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Outreach Screening and Treatment for Hepatitis C in a Drug Treatment Unit – An Exploratory Assessment of Feasibility and Cost Effectiveness

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HEOR

Imperial College Healthcare NHS Trust

INHSU 2016, Oslo

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Disclosures

The Speaker has acted as a Clinical Investigator, Advisor and/or has received research grants from the following companies:

Abbvie, BMS, Gilead, Janssen, Merck, Roche

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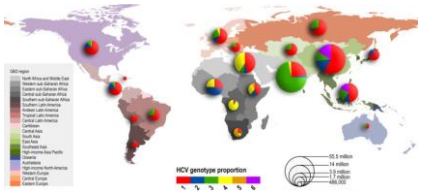
Background

- Chronic HCV - 180 million patients worldwide [1]
- An estimated 214,000 patients in the UK [2]
- Estimated 40-50% remain undiagnosed [3]
- Persons who inject drugs (PWID) highest risk group but have poor rates of treatment uptake and possibly adherence [2]

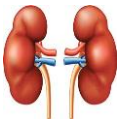


Messina et al. Hepatology. 2015 Jan; 61(1): 77–87.

HCV outcomes:

Liver-related complications

Extra hepatic



Productivity

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Objectives

This study aims to evaluate the cost-effectiveness of a pilot programme providing an outreach screening and treatment programme within an inner London Drug Treatment Unit (DTU)

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Methods: Screening programme

- Persons attending the North Westminster Drug and Alcohol Service between 1st April 2012 and 1st November 2014 were offered screening
- All positive diagnoses for HCV offered counselling, work-up and treatment by an outreach viral hepatitis team
- Treatment was performed at DTU or hospital as per patient wishes +/- key worker support to ensure adherence
- Treatment modalities as per physician discretion (and availability) and outcomes were recorded for all patients that initiated treatment by 1st August 2015
- Outcomes were used to inform a base case scenario for health economic evaluation

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Methods: Screening costs

Screening Component	Unit cost (£)	Resource use	Total cost (£)
Consultant/nurse time			
Nurse time	£150/half day	Half day per clinic (71 clinics)	£10,650
Consultant time	£2,500/year	3 years	£7,500
Testing			
Dry blood kits	£12.50	1 kit for each patient tested (216 patients tested)	£2,700
First consultation	£150	Cost of initial hospital visit for patient scheduled for HCV treatment (29 patients)	£4,350
Repeat patient episode	£25	Cost of initial hospital visit for patient scheduled for HCV treatment (375 visits)	£9,375
Fibroscan	£125	Cost per fibroscan (56 performed)	£7,000
Liver biopsy	£800	Cost per liver biopsy (5 performed)	£4,000
HCV anti-body test	£5.91	Cost per HCV anti-body test (216 performed)	£1,276.56
PCR test	£47	Cost per PCR test (71 initial tests performed based on positive HCV antibody testing, 5 confirmatory re-tests performed for those that initially had a negative PCR test result)	£3,337 + £235 = £3,572
Genotype testing	£44.50-126.66	Cost per genotype test performed (66 tests performed)	£8,360*
Liver screening	£150	Cost per liver screening test performed (66 tests performed)	£9,900
Total cost	-	-	**£68,683**

*So as not to bias towards the screening program, the larger cost (£126.66) was utilised
HCV, hepatitis C virus; PCR, polymerase chain reaction

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Cost-effectiveness analysis in hepatitis C

- A previously published and validated lifetime HCV disease progression and cost-effectiveness model was utilised [4-9]
- Patient characteristics (age, gender, fibrosis stage, alcohol use and current injecting status) were directly informed by the study data
- Published disease transition rates, costs and health utility values were utilised and outcomes discounted at a rate of 3.5% (see supplemental slides) [10-13]

