Public Health England

Protecting and improving the nation's health

Hepatitis C: interventions for patient case-finding and linkage to care

Evidence review: summary tables

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Abbreviations

anti-HCV	Hepatitis C antibody
aOR	Adjusted odds ratio
aRR	Adjusted risk ratio
BBV	Blood borne virus
CDC	Centers for Disease Control and Prevention
CEA	Cost-effectiveness analysis
CI	Confidence interval
CUA	Cost-utility analysis
DAA	Direct-acting antiviral
DBS	Dried blood spot
DOT	Directly observed treatment
DTS	Drug treatment service
ED	Emergency department
EIA	Enzyme immunoblot assay
ELISA	Enzyme-linked immunosorbent assay
EMR	Electronic medical records
GP	General practitioner
GUM	Genito-urinary medicine
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
ICER	Incremental cost-effectiveness ratio
IFN	Interferon
LY	Life year
MSM	Men who have sex with men
NPV	Net present value
NS	Non-significant
NSP	Needle and syringe programme
OR	Odds ratio
OST	Opioid substitution therapy
PCR	Polymerase chain reaction
PEG-IFN	Pegylated interferon
POC	Point of care
PWID	People who inject drugs
QALY	Quality-adjusted life year
RBV	Ribavirin
RCT	Randomised control trial
RNA	Ribonucleic acid
RR	Risk ratio
SVR	Sustained viral response
UK	United Kingdom
US	United States
WTP	Willingness to pay

Tables of included studies

Table 2. Interventions to increase HCV testing in drug treatment services (DTS)

Study	Intervention	Location	Type of evidence	Time frame	Sample size / size of intervention	Test uptake	Positivity (anti-HCV unless stated)	Cost-effectiveness
UK								
Hickman et al., 2008	DBS testing	UK	Cluster RCT (before/after study)	Jun to Dec 2004 (6 mo)	28 specialist drug clinics and 6 prisons In DTS: Intervention: 4,720 Control: 4,140	Intervention sites: 9% (441/4,720) Control sites: 3% (121/4,140)	Not reported	Not measured
Harrison et al., 2019	Facilitator, staff training, identify and contact patients for testing, DBS testing	UK	Pilot intervention study / service evaluation with control sites	2016-2017 (1 yr) vs 2014	3 intervention and 3 control drug treatment centres Intervention: Baseline 1,804 / Intervention 1,671 Control: Baseline 924 / Intervention 826	Interaction OR 3.9 (95% CI 2.7–5.5, p<0.001)	Intervention period Intervention: 23.8% Control: 20.9% (self-reported HCV positive)	Awaited
Abou-Saleh et al., 2013	DBS testing and self-administered DBS, care pathway improvements	UK	Prospective cohort (before/after)	Not reported	Not reported, total 556 tests done during 12 months of intervention	Intervention: 52 per 3 months Control: 1.75 per 3 months	Intervention: 30.2% Control not reported	Not measured
MacLeod et al., 2014	Introduction of DBS testing in DTS as part of Scotland's HCV Action Plan	Scotland, UK	Evaluation of national programme	2007-2011 vs 1999-2006	3 prisons, 11 specialist drug clinics and multiple settings including GP, hospital and GUM In DTS: 5,399	Average annual tests in DTS Intervention: 973 Control: 67	Intervention: 19% Control: 38%	Not measured
The Centre for Public Innovation, 2017	Peer education workshops, buddy scheme and workforce development	South West, UK	Pilot case study	Not reported	46 peers & 205 staff trained; 806 people attended peer education workshops	Month post workshop: 65 tests Month before workshop: 27 tests	Not reported	Not measured
Wolf, 2016 (HCV Action)	HCV nurse, offering testing on intake and repeatedly if initially refuse	Bristol, UK	Case study	2013 - 2016	One drug treatment centre	Intervention: 95% Control: 12%	Not reported	Not measured

Study	Intervention	Location	Type of evidence	Time frame	Sample size / size of intervention	Test uptake	Positivity (anti-HCV unless stated)	Cost-effectiveness
International								
Arain et al., 2016	Formal and peer HCV education and offsite Fibroscan	Belgium	Pilot (RCT)	Not reported	Intervention:25 Control: 27	Intervention: 20% (5/25) Control: 7% (2/27)	Not reported	Not measured
Hagedorn et al., 2007	Routine HCV & HBV testing on intake to DTS, educational session 3-4 weeks after intake, nurse consultation	US	Prospective cohort (before/after)	Jan - Nov 2005	Intervention: 171 Baseline: 104	Intervention: 66% (113/171) Control: 72% (75/104)	Intervention: 17% (19/113) 12% (14/113) RNA+ Control: 23% (17/75) 13% (10/75) RNA+	Not measured
Roux et al., 2016	Harm reduction education for PWID accessing harm reduction centres	France	Multisite intervention with control sites	2011-2013	Intervention: 114 Control: 127	Intervention OR 0.72 (95% CI 0.24-2.13) aOR 4.13 (95% CI 1.03-16.60)	Not reported	Not measured

Table 3. Interventions in DTS to increase linkage to care for PWID

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive patients unless stated)	RNA testing	Referral to treatment	Treatment uptake	Treatment adherence	Treatment outcome (SVR)	Cost-effectiveness
UK											
Harrison et al., 2019	Facilitator-led intervention to train staff, identify and contact patients for testing and provide DBS testing	UK	Pilot intervention study / service evaluation with control sites	2016-2017 (1 yr) vs 2014	3 intervention and 3 control drug treatment centres Intervention: Baseline 290 / Intervention 398 Control: Baseline 194 / Intervention 173	Not reported	Referral to hepatology interaction OR 16.0 (95% CI 8.0-32.2)	Treatment initiation interaction OR 21.4 (95% CI 8.2-56.1, p<0.001)	Engaging in treatment interaction OR 29.2 (95% CI 11.9-71.8, p<0.001)	Not reported	Awaited
Tait et al., 2010	Referral pathway with non-medical referrals and outreach clinics in hospital, drug treatment and prisons	Scotland, UK	Retrospective cohort (before/after)	2004-2008 Vs prior to 2004	Results for DTS patients not reported separately – overall results presented in Care Pathway section						
International											
Masson et al., 2013	Care coordination; motivational interviewing, counselling and case management to facilitate referrals to off-site hepatology clinic	US	RCT	Feb 2008 – Jun 2011	Intervention: 149 Control: 137	Not reported	Not reported	Attended hepatology appointment Intervention: 65% (97/149) Control: 37% (51/137) p<0.001	Not reported	Not reported	Not measured
Arain et al., 2016	Formal and peer HCV education and offsite Fibroscan	Belgium	Pilot (RCT)	Not reported	Not reported Intervention: 5 tested Control: 2 tested	Not reported	Not reported	Saw hepatologist Intervention: 1 Control: 0	Not reported	Not reported	Not measured

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive patients unless stated)	RNA testing	Referral to treatment	Treatment uptake	Treatment adherence	Treatment outcome (SVR)	Cost-effectiveness
Moussali et al., 2010	Onsite provision of HCV care by multi-disciplinary team, including Fibroscan, psychiatric evaluation and motivational interviewing to initiate treatment	US	Retrospective cohort with historical comparator	Jan 2002 – Dec 2004	RNA-positive patients Intervention:224 Control:113	N/A – RNA positives	Not reported	Intervention: 38% (85/224) Control: 2% (2/113) p<0.001	Completion Intervention: 82% (70/85) Control not reported	Intervention: 43% (37/85) Control not reported	Not measured
Curcio, 2010	Case management, weekly counselling, psychiatric evaluation for OST patients (PEG-IFN/RBV)	Italy	Prospective cohort with comparator	2004 - 2008	RNA-positive patients Intervention: 16 Control: 32	N/A – RNA positives	N/A	N/A	Intervention: 93% (15/16) Control: 41% (13/32)	Intervention: 69% (11/16) Control: 34% (11/32)	Not evaluated
Hagedorn et al., 2007	Routine HCV & HBV testing on intake to drug treatment, educational session 3-4 weeks after intake, nurse consultation and referral	US	Prospective cohort (before/after)	Jan to Nov 2005	Intervention: 19 Baseline: 17	Not reported	Intervention: 100% (9/9 not already in treatment) Baseline: 50%	Intervention: 78% (7/9) Control not reported	Not reported	Not reported	Not measured
Bonkovsky et al., 2008	DOT onsite in methadone clinics (PEG-IFN/RBV)	US	Pilot (RCT)	Not reported	RNA-positive patients Intervention: 24 Control: 24	N/A - RNA positives	N/A	N/A consenting patients	Completion Intervention: 83% 20/24 Control: 71% (71/24) p=0.3	Intervention: 54% (13/24) Control: 33% (8/24) p=0.15 OR 3.27, 95% CI 0.90-11.91, p=0.073	Not measured

