
Costs	Total cost in the societal perspective (£2007) Bristol: Total cost / Incremental cost

Current NSP	481 129 096	
Intervention to increase recruitment to high syringe coverage (% increase in 100% coverage recruitment rate: +12.5%)	481 248 303	119 207
Intervention to increase recruitment to high syringe coverage (% increase in 100% coverage recruitment rate: +100%)	481 318 473	189 377
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -12.5%)	481 245 327	116 231
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -75%)	481 224 069	94 973
Intervention to increase recruitment in OST (% increase in OST recruit rate: +13.5%)	473 111 950	-8 017 146
Intervention to increase recruitment in OST (% increase in OST recruit rate: +107.8%)	432 846 008	-48 283 088
	Total cost	Incremental cost
Current NSP (base case: 0%)	481 161 632	
Intervention to increase recruitment to HCV antiretroviral treatment (5%)	482 353 143	1 191 511
Intervention to increase recruitment to HCV antiretroviral treatment (10%)	483 396 578	2 234 946

	Teesside	
	Total cost	Incremental cost
Current NSP	375 057 269	
Intervention to increase recruitment to high syringe coverage (% increase in 100% coverage recruitment rate: +12.5%)	375 114 253	56 984
Intervention to increase recruitment to high syringe coverage (% increase in 100% coverage recruitment rate: +100%)	375 074 979	17 710
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -12.5%)	375 106 936	49 667
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -75%)	375 049 718	-7 551
Intervention to increase recruitment in OST (% increase in OST recruit rate: +13.5%)	368 578 145	-6 479 124
Intervention to increase recruitment in OST (% increase in OST recruit rate:	342 234 596	-32 822 673

	+107.8%)		
		Total cost	Incremental cost
	Current NSP (base case: 0%)	374 820 539	
	Intervention to increase recruitment to HCV antiretroviral treatment (5%)	375 454 450	633 911
	Intervention to increase recruitment to HCV antiretroviral treatment (10%)	375 300 508	479 969
Outcomes			

	Bristol	
	Total QALYs	Incremental effectiveness
Current NSP	10 563	
Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +12.5%)	10 566	3
Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +1000%)	10 583	20
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -12.5%)	10 565	2
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -75%)	10 586	23
Intervention to increase recruitment in OST (% increase in OST recruit rate: +13.5%)	10 612	49
Intervention to increase recruitment in OST (% increase in OST recruit rate: +107.8%)	10 861	298
	Total QALYs	Incremental effectiveness
Current NSP (base case: 0%)	10 266	
Intervention to increase recruitment to HCV antiretroviral treatment (5%)	10 380	114
Intervention to increase recruitment to HCV antiretroviral treatment (10%)	10 488	222

	Teesside	
	Total QALYs	Incremental effectiveness
Current NSP	10 998	
Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +12.5%)	11 000	2
Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +1000%)	11 010	12

	Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -12.5%)	11 000	2
	Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -75%)	11 013	15
	Intervention to increase recruitment in OST (% increase in OST recruit rate: +13.5%)	11 038	40
	Intervention to increase recruitment in OST (% increase in OST recruit rate: +107.8%)	11 201	203
		Total QALYs	Incremental cost
	Current NSP (base case: 0%)	10 898	
	Intervention to increase recruitment to HCV antiretroviral treatment (5%)	10 958	60
	Intervention to increase recruitment to HCV antiretroviral treatment (10%)	11 012	114

Cost-effectiveness

	Bristol		
	ICER	£20 000 Threshold	£30 000 Threshold
Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +12.5%)	38 679	Not cost-effective	Not cost-effective
Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +1000%)	4 359	321	526
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -12.5%)	45 821	Not cost-effective	Not cost-effective
Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -75%)	4 088	370	602
Intervention to increase recruitment in OST (% increase in OST recruit rate: +13.5%)	Dominant		
Intervention to increase recruitment in OST (% increase in OST recruit rate: +107.8%)	Dominant		
	ICER	£20 000 Threshold	£30 000 Threshold
Intervention to increase recruitment to HCV antiretroviral treatment (5%)	10 500	1 078	2213
Intervention to increase recruitment to HCV antiretroviral treatment (10%)	1 062	2 208	4429