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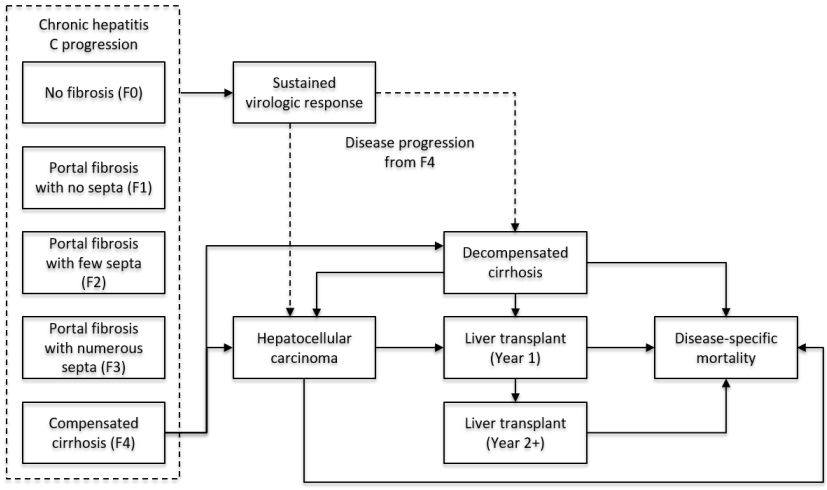
MONARCH cost-effectiveness model flow diagram



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Health state transition parameters

Transition	Functional form	Source
F0 to F1	exp*[-2.0124-0.07589×HCVD+0.3247×Design+0.5063×Male+0.4839×GT1*	[10]
F1 to F2	exp*-1.5387-0.06146×HCVD+0.8001×Alcohol*	
F2 to F3	exp*[-1.6038+0.0172×HCV Age-0.05939×HCVD+0.4539×Alcohol]*	
F3 to F4	exp*[-2.2898+0.01689×HCV Age-0.03694×HCVD+0.5963×IDU+1.1682×BT-0.4652×GT1*	

Transition	Mean	SE	Distribution	Source
F4 to DC	0.039	0.010	Beta	[11]
F4 to HCC	0.014	0.010	Beta	
DC to HCC	0.014	0.010	Beta	
DC to LT	0.030	0.012	Beta	
DC to Death	0.130	0.010	Beta	
HCC to LT	0.030	0.012	Beta	
HCC to Death	0.430	0.030	Beta	
LT (Yr 1) to Death	0.210	0.046	Beta	
LT (Yr 2+) to Death	0.057	0.012	Beta	

Alcohol, defined as alcohol consumption of more than 20g/day; BT, the proportion of individuals that were newly diagnosed with HCV at blood donor screening; DC, decompensated cirrhosis; Design, set to 0 if the study design is cross-sectional and set to 1 if the study design is retrospective-prospective; GT1, set to 1 for genotype 1 or 0 for non-1; HCC, hepatocellular carcinoma; HCV Age, age at cohort initiation; HCVD, length of time from the presumed date of infection to the date of liver biopsy; IDU, the proportion of individuals that acknowledged intravenous drug use (IDU) as the main risk factor for HCV infection; LT, liver transplant; SE, standard error; Yr, year.
The proportion of patients consuming excess alcohol and with a history of IDU were assumed to be 100% in line with the high risk status of the study population.
The average duration of infection was not recorded thus the mean profiles from the UK studies reported in Thein 2008 were used as proxies. Information on patient sex was not available, thus a 50:50 male:female ratio was utilised.

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Cost and utility parameters

	Cost parameters			Health utility parameters		
	Mean (£)	SE (£)	Source	Mean	SE	Source
Disease State (annual)						
F0/F1	177.47	35.01	[12]	0.77	0.015	[12]
F2/F3	922.08	97.82		0.66	0.031	
F4	1,463.50	297.45		0.55	0.054	
DC	11,728.61	1,954.09		0.45	0.031	
HCC	10,451.58	2,456.09		0.45	0.031	
LTx (Year 1)	47,310.55	6,843.48		0.45	0.031	
LTx (Year 2+)	1,781.15	456.57		0.67	0.066	
SVR from F0/F1*	333.08	62.05		0.82	0.043	
SVR from F2/F3*	922.08	97.74		0.72	0.048	
SVR from F4*	1,463.50	288.07		0.72	0.048	