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive patients unless stated)	RNA testing	Referral to treatment	Treatment uptake	Treatment adherence	Treatment outcome (SVR)	Cost-effectiveness
Litwin et al., 2011	Modified DOT onsite in methadone clinics (PEG-IFN/RBV)	US	RCT	Not reported	RNA-positive patients Intervention: 21 Control: 19	N/A RNA positive patients	N/A	N/A	Pill count at 12 weeks Intervention: 88% Control: 80% p=0.04	Intervention: 44% Control: 40% p=NS	Not measured
Bruce et al., 2012	Modified DOT onsite in a methadone clinic (PEG-IFN/RBV)	US	Pilot (RCT)	2007-2010	RNA-positive patients Intervention: 12 Control: 9	N/A RNA positive patients	Not reported	Intervention: 100% (12/12) Control: 44% (4/9)	Not reported	Intervention: 50% (6/12) Control: 11% (1/9) p=NS	Not measured
Litwin et al., 2017	DOT or group medical visit for patients receiving onsite DAA treatment in methadone maintenance clinic	US	RCT	Not reported	RNA-positive patients DOT: 51 Group medical visit: 48 Control: 51	N/A RNA positive patients	N/A	N/A, patients who initiated treatment	Not reported	Interim results, patients who had reached this time point DOT: 98% (45/46) Group medical visit: 93% (42/45) Control: 89% (40/45) p=0.19	Not measured
Reimer et al., 2013	Patient education for OST patients receiving PEG-IFN/RBV	Germany	Prospective cohort with control	Jan 2005 – Dec 2008	RNA-positive patients Intervention: 82 Control: 107	N/A RNA positive patients	N/A	N/A	Completion Intervention: 78% (64/82) Control: 68% (73/107) aOR 0.05, 95% CI 0.01-33.95, p=0.370	aOR 0.01, 95% CI 0.01-7.77, p=0.183	Not measured
Seaman et al., 2018	Treatment for OST patients vs those recruited through needle exchange programme (NSP)	US	Prospective cohort with comparator group	Not reported	RNA-positive patients NSP: 25 OST: 25	N/A RNA positive patients	N/A	Enrolled: NSP: 20/25 OST: 25/25	NSP: 75% (15/20) OST: 93% (23/25) Community standard: 98%	Interim results NSP: 45% (5/11) OST: 92% (22/24) Community standard: 93% (42/45)	Not measured

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive patients unless stated)	RNA testing	Referral to treatment	Treatment uptake	Treatment adherence	Treatment outcome (SVR)	Cost-effectiveness
Sulkowski et al., 2017	i) Financial incentives ii) Peer mentors iii) Usual care (control)	US	RCT	Not reported	RNA-positive patients i) 54 ii) 54 Control: 36	N/A RNA positive patients	N/A	i) 77% (41/53) (1 pending) (p>0.05) ii) 88% (45/51) (3 pending) (p=0.01) Control: 66% (24/36)	Not reported	90% of all patients who initiated treatment	Not measured

Table 4. Pharmacy interventions to provide HCV testing for PWID

Study	Intervention	Location	Type of evidence	Time frame	Sample size / size of intervention	Test uptake	Positivity (anti-HCV unless stated)	Cost effectiveness
UK								
Radley et al., 2017	Pharmacy DBS and treatment	Scotland, UK	RCT	Nov 2015 to Sep 2016 (10 mo)	Intervention: 4 pharmacies, 262 clients Control: 4 pharmacies, 244 clients	Intervention: 36% (94/262) Control: 24% (58/244) p<0.003	Intervention: 32% (30/94) Control: 29% (17/58)	Costs for treatment pathway £695 less per patient than traditional setting
Radley et al., 2017	Pharmacy DBS	Scotland, UK	Prospective cohort - quasi-experimental	Jan – Dec 2014 (1 year)	Intervention: 6 pharmacies, 143 clients Control: 561	Intervention: 30% (43/143) Control: 13% (75/561) p≤0.0001	Intervention: 28% (12/43) Control: Not reported	Not measured
Buchanan et al., 2016	Pharmacy DBS	Isle of Wight, UK	Service evaluation	Sep 2014 to May 2015 (9 mo)	22 intervention pharmacies, control was patients attending drug support centre	Intervention: 88 patients tested Control: 34 patients tested	Intervention: 7% (6/88) HCV RNA+ Control: 9% (3/34) HCV RNA+	Not measured

Table 5: Pharmacy interventions to increase linkage to care for PWID

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive patients unless stated)	RNA testing	Referral to treatment	Treatment uptake	Treatment adherence	Treatment outcome (SVR)	Cost effectiveness
UK											
Radley et al., 2017	Pharmacy DBS and treatment	Scotland, UK	RCT	Nov 2015 to Sep 2016 (10 mo)	Intervention: 4 pharmacies, 26 new anti-HCV+ diagnoses Control: 4 pharmacies, 15 new anti-HCV+ diagnoses	Attended for assessment blood test: Intervention 77% (20/26) Control 27% (6/15) p<0.002	N/A	Intervention: 11% (3/26) Control: 7% (1/15)	Completion Intervention: 100% (3/3) Control: 100% (1/1)	Not reported	Treatment pathway in pharmacy setting £695 less per patient than traditional setting
Buchanan et al., 2016	Pharmacy DBS	Isle of Wight, UK	Service evaluation	Sep 2014 to May 2015 (9 mo)	22 intervention pharmacies, control was patients attending drug support centre Intervention: 6 Control: 3	Intervention:100% (reflex testing) Control not reported	Intervention: 100% (6/6) attended point-of-diagnosis consultation Control: 100% (3/3) referred to hepatology	Intervention: 100% (6/6) in HCV care pathway 33% (2/6) had commenced treatment Control: 0% (0/3) had been seen by a hepatology specialist	Not reported	Not reported	Not measured

Table 6. Primary care testing interventions

Study	Intervention	Location	Type of evidence	Time frame	Sample size / size of intervention	Test uptake	Positivity (anti-HCV unless stated)	Cost effectiveness
UK								
Roberts et al., 2019	EMR identification of at-risk patients	South West, England	Cluster RCT	Not reported	22 intervention practices 13,097 patients with risk criteria 23 control practices 11,376 patients with risk criteria.	Intervention practices Intervention: 16% (2,071/13,097) Baseline: 4.6% (608/13,907) aRR 1.59, 95% CI 1.21-2.08, p<0.001	To be completed	ICER £7,507 per QALY for base case, 89.7% probability of being below £20,000 per QALY
Flanagan et al., 2018	Incentivised HBV and HCV testing for migrants in GP practices	Bradford, East and South London, UK (high migrant density areas)	Cluster RCT	Oct 2013 – Feb 2017	50 intervention practices; 58,512 patients 8 control practices; 31,738 patients	Intervention: 20% (11,386/58,512) Control: 2% (453/31,738) p=0.01	All patients: 0.9% (111/11,929) RNA+: 0.3% (36/11,929)	ICER £6,935 to £18,185 per QALY for HCV testing and treatment
		Oxford, UK (low migrant density area)	Prospective cohort	May 2015 – Apr 2017	9 intervention practices; 6,854 patients	Intervention: 8% (515/6,854) Control not reported	Not reported	Not reported
Lewis et al., 2011	Community outreach (Mosques), opportunistic or opt-out testing for Pakistani/British Pakistani patients	UK	Prospective cohort	Not reported	Mosques: 5,000 Opportunistic: 1,163 Opt-out: 1,134	Mosques: 0 Opportunistic: 2% (17/1,163) Opt-out: 20% (223/1,134) (p<0.0001)	Opportunistic: 0% Opt-out: 2.4%	Not reported
Anderson et al., 2009	HCV testing among birth cohort in GP practices	Glasgow, UK	Intervention with control	Nov 2003 - Apr 2004 (6 mo)	2 GP practices	Intervention: 20% (117/584) Control: 0	Intervention: 13% (15/117) 9% (11/117) HCV RNA+ Control N/A	Not measured
Cullen et al., 2012	EMR to identify former PWID for opportunistic testing in GP practices	Scotland, UK	Prospective cohort	Feb - Oct 2007 (6 mo)	Practices Intervention: 8 Control: 8	Intervention: 0.8% (105/13,037) Control: 0.3% (36/14,189)	Intervention: 70% (74/105) 41% (43/105) HCV RNA+ Control: 22% (8/36) 14% (5/36) HCV RNA+	Not measured
Leeds Sexual Health, 2017	Opt-out HBV, HCV and HIV testing in GP practices	UK	Pilot evaluation	Nov 2015 – Nov 2016	29 GP practices, 20,615 patients	18% (3,748/20,615) 250% increase in number of tests vs 8 months prior to intervention	0.8% HCV 0.29% HIV 3% HBV	£1,060 per BBV diagnosis