		Teesside		
		ICER	£20 000 Threshold	£30 000 Threshold
	Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +12.5%)	29 309	Not cost-effective	1
	Intervention to increase recruitment to high syringe coverage (% increase in 100% coveragerecruitment rate: +1000%)	1 483	221	341
	Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -12.5%)	31 106	Not cost-effective	Not cost-effective
	Intervention to reduce rate IDUs leave high coverage group (% decrease in 100% coverage leaving rate: -75%)	Dominant	295	438
	Intervention to increase recruitment in OST (% increase in OST recruit rate: +13.5%)	Dominant		
	Intervention to increase recruitment in OST (% increase in OST recruit rate: +107.8%)	Dominant		
		ICER	£20 000 Threshold	£30 000 Threshold
	Intervention to increase recruitment to HCV antiretroviral treatment (5%)	10 623	560	1156
	Intervention to increase recruitment to HCV antiretroviral treatment (10%)	4 232	1 788	2923
Sensitivity analysis	One-way sensitivity analysis showed that for OST interventions, most of the cost and utility variables did not influenced greatly the ICER.			
Conclusion	The scope for these NSP-related interventions to be cost-effective was high. However, quality of effectiveness data used was poor and more data from RCT are needed.			
Remarks	5) Result was mostly due to the impact on HIV infection 6) Quality of effectiveness data used was poor and more data from RCT are needed 7) Univariate sensitivity was limited and no probabilistic sensitivity analysis was performed. 8) Results are not generalisable to the Belgium setting (e.g. different HCV prevalence)			

Authors (Year)	Bayoumi AM, Zaric GS (2008)
Funding	No funding
Country	Canada
Design	CEA
Model	Dynamic compartmental model
Perspective	Health care system
Time window	10 years
Interventions	Supervised injection facility compared to other interventions such as needle exchange programs and methadone maintenance treatment without such supervised facility.

<table>
<tr><td>Population</td><td>Vancouvert population categorized in IDUs (with a distinction of those who received methadone maintenance treatment with tho se who did not), non IDUs, persons infected with HIV, person infected with HCV and those with combinations of these states.
Age: 15-64 years</td></tr>
<tr><td>Assumptions</td><td>1) 21% of the IDUs used the facility regularly. For these people and compared to those who used the facility irregularly or not at all , the following impact were considered:
- (1) Decreased needle sharing (odds ratio: 0.30)
- (2) Increase d use of safer practices during shared injections (odds ratio: 2.70)
- (3) Increased referral to methadone maintenance treatment (odds ratio: 1.84)
Sources: cohort studies
2) Decreased criminality was not taken into account.

Assumption related to HCV (other assumptions not detailed, see the article):
<table>
<tr><th>Parameter</th><th>Estimate</th></tr>
<tr><td>Sexual transmission</td><td></td></tr>
<tr><td>Annual risk of sexual HCV transmission per partner, %</td><td>0.3 (0–1)</td></tr>
<tr><td>Transmission through needle sharing</td><td></td></tr>
<tr><td>Risk of HCV transmission through needle sharing per act, %</td><td>4 (1–13)</td></tr>
<tr><td>Relative risk of HCV transmission through sharing of needles sterilized with bleach</td><td>0.35 (0.08–1.0)</td></tr>
<tr><td>Population parameters</td><td></td></tr>
<tr><td>Prevalence of hepatitis C virus infection among IDUs, %</td><td>88 (75–90)</td></tr>
<tr><td>Prevalence of hepatitis C virus infection among non-IDUs, %</td><td>0.8 (0–0.23)</td></tr>
<tr><td>Relative risk of death</td><td></td></tr>
<tr><td>Non-users with hepatitis C virus infection and no HIV infection (v. general population)</td><td>1.35 (1.0–2.0)</td></tr>
<tr><td>Injection drug users with hepatitis C virus infection and no HIV infection (v. injection drug users without hepatitis C virus or HIV infection)</td><td>1.0 (1.0–2.0)</td></tr>
<tr><td>Individuals with HIV and hepatitis C virus coinfection (v. HIV-positive individuals without hepatitis C virus infection)</td><td>3.0 (2.0–4.0)</td></tr>
<tr><td>Annual costs, $</td><td></td></tr>
<tr><td>Care for person with hepatitis C virus infection</td><td>2 650 (2 000–3 000)</td></tr>
<tr><td>Operating costs of supervised injection facility</td><td>2 948 101 (2 211 000–3 685 000)</td></tr>
</table>
Assumption on the population:
<table>
<tr><td>Total population</td><td>578 040</td></tr>
<tr><td>Population aged 15–64 years</td><td>428 125</td></tr>
</table>
</td></tr>
</table>