	Weekly cost (£) [13]	Duration (weeks)	
		Genotype 1	Genotype 3
Treatments			
IFN/RBV	191.35	48	24
TVR+IFN/RBV	TVR: 1,866.50, IFN/RBV: 191.35	TVR: 12, IFN/RBV: 48	NA
BOC+IFN/RBV	BOC: 700, IFN/RBV: 191.35	BOC: 44, IFN/RBV: 48	NA
SMV+IFN/RBV	2,057.85	12	NA
SOF+IFN/RBV	3,106.60	NA	12
DCV+SOF+RBV	5,025.35	NA	24
SOF+LDV	3,248.33	Assumed 12 weeks of SOF+LDV for both genotypes	

* Applied in the first year only.
BOC, boceprevir; DC, decompensated cirrhosis; DCV, daclatasvir; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; IFN, pegylated interferon α; LDV, ledipasvir; LTx, liver transplant; RBV, ribavirin; RNA, ribonucleic acid; SE, standard error; SMV, simeprevir; SOF, sofosbuvir; SVR, sustained virologic response; TVR, telaprevir.

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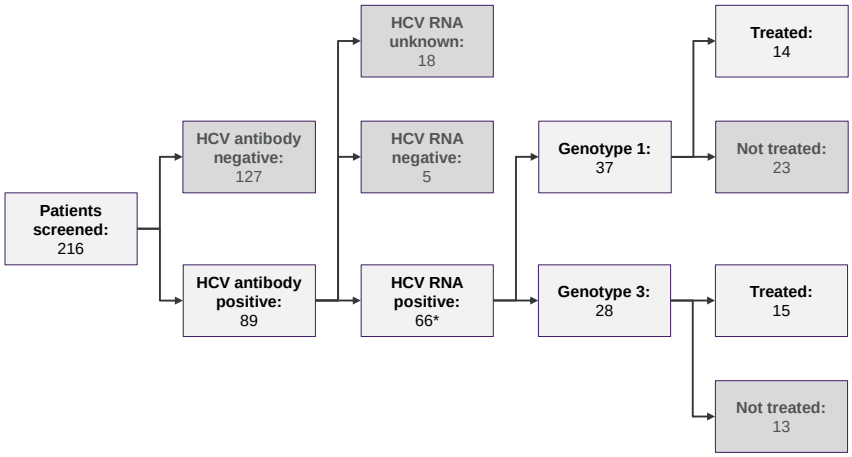
Results - Screening



*1 patient identified as HCV RNA positive had an unknown genotype, however was not treated.

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Baseline characteristics (1)

	Treated viraemic group N = 29	Untreated viraemic group N=37	P-value
Age	45 (31-61)	44 (24-58)	0.99
Male	22 (75%)	22 (60%)	0.20
Caucasian	27 (93%)	34 (92%)	0.99
Genotype 1 1a 1b 3	 2 (7%) 12 (41%) 0 15 (52%)	 8 (22%) 16 (43%) 1 (3%) 12 (32%)	 0.74
Prior HCV treatment	2 (7%)	1 (3%)	0.58
Reasons for non treatment Medical Mental Health Declined interferon Non engagement Moved location Rehab Deceased Unknown	 	 3 1 7 9 4 1 2 10	
Substance use	9 (31%)	19 (51%)	0.07
Alcohol consumption	3 (11%)	5 (14%)	**0.05**
Prescribed opiate substitution	19 (66%)	26 (70%)	0.24

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Baseline characteristics (2)