Study	Intervention	Location	Type of evidence	Time frame	Sample size / size of intervention	Test uptake	Positivity (anti-HCV unless stated)	Cost effectiveness
International								
Federman et al., 2017	EMR reminder to test birth cohort for HCV	US	Cluster RCT	Apr 2013 – Mar 2014	10 clusters, 25,821 study eligible visits Intervention: 15,010 Control: 10,811	Intervention: 20% Control: 2% p<0.0001	Intervention: 3.1% Control: 1.1% p<0.0001	Not measured
Brady, 2017	i) Repeated mailing	US	RCT	Feb 2013 – Oct 2013	8,992 patients, randomised 1:2	Intervention: 27% Control: 1% aRR 19.2, 95% CI 9.7-38.2	Not reported	$63 per test completed $7005 per HCV-positive case diagnosed
Brady, 2017	ii) EMR alert and automatic test order	US	Cluster RCT	Apr 2013 – Mar 2014	10 primary care practices, 14,475 patients	Intervention: 31% Control: 4% aRR 13.2, 95% CI 3.5-48.6	Not reported	$44 per test completed $4527 per HCV-positive case diagnosed
Brady, 2017	iii) Patient solicitation	US	Cluster randomised cross-over study	Dec 2012 – Jan 2014	4 internal medicine clinics, 8,873 patients	Intervention: 64% Control: 2.0% aRR 32.9, 95% CI 19.3-56.1	Not reported	$53 per test completed $4230 per HCV-positive case diagnosed
Cullen et al., 2006	Nurse-led education and awareness campaign for staff in methadone prescribing GP practices	Ireland	Cluster RCT	6 mo	Intervention: 13 practices, 104 patients Control: 12 practices, 94 patients	Intervention: 34% (35/104) Control: 26% (24/94) p=0.02	Not reported	Not measured
Castrejon, 2017	EMR reminder to test birth cohort for HCV	US	Before/after study	Aug 2015 – Jul 2016 vs Aug 2014 – Jul 2015	60 practices, ~180,000 registered patients	Intervention: 1,117 / month (Jul 2016) Control: 519 / month (Aug 2014) p<0.01 for trend	Intervention: 4.1% Control: 1.5% p<0.01 for trend	Not evaluated
de la Torre, 2016	EMR automated test order for HCV	US	Before/after study	Jul-Oct vs Jan-Jun 2016		Intervention: 1,187 per month Control: 245 per month	Intervention: 7.4% (151/1,473) Control: 10.3% (520/7,008)	Not evaluated
Gemelas, 2016	EMR alert, staff training, discussions with leadership and staff	US	Before/after study	Sep 2012 – Sep 2014	One clinic, ~6,500 patient population	Intervention:76% (593/785) (Dec 2014) Control: 5% (47/938) (Sep 2012)	Not reported	Not evaluated
Jain, 2018	EMR reminder to test birth cohort for HCV, staff training	US	Before/after study	Jun 2015 – Aug 2017 vs Jun 2013 – May 2015	Safety-net hospital system Intervention: 39,351 eligible patients seen Control: 56,727 eligible patients seen	Intervention:36% Control:10% aOR 5.42, 95% CI 5.22-5.62)	Not reported	Not evaluated

Study	Intervention	Location	Type of evidence	Time frame	Sample size / size of intervention	Test uptake	Positivity (anti-HCV unless stated)	Cost effectiveness
Konerman, 2017	EMR reminder, educational posters and patient portal, workflow design	US	Before/after study		Primary care health system, clinics at 13 sites Intervention: 27,789 eligible patients Control: 22,488 eligible patients	Intervention: 73% (19,847/27,789) Control: 7.6% (1,705/22,488) p<0.001	Intervention: 0.8% (178/19,847) Control: 2.1% (36/1,705)	Not reported
Magaldi, 2018	EMR automated test order (inc RNA testing), staff education	US	Before/after study	Oct 2016 – Sep 2017 vs Oct 2015 – Sep 2016	One health centre	Intervention: 78% (1,112 patients) Control: 57% (521 /909)	Intervention: 32.3% (359/1,112) Control: 12.7% (66/521)	Not measured
MacLean et al., 2018	EMR reminder to test birth cohort for HCV	US	Retrospective cohort (before/after)	Oct 2013 – July 2016	5 family medicine and 4 primary care internal medicine sites, 25,071 patients (all patients in age range who attended over study period)	Cumulative proportion: 12% before CDC recommendations 15% in 2 years after CDC recommendations 37% in 2 years after installation of EMR prompt p<0.001	6.4% before CDC recommendations 4.4% in 2 years after CDC recommendations 1.6% in 2 years after installation of EMR prompt p<0.001	Not measured
Golden et al., 2017	EMR reminder to test birth cohort for HIV / HCV	US	Retrospective cohort (before/after)	Jan 2011 – Dec 2015	3 primary care clinics Intervention: 3,336 Control: 3,773	Intervention: 36% Control: 18% p< 0.0001	Intervention: 10.4% Control: 19.8% p< 0.0001	Not measured
Goel et al., 2016	EMR reminder to test birth cohort patients, staff education, data feedback and patient navigation	US	Prospective cohort (before/after)	Nov 2013 – Nov 2015	2 primary care practices in 1 hospital Intervention: 9,101 Control: no data	Intervention: 75% Control: 55% p<0.01	Not reported	Not measured
Shahnazarian et al., 2015	EMR reminder to test birth cohort for HCV	US	Retrospective cohort (before/after)	May 2014 - Feb 2015 (10 mo) vs. Jan 2014	One hospital Intervention: 14,758 Control 1,207	Intervention: 88% (1,094/1,245) in final month[1] Control: 47% (570/1,207) p<0.001 final month vs control month	Intervention: 4% (326/8,989) Control: 2% (9/570)	Not measured
Teply, 2018	EMR alert to test birth cohort for HCV	US	Before/after study	Dec 2016 – May 2017 Vs Jun 2016 - Nov 2016	Health system with 35 primary care clinics	Intervention: 24% (8,928/37,424) Control: 1.7% (625/35,823)	Intervention: 1.7% (155/8,928) Control: 5.0% (31/625)	Not measured
Tzarnas, 2015	EMR alert to test birth cohort for HCV, staff education, improved test order	US	Before/after study	Jul-Aug 2014 vs May 2014	Intervention: 1,628 (Aug 2014) Control: 1,658	Intervention: 20% (Aug 2014) Control: 7%	Not reported	Not measured

Study	Intervention	Location	Type of evidence	Time frame	Sample size / size of intervention	Test uptake	Positivity (anti-HCV unless stated)	Cost effectiveness
Thuluvath, 2016	EMR alert to test birth cohort for HCV, invitation letters to patients with blood order form	US	Before/after study	Not reported	One community hospital	Testing rates increased by 300% compared to previous 12 months	Not reported	Not measured
Karliner, 2018	Quality improvement; staff education, EMR alert, educational posters, automated RNA testing	US	Before/after study	Jul 2016 – Mar 2017	1 internal medicine clinic	Intervention: 71% Control: 59%	2.85% (unclear what time period this refers to)	Not measured
Soo et al., 2018	EMR alert in a large healthcare system	US	Before/after	Jan 2017 – Apr 2018 Vs Dec 2016	One health system 76,288 patients screened overall	Intervention (Apr 2018): 55% Control (Dec 2016): 23%	Intervention overall: 4.6% (3,507/76,288) Control not reported	Not measured
Litwin et al., 2012	Clinical reminder stickers for risk based and birth cohort testing placed on progress notes	US	Serial cross sectional compared to baseline	Nov 2008-Mar 2009 and Mar-Jun 2009	Intervention: Risk screening: 8,981 Birth cohort: 10,165 Control: 6,591	Intervention: Risk screening: 13% Birth cohort: 10% Control: 6% p<0.001	Risk screening intervention: 5.3% Birth cohort intervention: 5.8%	Not measured
Nitsche, 2018	Continuous audit and staff education	US	Intervention with control sites	Mar-Sep 2015 Vs Aug-Oct 2014	3 intervention sites 4 control sites	Intervention: 6% at baseline, 18% in final month Control: 5% at baseline, 10% in final month p<0.001 for difference in intervention and control	Not reported	Not evaluated
Madhani et al., 2017	Educational intervention to improve staff knowledge of guidelines for HCV testing	US	Retrospective cohort (before/after)	Jan - Apr 2016 (4 mo) compared to 2013 data	Intervention: 100 Control: 200	Intervention: 13% (13/100) Control: 7% (13/200)	Not reported	Not measured
Wong, 2017	Staff education on testing age cohort for HCV, posters and educational handouts for patients	US	Before/after study	Feb-Jul 2016 vs Feb-Apr 2015	3 hospitals	Intervention: 10% (105/1,070) Control: 1% (16/1,268)	Intervention: 2.9% Control: 31.3%	Not evaluated