	Population of injection drug users: 7000 (3000–20000)
Data source for costs	For HCV treatment: Younossi 1999 and Krahn 2005 (cost-effectiveness models). For the cost of the facility: Scientific evaluation of supervised injecting (unpublished data from a cohort study).
Cost items included	Direct medical costs.
Data source for outcomes	Vancouvert-specific data from two cohort studies (published and unpublished data).
Discounting	5% for both costs and outcomes (according to the guidelines of the Canada). However, for outcomes, only undiscounted outcomes were published.

Costs

	Cost, $ (thousands) over 10 year (discounted at 5%)						
	Facility operation	HIV treatment	HCV treatment	Methadone maintenance treatment	Other	Total	Incremental
No facility	0	464 950	242 814	50 080	4 920 962	5 678 806	
Facility							
(1)	23 903	421 552	244 232	50 663	4 924 493	5 640 940	-37 866
(1) + (2)	23 903	414 310	244 499	50 757	4 925 067	5 634 633	-44 173
(1) + (2) + (3)	23 903	411 468	244 675	56 295	4 924 136	5 636 574	-42 232

(1) = Taken into account the impact of decreased needle sharing
(2) = Taken into account the impact of increased use of safer practices during shared injections
(3) = Taken into account the impact of increased referral to methadone maintenance treatment

Outcomes

Assumption	No. of infections averted		Undiscounted life-years gained
	HIV	HCV	
(1)	1191	54	1326
(1) + (2)	1400	60	1542
(1) + (2) + (3)	1517	68	1695

(1) = Taken into account the impact of decreased needle sharing
(2) = Taken into account the impact of increased use of safer practices during shared injections
(3) = Taken into account the impact of increased referral to methadone maintenance treatment

Cost-effectiveness	In terms of cost per life year gained: dominant strategy In terms of cost per HIV case averted: $20 100 (undiscounted) In terms of cost per HCV case averted: $444 500 (undiscounted)
Sensitivity analysis	Results were sensitive to assumptions related to injection frequency, the risk of HIV transmission through needle sharing, th e frequency of safe injection practices among users of the facility, the costs of HIV-related care and of operating the facility, and the pro¬portion of users who inject in the facility. The facility was not anymore cost saving if: - The average number of injection was < 490/year (1.3/day) or > 1762/year (4.8/day) (base case = 711; range **365-**1460) - If the number of IDUs who used the facility regularly was < 4.8% (base case: 21%) - If the annual operating costs were > $4.7 million (base case: $2 948 101; range: $2 211 000 - $3 685 000) - If the average annual cost of HIV-related care was < $10 339 (base case = $15 564; range: $12 000 - $30 000) The ICER was > $50 000/LYG if:

	- The average number of injection was < 284/year (0.78/day) (base case = 711; range 365-1460) - The proportion of injections in which needles were shared was less than 5.1% (base case: 13%; range: **5%**-21%) - If the odds ratio for the impact of the facility on needle sharing was > 0.79 (base case: 0.30 (95%CI: 0.11-**0.82**) (95%CI was provided by Kerr 2005) - If the proportion of users who followed safer injection practices > 72% (base case: 50%; range: 40%-60%)
Conclusions	Compared to other interventions, Vancouver's supervised injection site is a dominant strategy.
Remarks	1) Effectiveness data came for cohort studies (no RCT). 2) The sensitivity analysis showed that the ICER is > $50 000/LYG if the odds ratio for the impact of the facility on needle sharing was > 0.79. It should be noted that the 95%CI of this odds ratio is 0.11-0.82. In some cases, the ICER would therefore be > $50 000/LYG. 3) Results were mostly due to the impact of the facility on HIV prevalence. In terms of cost per HCV cases averted, results are not anymore cost-effective. 4) Sensitivity analysis on all parameters was not reported and no probabilistic sensitivity analysis was performed. 5) Results are not generalisable to the Belgium setting. The number of IDUs in the population (7000) and the prevalence of HIV (17%) and HCV (88%) among IDUs has an impact and differ between countries.