	Treated viraemic group N = 29	Untreated viraemic group N=37	P-value
HBV co-infection	1	0	0.44
HIV co-infection	0	3	0.25
F0-F1 fibrosis	11 (38%)	10 (27%)	0.23
F2-F3 fibrosis	12 (41%)	5 (14%)	0.53
F4 fibrosis	6 (21%)	2 (5%)	0.69
Unknown fibrosis stage	0	20 (54%)	
Haemoglobin (g/dL)	13.9 (10.3-16.4)	13.5(8-16.4)	0.34
Platelets (10^9/L)	191(46-427)	221(116-353)	**0.04**
INR	1.1(1-1.6)	1.1(1-1.4)	0.60
ALT (iU/L)	102(18-428)	58(8-145)	**0.02**
Albumin (g/dL)	39(26-45)	37(15-43)	**0.04**
Bilirubin (mmol/L)	13(4-49)	10(3-59)	**0.01**
Sodium (mmol/L)	139(132-143)	138(133-144)	0.75
Creatinine (µ/L)	77(54-259)	66(42-83)	0.16
HCV Viral Load (iU/mL)	$8x10^6$ ($1.23x10^5$-$152x10^6$)	$1.6x10^6$($1771-17x10^6$)	**0.03**

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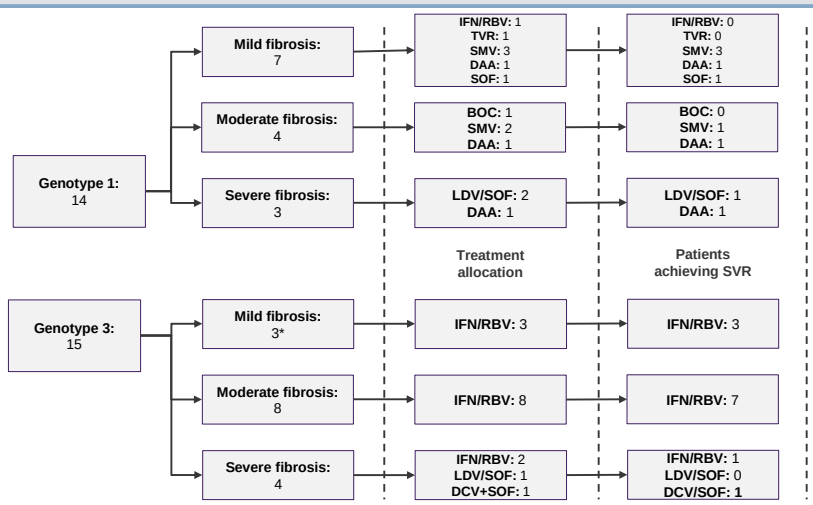
Results - Treatment



BOC, boceprevir + pegylated interferon alpha + ribavirin; DAA, direct-acting antivirals; IFN/RBV, pegylated interferon alpha + ribavirin; LDV/SOF, ledipasvir + sofosbuvir; SMV, simeprevir + pegylated interferon alpha + ribavirin; TVR, telaprevir + pegylated interferon alpha + ribavirin.
*1 genotype 3 patient achieved SVR with IFN/RBV therapy but had an unknown fibrosis severity at initiation, thus it was assumed that they had mild fibrosis, the most conservative assumption

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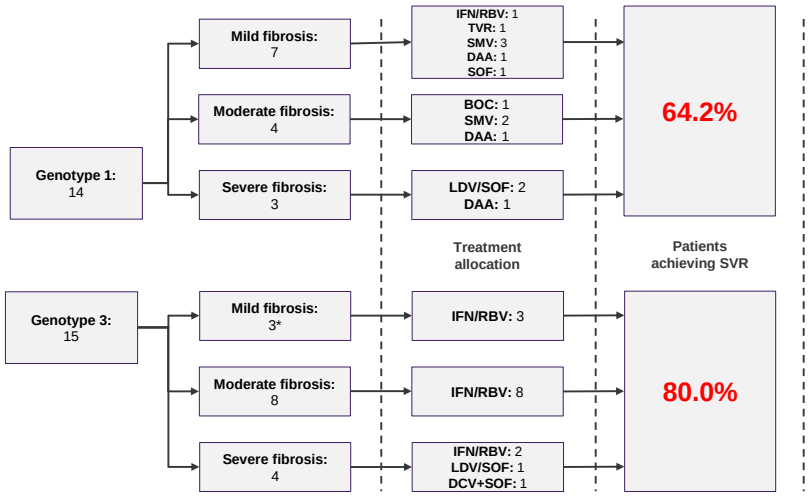