Study	Intervention	Location	Type of evidence	Time frame	Sample size / size of intervention	Test uptake	Positivity (anti-HCV unless stated)	Cost effectiveness
Murphy, 2016	Staff education on testing age cohort patients for HCV	US	Retrospective cohort (before/after)	4 weeks before/after intervention, 2011	One community clinic	Intervention: 69% (213/307) Control: 46% (156/339) p<0.001	Not reported	Not evaluated
Helsper et al., 2010	Awareness raising plus support programme for practitioners compared to awareness raising alone	Netherlands	Intervention with control	Oct 2007 - Jan 2008 (4 mo)	Intervention and control regions	Intervention region: Before intervention 57 tests After intervention 172 tests Control region: Before intervention 86 tests After intervention 118 tests	Intervention region: Before intervention 0% (0/57) After intervention 1.7% (3/172) Control region: Before intervention 1.7% (1.5/86) After intervention 0.8% (1/118)	Not measured
Franco et al., 2018	Community testing, awareness raising, patient navigation and treatment	US	Before/after and comparison of community sites vs tertiary care	July 2015 – May 2017 Vs 2013-2015	Multi-site state-wide intervention, >40 locations	2.7-fold increase in quarterly testing	2.2-fold increase in quarterly diagnosis	Not measured
Ho et al., 2018	Community POC HBV and HCV testing for migrants	Belgium	Prospective cohort comparing 2 screening protocols	Oct 2014 – Dec 2017	Not reported	Intervention: 108 Control: 460	Intervention: 0.2% (1/108) Control: 0% (0/460) HBV Intervention: 6% (6/108) Control: 7% (32/460)	Intervention: €25.5 per person screened Control: €54.0 per person screened

Table 7. Primary care interventions to increase linkage to care

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive patients unless stated)	RNA testing	Referral to treatment	Treatment initiation	Treatment adherence	Treatment outcome (SVR)	Cost effectiveness
UK											
Roberts et al., 2019	Treatment in primary care for patients identified via EMR risk algorithm and diagnosed	South West, England	Cluster RCT	Not reported	22 intervention practices, 13,097 patients with risk criteria 23 control practices, 11,376 patients with risk criteria	Intervention: 93% (120/129) Control: 98% (50/51)	Intervention: 46% (20/43) PCR positive patients Control: 23% (3/13) PCR positive patients aRR 5.78, 95% CI 1.55-21.61)	Not reported	Not reported	Not reported	ICER £7,507 per QALY for base case, 89.7% probability of being below £20,000 per QALY
Flanagan et al., 2018	Community care for migrant patients diagnosed with HCV in primary care	Bradford, East and South London, UK (high migrant density areas)	Cluster RCT	Oct 2013 – Feb 2017	Intervention: 8 Control: 27	Not reported	N/A – patients randomised after referral	100% (8/8) 100% (27/27)	100% (8/8) 100% (27/27)	Not reported	Not measured
International											
Arora et al., 2011	Telehealth / Training and support via videoconferencing / teleconferencing for primary care providers to deliver HCV care	US	Prospective cohort	Sep 2004 – Feb 2008	RNA-positive patients Intervention:261 Control: 146	N/A	N/A	N/A	Not reported	Intervention: 58% (152/261) Control: 58% (84/146)	Not measured
Wade et al., 2018a	Pathway to support primary care to deliver HCV care	Australia	Before/after	Jul 2016 – Jun 2017 vs Jul 2015 – Jun 2016	Not stated Intervention: 442 Control: 226	Not reported	N/A	Intervention: 40% (178/442) Control: 8% (18/226)		Intervention: 73% Control not reported	Not measured

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive patients unless stated)	RNA testing	Referral to treatment	Treatment initiation	Treatment adherence	Treatment outcome (SVR)	Cost effectiveness
Wade et al., 2018b	Providing DAA treatment in primary care	Australia	RCT	Not reported	Not stated 'people with HCV' Intervention: 70 Control: 66	Not reported	Completed assessment Intervention: 87% (61/70) Control: 64% (42/66)	Of eligible patients Intervention: 75% (43/57) Control: 34% (18/53) p<0.001		Intervention: 47% (27/57) Control: 30% (16/53) p=0.065	Not measured
Mohsen et al., 2018	Tele-mentoring to support primary care staff to treat	Australia	Retro-spective cohort	Jul 2016 – Apr 2017	RNA-positive patients Intervention: 100 Control: 100	N/A	N/A – referred patients	Intervention: 78% (78/100) Control: 81% (81/100)		Intervention: 60% (60/100) Control: 67% (67/100)	Not measured
Fox, 2015	Patient navigator and treatment in primary care	US	Prospective cohort (before/after)	2009 - 2014	Not reported	Not reported	Intervention: 33 Control: 12 Completed referral Intervention: 73% 24/33 Control: 33% 4/12 p=0.03	Intervention: 18% 6/33 Control: 8% 1/12 p=NS	Not reported	Intervention: 9% 3/33 Control: 8% 1/12 p=NS	Not measured
Franco et al., 2018	Community testing, awareness raising, patient navigation and treatment	US	Before/after and comparison of community sites vs tertiary care	July 2015 – May 2017 Vs 2013-2015	Multi-site state-wide intervention, >40 locations	Confirmed RNA+ Intervention: 57% (1,164/2,042) Control: 72% (5,362/7,464) p<0.001	Not reported	Intervention: 29% (339/1,164) Control: 29% (1,563/5,362) p=0.97	Not reported	Intervention: 13% (148/1,164) Control: 24% (1,285/5,362)	Not measured
Ho et al., 2018	Community POC HBV and HCV testing for migrants	Netherlands	Prospective cohort comparing 2 screening protocols	Oct 2014 – Dec 2017	Not reported	Not reported	Linkage of HBV and HCV diagnosed Intervention: 86% Control: 34% P=0.02	Not reported	Not reported	Not reported	Cost for linkage to care not reported

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive patients unless stated)	RNA testing	Referral to treatment	Treatment initiation	Treatment adherence	Treatment outcome (SVR)	Cost effectiveness
Magaldi et al., 2018	EMR automated test order (inc RNA testing), staff education	US	Before/after study	Oct 2016 – Sep 2017 vs Oct 2015 – Sep 2016	One health centre	Intervention: 99.7% (358/359) Control: 81% (66/81)	Attended 1st appointment: Intervention: 76% (273/359) Control:76% 62/81)	Intervention: 33% (118/359) Control: 14% (11/81)	Completion: Intervention: 21% (75/359) Control: 14% (11/81)	Intervention: 9% (33/359) Control: 14% (11/81)	Not measured
Hirsch et al., 2014	Quality improvement to increase timely RNA testing: i) RNA testing at outpatient clinics ii) Reflex RNA testing policy iii) Improvement team to address failures in RNA testing policy	US	Before/after (interrupted time series)	i) 2008 – 2010 ii) 2010-2011 iii) 2011-2013 vs 2005 - 2008	One healthcare system (i) 672 (ii) 395 (iii) 568 Control: 1,404	(i) 68% (457/672) (ii) 96% (380/395) (iii) 100% (568/568) Control: 45% (638/1,404) p<0.001	Not reported	Not reported	Not reported	Not reported	Not measured
Castrejon et al., 2017	EMR alert and patient navigator to improve RNA testing	US	Retrospective cohort (before/ after)	Jan-Jul 2016 Vs Jan-Jul 2015	Intervention: 131 Control: 87	Intervention: 95% (124/131) Control: 84% (73/89)	Linked to care, of RNA positives Intervention: 94% (46/49) Control: 88% (35/40)	Not reported	Not reported	Not reported	Not measured
Cullen et al., 2006	Nurse-led education and awareness raising for staff in methadone prescribing GP practices	Ireland	Cluster RCT	6 mo	Intervention: 13 practices, 73 patients Control: 12 practices, 41 patients	Intervention: 56% (41/73) Control: 22% (9/41) P=0.05	Intervention: 60% (44/73) Control: 32% (13/41) p = 0.06	Attended Intervention: 51% (37/73) Control: 22% (9/41) p=0.04 Initiated treatment Intervention: 7% (5/73) Control: 3% (1/41) p=0.20	Not reported	Not reported	Not measured

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive patients unless stated)	RNA testing	Referral to treatment	Treatment initiation	Treatment adherence	Treatment outcome (SVR)	Cost effectiveness
Jain, 2018	EMR best practice alert and staff education	US	Before/after study	Jun 2015 – Aug 2017 vs Jun 2013 – May 2015	Safety-net hospital system Intervention: 1,207 Control: 1,117	Intervention: 75% Control: 54% aOR 2.38, 95% CI 1.95-2.90	Of RNA positives Intervention: 45% Control: 43% aOR 1.61, 95% CI 0.88-1.54	Not reported	Not reported	Not reported	Not measured
Konerman, 2017	EMR reminder, educational posters and patient portal, workflow design	US	Before/after study		13 primary health care sites Intervention: 178 Control: 36	Intervention: 94% (168/178) Control: 86% (31/36)	Intervention: 100% (53/53) Attended referral Intervention: 87% 46/53 (1 pending) Control not reported	Intervention: 38% (20/53) (interim results) Control not reported	Not reported	Interim results Intervention: 45% 9/20 Control not reported	Not measured