Authors (Year)	Pollack HA (2001)
Funding	Center for Substance Abuse Prevention Faculty Development Program
Country	USA
Design	CEA
Model	Epidemiological model (Susceptible-infected random-mixing model of disease spread)
Perspective	Not specified
Time window	Not specified
Interventions	Syringe exchange program (SEP) versus a do-nothing approach
Population	IDUs (no more specifications)
Assumptions	SEP created a 1/3 proportional reduction short-term disease incidence
	It was assumed that SEP do not reduce the frequency or duration of IDUs
	Exit rates are independent of HCV sereostatus
	All IDUs have identical risk behavior
	Sexual risks were not considered
	Sharing occurred through a process of random mixing across the IDU population
	Parameters of the model:

Variable	Estimate	Source
Arrival rate into IDU population of uninfected individuals	0.5/day	/
Arrival rates into shooting galleries*	1/(7 days)	Kaplan 1992
Infectivity**	Range of 0.005 (based on HIV) to 0.05 (HCV in high risk population)	MacDonald 1996, Coutinho 1998, Kaplan 1992
Exit rate from active IDU population	1/(4000 days), with a feasible range between (1/6320) and (1/2920)	Kaplan 1989 and Vlahov 1995

	Cost of intervention/client/day: $5 (Lurie 1993) Proportional reduction in short-term disease incidence attributable to a syringe exchange program (SEP): 1/3 (Kaplan 1994) Prevalence in the absence of treatment: Range of 0.65 to 0.965 (Analytically computed) Reproductive rate of infection***: Range of 1.14 to 28.6 (Analytically computed) *frequency of high-risk needle sharing **ability of a pathogen to establish an infection (=how frequently it spreads among hosts that are not in a parent-child relationship) ** mean number of secondary cases caused by an individual infected soon after disease introduction into a population with no pre-existing immunity to the disease in the absence of interventions to control the infection
Data source for costs	Not clear (reference given not found)
Cost items included	Not described
Data source for outcomes	See in the assumptions. For the effectiveness of SEP: Kaplan 1994 (study based on the circulation theory model for HIV)
Discounting	No discounting
Costs	SEP = $5 per client per day
Outcomes	SEP created a one-third proportional reduction in short-term disease incidence (based on the study of Kaplan 1994)
Cost-effectiveness	Cost per HCV infection averted >$250 000 across the empirically pertinent range and >$1 000 000 within the range of observed HCV prevalence in high-risk populations
Sensitivity analysis	The reproductive rate of infection is a critical variable: Variable: Arrival rates into shooting galleries; Estimate: Not specified; Reproductive risk of infection: 10; Cost per averted infection: $400 000 Variable: Arrival rates into shooting galleries; Estimate: Not specified; Reproductive risk of infection: 8; Cost per averted infection: $320 000 Variable: Infectivity; Estimate: 0.015; Reproductive risk of infection: 8.57; Cost per averted infection: $342 857 Variable: Infectivity; Estimate: 0.013125; Reproductive risk of infection: 7.5; Cost per averted infection: $300 000 Variable: Exit rate from active IDU population; Estimate: 1/(3500 days); Reproductive risk of infection: 7.5; Cost per averted infection: $262 500
Conclusions	In terms of HCV incidence and prevalence among IDUs, SEP are not cost-effective. More comprehensive harm reduction models must complement SEP to successfully contain HCV.
Remarks	1) Effectiveness of SEP was based on a mathematical model of HIV transmission among IDUs. More reliable data on the impact of SE P on HCV incidence from RCT are needed. Moreover, the uncertainty of this parameter was not handled by a sensitivity analysis. 2) It was not possible to determine the validity of the cost used and the perspective adopted was not specified. Moreover, the u ncertainty of this parameter was not handled by a sensitivity analysis. 3) Univariate sensitivity was limited (only on three parameters) and no probabilistic sensitivity analysis was performed. 4) Only the impact on HCV incidence was considered. Long term impact of HCV infect ion on costs and outcomes was not considered. 5) Results are not generalisable to the Belgium setting.