Table 8. Interventions to increase HCV testing in prisons

Study	Intervention	Location	Type of evidence	Time frame	Sample size / size of intervention	Test uptake	Positivity (anti-HCV unless stated)	Cost effectiveness
UK								
Craine et al., 2015	DBS testing	Wales, UK	Step-wedged RCT	Mar 2011 – Sep 2012	Intervention: 2,237 Control: 13,108	OR=0.84 (95% CI: 0.68-1.03)	Overall: 13.3%	Not measured
Hickman et al., 2008	DBS testing	UK	Cluster RCT (before/after study)	Jun to Dec 2004 (6 mo)	28 specialist drug clinics and 6 prisons. Intervention: 6550 Control: 5800	Intervention: 12% (791/6550) Control: 4% (243/5800)	Not reported	Not measured
Morey et al., 2019	Opt-out DBS testing	North East, UK	Before/after	Mar 2016-Feb 2017 vs 2013-2014	1 prison Intervention: 4,280 Control: ~7,000	Intervention: 35% (1,495/4,280) Control: 2% (164/7,000)	Intervention: 6.4% (95/1,495) 3.1% (47/1,495) HCV RNA+	Not measured
Jack et al., 2019	Opt-out DBS testing	East Midlands, UK	Before/after	Jul 2016 – Jun 2017	14 prisons	Intervention: 14% (2,706/20,075) Number tested year before intervention: 1,972 Year post intervention: 3,440	Intervention: 9.3% (152/1,643, DBS tests only)	Not measured
Arif et al., 2018	Opt-out DBS testing	Birmingham, UK	Before/after	2015 Vs 2013	1 prison Intervention: 4,998 Control: 6,452	Intervention: 8% (380/4998) Control: 0%	Not reported	Not measured
Abou-Saleh et al., 2013	DBS testing and self-administered DBS testing, care pathway improvements	UK	Prospective cohort (before/after)	Not reported	Not reported	Intervention: 43 per 3 months Control: 0.5 per 3 months	Intervention: 32.6% Control not reported	Not measured
MacLeod et al., 2014	Complex intervention; improved accessibility of HCV testing and targeted activities to promote HCV testing	Scotland, UK	Evaluation of national programme	2007-2011 (vs 1999-2006)	14 sites including 3 prisons In prisons: 4,200	In prisons: average annual tests Intervention: 429 Control: 257	Intervention: 44% Control: 27%	Not measured
International								
Winter et al., 2015	Nurse-led clinic	Australia	Before/after	Dec 2005 – Jul 2008	Intervention: 280 Control: 285	Intervention: 25% Control: 13% p<0.001	Not reported	Not measured
De la Flor et al., 2017	Opt-out HIV/HCV testing	US	Before/after	Jun 2015 – Nov 2016 Vs Jun 2015	Not reported	Intervention: 269 (Jan 2016) Control: 118 (Jun 2015)	Intervention: 16.4% (500/3,042) over 6 months Control not reported	Not measured

Table 9. Interventions to increase HCV linkage to care in prisons

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive unless stated)	RNA testing	Referral to treatment	Treatment uptake	Treatment adherence	Treatment outcome (SVR)	Cost effectiveness
UK											
Morey et al., 2019	Telemedicine HCV clinic in prison	North East, UK	Before/after	Mar 2016-Feb 2017 vs 2013-2014	Intervention: 80 patients initially reviewed Control: 29 HCV RNA+ patients	Not reported	Not reported	Intervention: 71% (57/80) Control: 14% (4/29)	Completion Intervention: 53% (42/80) Control not reported	Not reported	Not measured
Tait et al., 2010	Referral pathway; non-medical referrals and outreach clinics in hospital, DTS and prisons	Scotland, UK	Retrospective cohort (before/after)	2004-2008	In prisons: not reported	Not reported	Intervention: 75 Control: 4	Not reported	Not reported	Not reported	Not measured
International											
Saiz de la Hoya et al., 2014	DOT (PEG-IFN/RBV) compared to self-administered treatment	Spain	RCT	Jul 2006 – Sep 2008	25 prisons RNA-positive patients Intervention: 109 Control: 135	N/A	N/A	N/A	Intervention: 81% Control: 84% p=0.091	Intervention: 61% Control: 66% RR 0.92, 95% CI 0.76-1.12	Not measured

Table 10. Interventions to increase HCV linkage to care for homeless populations

Study	Intervention	Location	Type of evidence	Time frame	Sample size / size of intervention	RNA testing	Referral to treatment	Treatment uptake	Treatment adherence	Treatment outcome (SVR)	Cost effectiveness
UK											
Stagg et al., 2019	Peer support within outreach substance misuse and homelessness services	UK	RCT	Aug 2013 – Apr 2016	Intervention: 63 Control: 38	N/A RNA positive patients randomised	Not reported	Engagement with services Intervention: 37% (23/63) Control: 18% (7/38)	Engage in services 3 times or more: Intervention: 37% (23/63) Control: 18% (7/38) p=0.04 OR 2.55 (95% CI 0.97-6.70, p=0.06)	Intervention: 0 Control: 0	Not measured
International											
Hodges et al., 2018	Integrated medical, mental health and case management for people who are homeless or at risk of homelessness	US	Prospective cohort	Mar 2016 - ?	102 patients attended at least one intervention appointment 78 continued in intervention 26 opted for individual treatment	Not reported – assumed all RNA positive	N/A	N/A	Completion Intervention: 99% (77/78) Individual treatment: 88% (23/26)	Intervention: 91% (71/78) Individual treatment: 69% (18/26)	Not measured
Singh et al., 2017	Multidisciplinary care for PWID, comparing outcomes for homeless and stably housed individuals	Canada	Not reported	Not reported	74 individuals 43 homeless 31 with stable housing	Not reported	Not reported	Not reported	Not reported	Homeless: 88% (38/43) Stably housed: 97% (30/31) p=0.19	Not measured

Table 11. Emergency department (ED) interventions to increase testing

Study	Intervention	Location	Type of evidence	Time frame	Sample size / size of intervention	Test uptake	Positivity (anti-HCV unless stated)	Cost effectiveness
UK								
Bradshaw et al., 2018	Opt-out testing with quality improvement interventions; training, staff rewards, testing champions, common order set	UK	Pilot	Nov 2015 – Dec 2016	1 ED	Final 10 weeks: median 180 tests, 96% BBV tests (vs standalone HIV test) First 10 weeks: median 121 tests, 55% BBV tests P<0.01	0.5% (32/1,608)	Cost per case (HCV RNA) £4,682
Geretti et al., 2018	Effect of concomitant HIV testing offer on point of care HCV testing uptake	UK	Prospective cohort	Mar-Jun 2017	1 ED	HCV test only: 47% (211/451) With concomitant HIV test: 31% (113/363)	0.31% (1/324) HCV RNA+ overall	Not measured
International								
Merchant et al., 2014	Brief intervention promoting rapid HIV/HCV screening for drug users (not PWID)	US	RCT	Feb 2011 – Mar 2012	2 EDs Intervention: 198 Control: 197	Intervention: 65% Control:65%	Intervention: 4 Control: 3	Not measured
Merchant et al., 2015	Brief intervention for drug-misusing ED patients (HCV & HIV testing)	US	RCT	Jul 2010 - Dec 2012	2 EDs 1,057 patients	Intervention: 37% (175/475) Control: 43% (185/432) p=0.09	Not reported	Not measured
Schechter-Perkins et al., 2018	Opt-out testing using EMR alert for all patients aged over 13 years	US	Before/after	Nov 2016 – Jan 2017	1 ED 19,905 unique patient visits	Intervention: 1,269 per month Control: 18 per month	Intervention: 13.7% (504/3,808) 7.7% (292/3,808) HCV RNA+ Control not reported	Not measured

Table 12. Interventions to increase HCV testing in other settings

Study	Intervention	Location	Type of evidence	Time frame	Sample size / size of intervention	Test uptake	Positivity (HCV antibody unless stated)	Cost effectiveness
International								
Rosenberg et al., 2010	HBV and HCV testing, risk reduction, referral and support into treatment for people with dual diagnosis (severe mental illness and substance misuse) in community mental health	US	RCT	2006 - 2008	Intervention: 118 Control: 118	Intervention: 86% (70/81) Control: 15% (10/69) P<0.01	Intervention: 25% (26/106) Control: No data	Intervention: $240 per client (in addition to costs of tests and vaccines)
Sahajian et al., 2010	Education and pre-test counselling with onsite testing for people living in shelters	France	Cluster RCT	Oct 2007 - Apr 2009 (18 mo)	(i) education and referral to testing (6 shelters) (ii) education and on-site testing (6 shelters) (iii) control (6 shelters)	(i): 43% (95/222) (ii): 60% (145/243) Control: 2% (12/811)	(i): 3% (3/95) (ii): 3% (4/145) Control: 0% (0/12)	Not measured
Jen et al., 2016	Inpatient testing in hospital coordinated by interdisciplinary ward round	US	Before/after	Oct- Dec 2015 vs Oct- Dec 2014	1 hospital Intervention: 506 Control: 522	Intervention: 28% Control: 4%	Intervention: 7.7% Control not reported	Not measured
Lacey et al., 2007	HCV education and counselling and offer of testing for psychiatric inpatients	Australia	Prospective cohort (before/after)	Aug 2002 – Jan 2003 (vs Feb – Jul 2002)	One psychiatric unit Intervention: 402 Control: 430	Intervention: 18% (71/402) Control: 9% (40/430) P<0.01)	Intervention: 19.7% (14/71) Control not reported	Not measured

Table 13. HCV linkage to care in other settings

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive unless stated)	RNA testing	Referral to treatment	Treatment initiation	Treatment adherence	Treatment outcome	Cost effectiveness
International											
Rosenberg et al., 2010	HBV and HCV testing, risk reduction, referral and support into treatment for people with dual diagnosis (severe mental illness and substance misuse)	US	RCT	2006 - 2008	Self-reported HCV-positive Intervention: 21 Control: 16	Not reported	Not reported	Intervention: 81% (17/21) Control: 75% (12/16)	Not reported	Not reported	Intervention: $240 per client (in addition to costs of tests and vaccines)

Table 14. Care pathway changes

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV-positive unless stated)	RNA testing	Referral to treatment	Treatment initiation	Treatment adherence	Treatment outcome (SVR)	Cost effectiveness
UK											
Howes, 2019	Pathway redesign including reflex RNA testing, annotation of laboratory results to recommend referral, staff education, HCV clinics in DTS (PEF/IFN/RBV)	UK	Before/after study	Jan 2010 – Jan 2012 Vs Nov 2000 – Oct 2002	One healthcare region Newly diagnosed anti-HCV positive patients Intervention: 377 Control: 256	Intervention: 94% (348/377) Control: 27%	Intervention: 80% RNA positives (190/237) Control: 49% anti-HCV positives (125/256)	Attended assessment Intervention: 70% RNA positives (165/237) Control: 27% anti-HCV positives (68/256) Initiated treatment Intervention: 38% RNA positives (91/377) Control: 10% anti-HCV positives (26/256)	Not reported	Not reported	Not evaluated
Tait et al., 2010	Referral pathway with non-medical referrals and outreach clinics in hospital, drug treatment and prisons	Scotland, UK	Retrospective cohort (before/after)	2004-2008 Vs prior to 2004	Intervention: 1,767 patients, 1,012 still alive and registered with GP Control: 1,243	Intervention: 70% 1243/1767 Control not reported	Intervention: 87% (875/1012) Control: 35% (430/1243)	Intervention: 82% (721/875) Control: 66% (282/430) p<0.0001	Completion[1] Intervention: 74% (98/133) Control: 66% (43/65) p=0.2	Intervention:[1] 61% (81/133) Control: 51% (33/65) p=0.2	Not measured
Tait et al., 2017	Managed care network, DBS testing in DTS and needle exchanges, nurse specialist, increase in outreach clinics, DAA treatment	Scotland, UK	Retrospective cohort (before/after)	2009-2014 Vs pre 1999	Intervention: 1,207 Control: 688	Intervention: 95% (1150/1207) Control: 63% (432/688)	Of RNA positive patients Intervention: 98% (801/821) Control: 96% (279/292)	Within 1 year of diagnosis Intervention: 13% (133/821) Control: 2% (6/292)	Not reported	Intervention: 77% Control: 61%	Not measured

* Assessed for patients who received treatment pre 2004 and between 2004-2007 – different set of patients from those referred

Table 15. Multidisciplinary care coordination interventions

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive unless stated)	RNA testing	Referral to treatment	Treatment initiation	Treatment adherence	Treatment outcome (SVR)	Cost effectiveness
UK											
Ahmed et al., 2013	Integrated multidisciplinary care in established HCV clinics	UK	Before/after (retrospective cohort)	2002 onwards Vs 1998 - 2002	RNA-positive patients Intervention: 26 Control: 56	N/A RNA positive patients	N/A	Attended Intervention: 96% (25/26) Control: 89% (50/56) Initiated treatment Intervention:92% (24/26) Control: 82% (46/56)	Completion Intervention: 88% (23/26) Control: 39% (22/56)	Intervention: 69% (18/26) Control: 20% (11/56)	Not measured
International											
Ho et al., 2015	Multidisciplinary care coordination and case management for people with mental illness in established HCV clinics	US	RCT	Mar 2009 – Feb 2011	RNA-positive patients Intervention: 182 Control: 181	N/A	N/A	Intervention: 32% (58/182) Control: 19% (34/181) (p=0.005)	Adherence to planned therapy duration: Intervention: 70% Control: 62%	Intervention: 16% (29/182) Control: 8% (14/181) p=0.018	Not measured
Groessl, 2017	Case management and brief psychological interventions for patients with psychiatric comorbidities or substance misuse (DAAs)	US	RCT	Jan 2012 – Feb 2013	RNA-positive patients Intervention: 40 Control: 39	N/A RNA positive	N/A	Intervention: 45% (18/40) Control: 23% (9/39) p=0.032	100% planned therapy duration Intervention: 78% (14/18) Control: 56% (5/9)	Intervention: 30% (12/40) Control: 13% (5/39)	Not evaluated
Rosenberg et al., 2010	HBV and HCV testing, risk reduction, referral and support into	US	RCT	2006 - 2008	Self-reported HCV-positive Intervention: 21 Control: 16	Not reported	Not reported	Intervention: 81% (17/21) Control: 75% (12/16)	Not reported	Not reported	Intervention: $240 per client (in addition to costs of tests and vaccines)

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive unless stated)	RNA testing	Referral to treatment	Treatment initiation	Treatment adherence	Treatment outcome (SVR)	Cost effectiveness
	treatment for people with dual diagnosis (severe mental illness and substance misuse)										
Deming et al., 2018	Care coordination (DAAs)	US	Intervention with propensity-score-matched comparator group	2015	RNA-positive patients 1,098 matched sets of enrolees and controls	N/A – RNA positives	Not reported	Intervention: 72% (790/1103) Control: 36% (11960/32819) p<0.001		Intervention: 47% (514/1103) Control: 17% (5641/32819) P<0.001	Not evaluated
Carrion et al., 2013	Multidisciplinary support programme (PEF-IFN/RBV)	Spain	Intervention with historical control group	Jan 2003 – Jan 2009	RNA-positive patients Intervention: 131 Control: 147 Intervention validation: 169	N/A – RNA positives	N/A	N/A	Adherence: Intervention: 94.6% Intervention validation: 91.7% Control: 78.9% (p<0.05)	Intervention: 77.1% Intervention validation: 74.6% Control: 61.9% (p<0.05)	Cost per patient Intervention: €13,319 Control: €16,184

Table 16. Psychosocial and educational adherence and uptake interventions

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive unless stated)	RNA testing	Referral to treatment	Treatment initiation	Treatment adherence	Treatment outcome	Cost effectiveness
International											
Weiss et al., 2017	4-session behavioural intervention to address barriers to treatment initiation (DAAs)	US	RCT	Not reported	HIV/HCV coinfected Intervention: 29 Control: 26	N/A	Not reported	Prescribed medication Intervention: 59% Control: 27% p=0.018 OR 3.85, 95% CI 1,23-12.01 Initiated treatment Intervention: 48% Control: 23% p=0.052 OR 3.11, 95% CI 0.97-10.00	Not reported	Not reported	Not measured
Hussein et al., 2010	24/7 access to a nurse, motivational and educational mail, support phone calls (PEG-IFN/RBV)	US	Intervention with propensity-score matched comparator	Jan 2004 – Jun 2006	RNA-positive patients Intervention: 780 Control: 8,572	N/A	N/A	N/A	Fill ≥12 injections within 12 weeks of initiation Intervention: 72% Control: 64% p<0.001	Not reported	Not measured
Renou et al., 2009	Therapeutic education (PEG-IFN/RBV)	France	Prospective cohort with control	Not reported	RNA-positive patients Intervention: 98 Control: 326	N/A	N/A	N/A	Early cessation Intervention: 18% Control: 30% p=0.02	Intervention: 71% Control: 53% p=0.001 Genotype 2,3 Intervention: 78% Control: 69% p=0.268	Not measured
Larrey et al., 2009	Nurse-led education	France	Prospective cohort with control	Not reported	RNA-positive patients Intervention: 123 Control: 121	N/A	N/A	N/A	Intervention: 74% Control: 63%	Intervention: 38% Control: 25% p<0.02	

Study	Intervention	Location	Type of evidence	Time frame	Sample size (anti-HCV positive unless stated)	RNA testing	Referral to treatment	Treatment initiation	Treatment adherence	Treatment outcome	Cost effectiveness
Lubega et al., 2013	Patient education to improve treatment adherence (PEG-IFN/RBV)	US	Before/after (retrospective cohort)	Jan 2006 – Jun 2011	RNA-positive patients One healthcare system	N/A RNA+ patients	Not reported	Intervention: 60 Control: 58	Intervention: 86% (49/60) Control: 88% (51/58) p=0.79	Intervention: 68% (34/60) Control: 50% (25/58) p=0.07 aOR 3.0, 95% CI 1.1-1.79, p=0.031	Not measured