Authors (Year)	Sheerin IG, Green FT, Sellman JD (2004)
Funding	Research council of New Zealand
Country	New Zealand
Design	CEA
Model	Markov model

<table>
<tr><td>Perspective</td><td>Taxpayer (private costs to patients are not included).</td></tr>
<tr><td>Time window</td><td>Lifelong</td></tr>
<tr><td>Interventions</td><td>⇨ No Methadone maintenance therapy (MMT) and no HCV treatment
⇨ MMT and no HCV treatment
⇨ MMT and HCV treatment with interferon + ribavirin
⇨ MMT and HCV treatment with pegylated interferon + ribavirin
+ various assumptions on the number of patients receiving treatment (5% or all eligible patients (% not clear)) and on the be ginning age of treatment and age of stabilizing on MMT (26 and 31 years old).
Because interferon and ribavirin are not the current treatment, only results for pegylated interferon and ribavirin will be presented:
(1) No MMT and No treatment
(2) MMT and No treatment
(3) MMT and Pegylated interferon at age 31
(4) MMT and Pegylated interferon at age 26</td></tr>
<tr><td>Population</td><td>IDUs</td></tr>
<tr><td>Assumptions</td><td>Average dose of 70mg of methadone per day.

Cost of pegylated interferon was assumed to be 20% higher than interferon.

Patients commence injecting drugs at age 18
Excess mortality for Maori is the same as for non-Maori
IDUs are one-quarter as likely to die while in MMT compared to not in MMT
First admission to MMT at age 23
50% retention in MMT after first admission
Base case: stabilization on MMT at age 31
After stabilization on MMT, 16% per annum drop out of MMT. Patie nts retained in MMT for 11 years
84% have HCV of which 70 – 80% become chronic cases

Progression of HCV disease:
<table>
<tr><th>States</th><th>Community acquired HCV (lower rates) =Base case</th><th>Patients presenting to Liver clinic (higher rates)</th></tr>
<tr><td>Chronic hepatitis C - cirrhosis</td><td>0.010</td><td>0.0221</td></tr>
<tr><td>Chronic hepatitis C - HCC</td><td>0.001</td><td>0.001</td></tr>
<tr><td>Cirrhosis – decompensated cirrhosis</td><td>0.025</td><td>0.050</td></tr>
<tr><td>Cirrhosis– HCC</td><td>0.015</td><td>0.020</td></tr>
<tr><td>Decompensated cirrhosis – death</td><td>0.100</td><td>0.130</td></tr>
<tr><td>Decompensated cirrhosis – liver transplant</td><td>0.200</td><td>0.200</td></tr>
<tr><td>HCC – death</td><td>0.500</td><td>0.800</td></tr>
<tr><td>Liver transplant – death</td><td>0.020</td><td>0.020</td></tr>
<tr><td>All-cause death</td><td colspan="2">Variable according to age, gender and status*</td></tr>
<tr><td>Excess mortality rate due to intravenous drug use</td><td colspan="2">Range between 1 and 13.5 times the expected mortality according to age and gender</td></tr>
</table>
*Maori or non Maori
Sources: Dusheiko 1995; Wong 1995; Tong 1995</td></tr>
</table>

Effectiveness of MMT: Reduced risk of mortality: RR = 0.25

Effectiveness of treatment:
SVR rates:

	Interferon + ribavirin (Poynard 1998)	Pegylated Interferon + Ribavirin (Manns 2001)
Genotype 1 (60%)	31%	42%
Other genotypes (40%)	64%	80%

Anti-viral therapy is started 12 months after patients stabilize on MMT.
Patients eligible for treatment: around 25% (own calculation: 75% have elevated ALT and of those, 33% commence combination th erapy)
Length of treatment : 48 weeks for genotype 1 and 24 weeks for other types.
19% non-compliance with conventional COT.
14% non-compliance with pegylated interferon and ribavirin.

- ⇨ % of patients who completed the treatment: about 4.7% for interferon + ribavirin and 3.4% for pegylated interferon and ribavirin (own calculation).

Data source for costs

Christchurch Methadone Programme, New Zealand government, Australian Pharmaceutical Benefit Schedule.

Cost items included

For MMT: Operating costs: Staff, facilities, laboratory testing, methadone, etc.($2000)
For HCV treatment (Interferon + ribavirin): screening, follow-up, liver biopsy, laboratory tests and pharmaceuticals.

Data source for outcomes

Literature. Source of data for the effectiveness of MMT was not clear.

Discounting

0%, 3% and 5%

Costs

Cost per IDU (only reported for non-maori; not discounted)

	No MMT	MMT only	MMT + treatment at age 31	MMT + treatment at age 26	Incremental cost		
	(1)	(2)	(3)	(4)	(2) - (1)	(3) - (1)	(3) - (2)
Non-Maori men	28 112	64 441	68 235	57 541	36 329	40 123	3 793
Non-Maori women	31 123	72 769	73 212	65 211	41 646	42 089	443

Outcomes

Life-year gained per IDU (not discounted):

	No MMT	MMT only	MMT + treatment at age 31	MMT + treatment at age 26	Incremental LYG		
	(1)	(2)	(3)	(4)	(2) - (1)	(3) - (1)	(3) - (2)
Non-Maori men	NA	NA	NA	NA	2.44	3.24	0.81
Non-Maori women	NA	NA	NA	NA	4.13	5.05	0.93

NA: not available

Cost-effectiveness

Cost per life-year gained:

	ICER			
	(2) - (1)	(3) - (1)	(4) - (1)	(3) - (2)

	Non-Maori men	0%	14 920	12 368	8 129	4 689
		3%	25 397	25 505	19 102	NA
		5%	33 421	35 722	28 549	NA
	Non-Maori women	0%	10 096	8 334	6 227	479
		3%	25 035	24 757	19 054	NA
		5%	40 832	42 534	34 165	NA

NA: not available

Sensitivity analysis	Tested on: - Mortality (IDUs on MMT compared to not on MMT: 25% and 33%) - Higher progression rate - Lower compliance (70% instead of 86%) - Age to start MMT Similar results were found (not always reported).
Conclusions	Treating IDUs under MMT is a cost-effective strategy.
Remarks	1) SVR rates and compliance to treatment are not based on IDUs (Manns 2001). 2) Effectiveness data used to assess the impact of MMT are based on a cohort study (RR: 0.25; 95%CI: 0.19-0.33). 3) Transition probabilities varied among studies. More data are needed. 4) Sensitivity analysis on all parameters was not reported and no probabilistic sensitivity analysis was performed. 5) Results are not generalisable to the Belgium setting. 6) They adopted the perspective of the taxpayer. For this topics, the societal perspective is needed (e.g. To include the cost of IDUs associated crimes)

Authors (Year)	Martin NK, Vickerman P, Miners A, Graham RF, Hutchinson SJ, Goldberg DJ, Hickman M 2011
Funding	Scottish government hepatitis C action plan
Country	UK
Design	CUA
Model	Open dynamic HCV transmission model (cycle length = 6 months)
Perspective	Health care provider
Time window	10 years of treatment and 50 years of follow-up (40 + 10).
Interventions	Treatment of IDUs (10 treatments per 1000 IDU annually for 10 years) compared to treating ex- or non- IDUs (10 treatment annually for 10 years) or compared to no treatment.
Population	IDUs
Assumptions	Prevalence of chronic hepatitis C in the IDUs population: 3 scenarios: 20%, 40% and 60%
	Genotype distribution: genotype 1: 50% and genotype 2/3: 50%.