Table 17: Economic evaluations of interventions for PWID

Study	Year	Intervention	Location	Type of study	Perspective	Results	Sensitive to
UK							
Leal	1999	One round of screening in drug service	UK	CUA	Health service	£9,300 per QALY	discount rates, acceptance of liver biopsy, acceptance of treatment, continuation of treatment
Stein	2003	Screening former PWID in GUM	UK	CUA	Health service	£27,138 per QALY	prevalence, acceptance of testing, acceptance of liver biopsy, acceptance of treatment
Stein	2004	One round of screening in drug service	UK	CUA	Health service	£28,000 per QALY (IFN+RBV) £14,000 (PEG-IFN/RBV)	acceptance of liver biopsy, acceptance of treatment, treatment response, disease staging of the population, mortality rate of biopsy complications, utility assumptions for chronic hepatitis and successful drug treatment
Castelnuovo	2006	Opportunistic testing for former PWID in primary care	UK	CUA	Health service	£16,493 per QALY	discount rates, distributions of disease severity in the population
		Testing former PWID in drug and alcohol service	UK	CUA	Health service	£17,515 per QALY	discount rates, distributions of disease severity in the population
Thompson-Coon	2006	Opportunistic testing for former PWID in primary care	UK	CUA	Health service	£16,493 per QALY	Discount rates, Disutility associated with presentation and treatment, Utility associated with SVR and avoidance of long-term consequences of HCV
Martin	2013	DBS testing in DTS compared to venepuncture as usual care	UK	CUA	Health service	£14,600 per QALY	discount rates, treatment rates, assumptions on the disutility of diagnosis
Bennet	2015	Effect of improved treatment uptake on life years and QALYs gained from treatment	UK	CEA and CUA?	Health service	Increasing treatment to 250 per 1,000 PWID, among 4,240 PWID: Discounted gain of 300 LY Gain of 1,700 QALYS £5,4 million cost saving	Not reported
Radley	2017	DBS testing and treatment for OST patients in pharmacies	Scotland, UK	Cost analysis	Health service	£695 less per patient than traditional pathway	Costs of intervention
Bennett	2017	Effect of improved treatment uptake on cost-effectiveness of DAA treatment	UK	CUA	Health service	36-79% improvement in cost-effectiveness of treatment at 10 to 100% treatment uptake	Treatment uptake, time horizon

Selvapatt	2017	Testing and onsite treatment in drug treatment: i) standard treatment (real case – varied treatments) ii) all DAAs (hypothetical 95% SVR)	UK	CUA	Health service	i) Dominates ii) ICER £1,029 per QALY	Discount rate, health state costs, treatment costs
International							
Loubiere	2003	Screening PWID using 2 enzyme immunoblot assay (EIA) tests compared to no screening	France	CEA	Health service	£3,302 per LY gained	
Honeycutt	2007	HCV counselling, testing and referral for PWID sexual health clinic attendees	US	CEA	Health service	£43 per true positive client who returned for results	Cost of testing
Tramarin	2008	Screening for PWID in a population in Italy	Italy	CUA	Health service	Dominates (-£2,814 per QALY)	Prevalence of genotypes 1 and 4
Helsper	2012	Awareness campaign for hard drug users	Netherlands	CUA	Health service	£5,804 per QALY	age at testing, costs, disease progression parameters
Cipriano	2012	Screening individuals in OST for HIV, HCV or both	US	CUA	Health service	>£78,740 per QALY for strategies which included HCV screening	disutility of awareness of HCV diagnosis, behaviour change resulting from known diagnosis
Schackman	2015	Screening in drug treatment (including non-PWID)	US	CUA	Health service	£14,173 per QALY	none
Helsper	2017	National awareness-raising campaign	Netherlands	CUA	Health service	£7,813 per QALY, >99.9% probability of being below £11,668 per QALY threshold If DAAs used: £9,521 per QALY	proportion of PWID who chose to be treated, cost of treatment
Cousien	2018	(i) current practice	France	CUA	Health service		treatment costs, incidence, connectivity of the social network
		(ii) improved needle/syringe programmes and OST				Extended dominance	
		(iii) faster diagnosis/linkage to care				Extended dominance	
		(iv) treatment initiation Fibrosis stage 0 (vs initiation at stage 2)				Extended dominance	
		(v) (iii) and (iv) combined				£4,574 per QALY	
		(vi) (ii) – (iv) combined				£91,129 per QALY	
Schackman	2018	(i) No intervention	US	CUA	Health service		None
		(ii) HCV screening and education (control)				Extended dominance	
		(iii) HCV screening, education and care coordination				ICER £18,771 per QALY vs no intervention ICER £58,377 per QALY vs control	

Table 18. Economic evaluations of screening in prisons

Study	Year	Intervention	Location	Type of study	Perspective	Results	Sensitive to
UK							
Sutton	2006	Case-finding on reception into prison	UK	CEA	Health service	£6,388 per case	Number of prisoners attending lecture, acceptance of testing
Sutton	2008	Screening and educational session for people who disclose as PWID on reception into prison	UK	CUA	Health service	£54,852 per QALY	Disease progression rates, discount rates, rates of re-presentation for testing in the community
Castelnuovo	2006	Lecture on BBV during induction to prison, testing offered to all aged 20-69	UK	CUA	Health service	£20,083 per QALY	discount rates, distributions of disease severity in the population
		Lecture with a specific focus on injecting drug use as a risk factor for HCV, testing offered to all aged 20-69				£16,484 per QALY	
Martin	2013	DBS testing compared to venepuncture as usual care	UK	CUA	Health service	£59,400 per QALY	treatment initiation, continuity of care
Martin	2016	DBS testing and treatment in prison	UK	CUA	Health service	£19,850 per QALY (standard treatment)# £15,090 per QALY (DAA treatment)	Treatment uptake and completion
International							
He	2016	Different screening strategies: one-time risk-based screening for active or former PWID current inmates and new entrants for one year, one-time opt-out universal HCV screening of current inmates followed by opt-out screening of all incoming inmates for up to one year, 5 years, and 10 years	US	CUA	Societal	from £14,178 per QALY gained for 1 year risk-based to £20,240 per QALY gained for 10-year universal program	cost of treatment, timeliness of treatment initiation (soon after diagnosis and early disease stage more cost-effective)

Current treatments: genotype 1: sofosbuvir/ ledipasvir for patients without cirrhosis (8 weeks) / with cirrhosis (12 weeks); genotype 2: PEG-IFN/RBV for 24 weeks; genotype 3: PEG-IFN/RBV for 24 weeks for patients without cirrhosis and sofosbuvir1 PEG-IFN/RBV for 12 weeks for patients with cirrhosis; genotype 4: sofosbuvir/ledipasvir for 12 weeks

Table 19. Economic evaluations of screening for migrants

Study	Year	Intervention	Location	Type of study	Perspective	Results	Sensitive to
UK							
Miners	2014	Inviting South Asian immigrants via letter for 'opt-out' screening in GP practices	UK	CUA	Health service	£23,200 per QALY	prevalence, intervention effect, intervention cost, treatment uptake
Flanagan	2018	Incentivised testing for first-and second generation migrants in GP practices	UK	CUA	Health service	£8,540 per QALY (base case) Range £6,935 -£18,185 per QALY for pure DAA regimes	Cost and duration of treatment, age of cohort (older less cost-effective)

Table 20. Economic evaluations of screening for MSM

Study	Year	Intervention	Location	Type of study	Perspective	Results	Sensitive to
International							
Linas	2012	Different screening strategies for HIV-positive MSM	US	CUA	Health service	ICER £34,388 per QALY for screening using 6-monthly LFTs and 12-month anti-HCV test compared to symptom-based screening with IFN+RBV treatment. Adding protease inhibitors to the treatment increased ICER to £45,483 per QALY	Incidence, treatment efficacy, disease progression, follow up of positive LFT results

Table 21. Economic evaluations of antenatal screening

Author	Year	Intervention	Location	Type of study	Perspective	Results	Sensitive to
UK							
Selvapatt	2015	Universal antenatal screening	London, UK	CUA	Health service	£2,400 per QALY for RBV only, £9,139 per QALY for Sofosbuvir only £3,105 per QALY for RBV then Sofosbuvir	Prevalence, treatment uptake
International							
Plunkett	2004	Universal antenatal screening	US	CEA	Health service	Dominated	None
		As above plus caesarean for diagnosed mothers				£927,926 per QALY	
Urbanus	2013	Universal antenatal screening i) Whole population	Netherlands	CEA	Health service	£39,138 per life year gained	Prevalence, treatment costs, treatment outcome, costs of testing, discount rates, disease state transition and treatment uptake, disease state transition
		ii) First generation non-Western migrants				£35,140 per life year gained	