Progression of HCV disease:

Parameter	Mean value [95% interval]	Distribution
Mild to Moderate transition probability, TP[a]	0.025[0.018-0.033]	Beta(38.086, 1485.3516)
Moderate to Cirrhosis TP[a]	0.037[0.025-0.052]	Beta(26.905,700.2582)

Cirrhosis to decompensated cirrhosis TP[a]	0.039 [0.030-0.083]	Beta(14.617,260.1732)
Cirrhosis/decompensated cirrhosis to HCC TP[a]	0.014 [0.002-0.039]	Beta(1.9326,136.1074)
Decompensated cirrhosis/HCC to transplant TP[a]	0.03[0.012-0.056]	Beta(6.5256,210.9945)
Transplant to death TP[a]	0.21 [0.127-0.307]	Beta(16.276,61.2294)
Post transplant to death TP[a]	0.057 [0.037-0.082]	Beta(22.902,378.8825)
Decompensated cirrhosis to death TP[a]	0.13 [0.111-0.150]	Beta(147.03, 983.97)
HCC to death TP[a]	0.43 [0.372-0.489]	Beta(117.1, 155.23)

SVR rate:

Parameter	Mean value	Distribution
SVR Genotype 1	0.45	Uniform(0.40,0.50)
SVR Genotype 2/3	0.8	Uniform(0.75,0.80)

Parameters related to IDUs:

Parameter	Mean value	Distribution
Average lifespan (age 20 in 2010)	76 [75.9-76.1]	Normal(76,0.06)
Average injecting duration[b]	11 [6.25-15.75]	Uniform(6,16)
Average excess IDU death rate (excluding HCV related death)	0.01	Poisson
Rate IDUs enter the IDU population	Fit to total population of 1000 injectors	-
Infection rate	Fit to give prevalence considered	-

Utility values:

Parameter- utility values	Mean yearly value [95% interval]	Distribution
Uninfected		
Ex/non-IDU	1	N/A
IDU	0.85	Uniform [0.8-0.9]
HCV		
Mild[a]	0.77 [0.74-0.80]	Beta(521.238,155.6943)
Moderate[a]	0.66 [0.60-0.72]	Beta(168.246,86.6723)
Cirrhosis[a]	0.55 [0.44-0.65]	Beta(47.1021,38.5381)
Decompensated cirrhosis[a]	0.45 [0.39-0.51]	Beta(123.75,151.25)
HCC[a]	0.45 [0.39-0.51]	Beta(123.75,151.25)
Liver transplant[a]	0.45 [0.39-0.51]	Beta(123.75,151.25)
Post transplant[a]	0.67 [0.53-0.79]	Beta(32,16)
On treatment		
Mild[a]	0.66 [0.59-0.73]	Beta(115.706,59.6063)
Moderate[a]	0.55 [0.44-0.65]	Beta(47.1021,38.5381)
SVR		
Mild[a,b]	0.82 [0.73-0.90]	Beta(65.8678, 14.4588)

	Moderate[a] 0.72 [0.62-0.81] Beta(58.0608, 22.5792) **HCV infection related costs:**

Parameter- costs	Mean 2003-2004 value*	Distribution	Units
Mild HCV	138	Gamma(25.7,5.3698)	£ per year
Moderate HCV	717	Gamma(88.85,8.0698)	£ per year
Cirrhosis	1138	Gamma(24.234,46.984)	£ per year
HCC	8127	Gamma(18.108,448.8045)	£ per year
Decompensated cirrhosis	9120	Gamma(36.0249,253.1582)	£ per year
Liver transplant	27330	Gamma(89.7536,304.5004)	£ per transplant
Hospital costs year of transplant	9458	Gamma(13.7788,686.4168)	£ per year
Post transplant	1385	Gamma(15.2189,91.0053)	£ per year
Mild SVR	259	Gamma(28.8141, 8.9887)	£ per year
Moderate SVR	717	Gamma(89.004,8.0557)	£ per year
Cirrhosis SVR	1138	Gamma(25.81,44.091)	£ per year

Antiviral treatment delivery costs:
Cost per item can be found in the publication and include staff time and test costs required for undertaking treatment (distr ibution: +/-20%).