Table 22. Economic evaluations of screening in sexual health

Study	Year	Intervention	Location	Type of study	Perspective	Results	Sensitive to
UK							
Stein	2003	Screening for GUM clinic attendees	UK	CUA	Health service	£85,000 per QALY	prevalence, acceptance of testing, acceptance of liver biopsy, acceptance of treatment
International							
Honeycutt	2007	HCV counselling, testing and referral in GUM	US	CEA	Health service	Cost per true positive client who returned for results: £142 for non-PWID men aged 40+ with 100 or more sexual partners, £1,098 for non-PWID men aged 40+ with <100 sexual partners, £2,367 for non-PWID women aged 40+	prevalence

Table 23. Economic evaluations of risk-based screening

Author	Year	Intervention	Location	Type of study	Perspective	Results	Sensitive to
UK							
Batra	2001	Opportunistic risk-based testing in any service	South West Kent, UK	Financial option appraisal and commissioning model for purchasers	Health service	NPV -£25,407 to -£32,471 for opportunistic screening of high-risk individuals to prevent one patient developing cirrhosis in 10 to 20 years	Not assessed
Roberts	2019	Complex intervention using EMR flagging of at-risk patients for GP testing	South West England, UK	CUA of cluster RCT	Health service	ICER £7,507 per QALY, 89.7% probability of being below £20,000 per QALY	Linkage to care, test yield, utility, drug costs
International							
Lapane	1998	Risk-based screening	US	CEA		£247 per case detected	
Josset	2004	Screening for people who received blood transfusions before 1991 and current or former drug users (injection or inhalation) in primary care	France	CEA	Health service	£590 to £1,970 per positive test, depending on which costs were included	Prevalence, proportion of practice population in risk groups
Tramarin	2008	Screening for people who had surgery	Italy	CUA	Health service	£727,907 per QALY	Prevalence of genotypes 1 and 4
Liu	2013	One-time screening based on risk factors at routine medical visit	US	CUA	Societal	Not reported – states not cost-effective	Treatment uptake, disease stage (more advanced is more cost-effective)
Helsper	2017	Public awareness campaign for risk groups and training and awareness raising for health professionals	Netherlands	CUA	Health service	ICER £15,882 per QALY If DAAs used: ICER £12,485 per QALY	Number of HCV patients identified, cost of the campaign

Table 24. Economic evaluations of birth cohort screening

Study	Year	Intervention	Location	Type of study	Perspective	Results	Sensitive to
UK							
Williams	2019	Add-on HCV testing to the NHS health check for individuals born in birth cohorts between 1950 and 1979	UK	CUA	Health service	ICER £31,695 to £105,568 Low probability of cost-effectiveness for all birth cohorts (0-5%) at £20,000 per QALY	Probabilities of HCV disease state transition, probability of referral and receiving treatment, prevalence
Castelnuovo	2006	Opportunistic testing for population aged 30-54 in primary care in area of assumed high HCV prevalence	UK	CUA	Health service	£15,493 per QALY	Discount rates, distributions of disease severity (for general case)
Selvapatt	2016	Testing for patients born 1950 to 1980	UK	Threshold CUA	Health service	To meet the £20,000 per QALY threshold, the intervention needed to cost ≤£24.52 per screened patient, or ≤£41.31 if DAAs were used – not cost-effective	Treatment uptake, prevalence
International							
Coffin	2012	One-time screening for population born 1945-1965 with PEG-IFN/RBV treatment	US	CUA	Health service	£4,281 per QALY	Disutility from disease stages before liver disease, discount rates, probability of SVR for genotype 1
Liu	2012	Screening for people aged 40-74	US	CUA	Health service	£48,036 per QALY for treatment with IL-28B-guided triple therapy £52,126 for treatment with universal triple therapy	fibrosis stage of diagnosed patients, disutility of knowledge of diagnosis, healthcare costs from knowledge of HCV status, treatment uptake, treatment adherence, reduction in non-liver related mortality from treatment
McEwan	2013	Birth cohort compared to risk-based screening for 1945-1965 birth cohort	US	CUA	Health service	£22,685 per QALY	Treatment uptake, prioritisation of treatment by disease staging
McGarry	2012	Birth cohort screening compared to risk-based for 1945-1965 birth cohort	US	CUA	Health service	£29,889 per QALY	time horizon, treatment uptake, treatment efficacy
Rein	2012		US	CUA	Health service	£12, 452 per QALY (PEG-IFN/RBV) £28,314 per QALY (DAAs for patients with genotype 1 and PEG-IFN/RBV for genotypes 2 and 3)	disutility from disease stages before liver disease, discount rates, probability of SVR for genotype 1
Ruggeri	2013	One-time screening to population aged 35+, compared to no screening (patients identified only when symptomatic)	Italy	CUA	Health service	£4,101 per QALY (PEG-IFN/RBV)	age of target population (older age groups had increased costs per QALY), time horizon (more cost-effective at longer time horizons), prevalence

Wong	2015	One-time screening compared to no screening, 3 different treatment strategies: i) PEG-IFN/RBV; ii) simeprevir-based combination therapy (genotype 1 patients), sofosbuvir-based combination therapy (genotype 2 and 3 patients), or PEG-IFN/RBV (other genotypes); iii) as in ii) but genotype 1 patients treated with DAA a) population aged 25-64	Canada	CUA	Health service	i) £30,231 per QALY ii) £33,626 per QALY iii) 27,587 per QALY	Costs and utilities of HCV infection, prevalence, acceptance of screening, costs of screening, rate of known infections
		b) population aged 45-64				i) £25,250 per QALY ii) £28,205 per QALY iii) £34,924 per QALY	
Rein	2017	One-time screening for: (i) those with risk factors, (ii) population aged 18+, (iii) population born 1945-1965	US	CUA	Health service	(iii) vs (ii) £37,513 per QALY (ii) vs (i) £61,775 per QALY (iii) vs (i) £43,405 per QALY (iii) dominates (ii)	Drug costs, treatment uptake, testing uptake

Table 25. Economic evaluations of general population screening

Study	Year	Intervention	Location	Type of study	Perspective	Results	Sensitive to
UK							
Leeds Sexual Health	2016	Opt-out testing in GP practices	UK	CEA	Health service	£1,060 per BBV diagnosis	Prevalence
International							
Singer	2001	Universal screening in primary care for those attending routine check-ups using 2 testing strategies: ELISA then PCR, or PCR only	US	CUA	Societal	Both strategies dominated by no screening	treatment uptake, disease progression rate, disutility of knowledge of diagnosis
Coffin	2012	One-time screening to the population aged 20-69 with PEG-IFN+RBV treatment	US	CUA	Health service	£6,243 per QALY	None
Helsper	2012	General publicity campaign	Netherlands	CUA	Health service	No extra diagnoses	N/A
		Support programme for primary care				£10,136 per QALY	number of cases identified during the campaign, rate of referral to treatment
Eckman	2013	Population screening followed by treatment with boceprevir	US	CUA	Health service	£37,364 per QALY	prevalence, risk of fibrosis progression, proportion with genotypes 2 and 3, disutility of receiving treatment, age at time of infection, treatment cost, test characteristics, and treatment efficacy

Table 26. Economic evaluations of ED screening

Study	Year	Intervention	Location	Type of study	Perspective	Results	Sensitive to
UK							
Williams	2019	Opt-out testing in ED	UK	Threshold CUA	Health service	At £20,000 WTP threshold, 0.26% HCV RNA prevalence required for ED testing to be cost-effective	Costs of diagnostic tests, costs of treatment, linkage to care (proportion of patients contacted, attending referral and accepting treatment)
Bradshaw	2018	Opt-out testing in ED	UK	CEA	Health service	£4,682 per diagnosis	Prevalence, cost of diagnostic tests
Orkin	2016	Opt-out testing in ED	UK	CEA	Health service	£988 per diagnosis	Prevalence, cost of diagnostic tests

Table 27. Economic evaluations of other care pathway interventions

Study	Year	Intervention	Location	Type of study	Perspective	Results	Sensitive to
International							
Carrion	2013	Multidisciplinary support programme in secondary care (PEG-IFN/RBV)	Spain	CUA	Health service	Intervention cost less per patient than control (£11,505 vs £13,977) and achieved more QALYs (16.317 vs 15.814)	
Slade	2013	Hepatitis education, testing, referral and support into treatment for people with dual diagnosis (severe mental illness and substance misuse) in community mental health	US	Cost analysis	Health service	Intervention cost £305 more per participant than treatment as usual, £541 per additional participant receiving HCV test	Volume of new clients seen
Whitty	2014	Rapid access to treatment model using Fibroscan, compared to liver biopsy	Australia	Cost analysis	Health service	Intervention cost on average £1,660 less per patient	N/A
Rattay	2017	Telementoring to support primary care to test and treat (Project ECHO)	US	CUA	Health service	ICER £7,923 per QALY	Age of patients treated (younger more favourable), discount rate