Treating IDUs accrues additional treatment delivery costs (2 psychiatric sessions prior to treatment, double the number of bas ic assessments during treatment, and 50% additional nursing time at each hospital visit

Antiviral treatment cost (=drug cost):
Mean cost £5,406 for 24 weeks, sampled uniformly between £4,806 -£6,418, and halved/doubled for treatment durations of 12/48 weeks

Follow-up cost:
Includes inpatient/outpatient services, investigations, procedures, and blood tests

Data source for costs	HCV infection related cost and treatment delivery cost: hospital community health services pay and prices index Treatment cost: British National Formulary Treatment delivery cost: Shepherd et al
Cost items included	2010 UK £ Direct health care costs.
Data source for outcomes	Literature
Discounting	3.5% for both costs and outcomes
Costs	

Scenario	Mean total costs (95% CI)
20% prevalence	
No treatment	20 010 000 (12 654 000-32 344 000)
Treat IDUs	20 163 000 (12 986 000-32 246 000)

	Treat ex/non-IDUs	20 552 000 (13 243 000-32 788 000)
	40% prevalence	
	No treatment	40 774 000 (26 053 000-65 483 000)
	Treat IDUs	41 119 000 (26 536 000-65 873 000)
	Treat ex/non-IDUs	41 316 000 (26 610 000-66 035 000)
	60% prevalence	
	No treatment	61 475 000 (39 424 000-98 863 000)
	Treat IDUs	62 066 000 (40 048 000-99 456 000)
	Treat ex/non-IDUs	62 017 000 (39 969 000-99 413 000)
Outcomes	QALYs gained:	
	Scenario	Mean total QALYs (95% CI)
	20% prevalence	
	No treatment	137 066 (96 704-206 932)
	Treat IDUs	137 360 (96 916-207 307)
	Treat ex/non-IDUs	137 146 (96 762-207 057)
	40% prevalence	
	No treatment	123 053 (87 031-185 394)
	Treat IDUs	123 217 (87 191-185 618)
	Treat ex/non-IDUs	123 133 (87 129-185 488)
	60% prevalence	
	No treatment	109 084 (76 883-163 857)
	Treat IDUs	109 161

	(76 978-163 961)
Treat ex/non-IDUs	109 163 (76 979-163 972)

Cost-effectiveness

Scenario	Mean ICER (£/QALY) (95%CI)
20% prevalence	
Treat IDUs	521 (Dominant - 1839)
Treat ex/non-IDUs	Dominated
40% prevalence	
Treat IDUs	2539 (1262-4822)
Treat ex/non-IDUs	Dominated
60% prevalence	
Treat ex/non-IDUs	6803 (Dominant-38 570)
Treat IDUs	Dominated

Sensitivity analysis

Probabilistic analysis (see the CI95%)
Linear regression ANCOVA analysis: % variability in the ICER at 40% prevalence results from:

- Health care costs of the different HCV progression states (55%)
- Mild SVR utility value (6%)
- Transition probabilities from mild to moderate (6%), moderate to cirrhosis (12%), cirrhosis to decompensated cirrhosis (5%), and IDU death (7%).
- Uninfected IDU utility value and costs related to antiviral treatment contributes little to the variablity in projections.

Univariate sensitivity analysis: No change in conclusion. Performed on:

- IDU SVR rate (1/2 or 3/4 of non/ex-IDU SVR)
- Genotype (all genotype 1 or all genotype 2/3)
- Time horizon (100 or 200 years),
- Discount rate (0% for outcomes)
- Treatment number (5 or 20 treatments per year),

	• Treatment duration (5 or 20 years) • Treatment delivery costs for IDU (equal or double the mean cost for an ex/non- IDU). • Ex-IDU uninfected utility values are reduced (from 1 to 0.9) • Average lifespan for both IDU and ex-IDU is reduced by 7 years • Treatment at a moderate stage instead of a mild stage.
Conclusions	Providing antiviral treatment to IDUs is the most cost-effective policy option in chronic prevalence scenarios of 20% and 40%. In chronic prevalence scenarios of 60%, providing antiviral treatment to ex/non-IDUs is slightly more cost-effective than treating IDUs.
Remarks	A prevalence of 60% is the more realistic scenario. At this level, the probability that treating IDUs was the most cost-effective option is inferior to 50% for every threshold values and this strategy is dominated compared to treating ex/non IDUs (slightly more costly and sli ghtly less effective). Confidence for this latest result would have been interesting. Limits: Important uncertainty around several parameters (SVR rate for active IDUs in the community; data related to IDUs and ex-IDUs utility values and lifespan) Heterogeneity in infection risk and treatment acceptability was not taken into account. Lack of age-structure in the model (e.g. no age-specific death rates)

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