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Cost-effectiveness analysis in hepatitis C

- Analysis was undertaken to investigate the following scenarios:
  - **Scenario 1:** No screening and no treatment
  - **Scenario 2:** Screening and treatment, as observed within the study population
  - **Scenario 3:** Screening and treatment, assuming all patients treated with a hypothetical DAA therapy with an SVR rate of 95%
- In order to assess the incremental cost-effectiveness of screening, scenario 2 and 3 were compared to scenario 1

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Results – Cost-effectiveness

Result per patient	No screening and treatment	Screening and treatment (base case)		Screening and treatment (all treated with DAAs)	
	Total	Total	Incremental (versus no screening and treatment)	Total	Incremental (versus no screening and treatment)
Screening cost (£)	0	2,368	2,368	2,368	2,368
Treatment cost (£)	0	22,716	22,716	38,980	38,980
Complication cost (£)	43,360	15,778	-27,583	7,506	-35,854
Total cost (£)	43,360	40,862	-2,498	43,360	5,494
Life years	14.02	17.48	3.46	18.45	4.42
QALYs	7.94	12.03	4.10	13.27	5.34
ICER: £/life year	-	-	-723	-	1,242
ICER: £/QALY	-	-	-610	-	1,029

DAAs, direct-acting antivirals; ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life years

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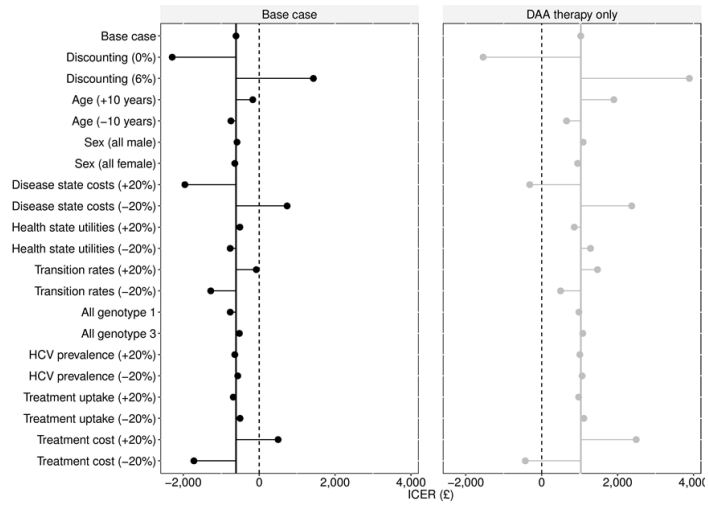
Results - Sensitivity analysis



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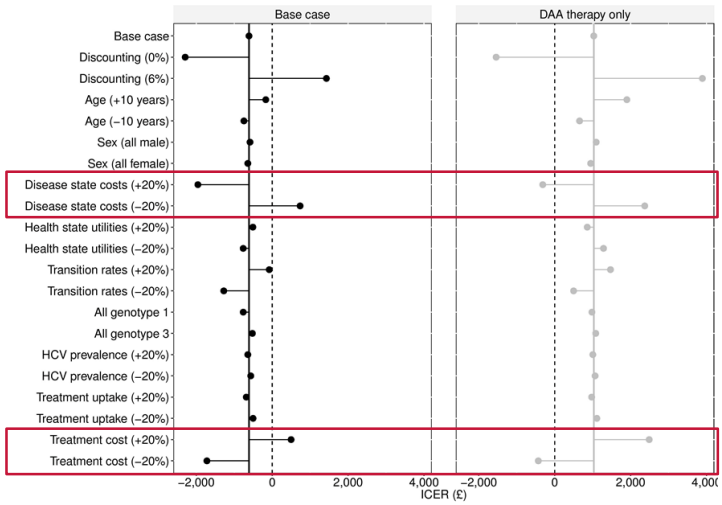

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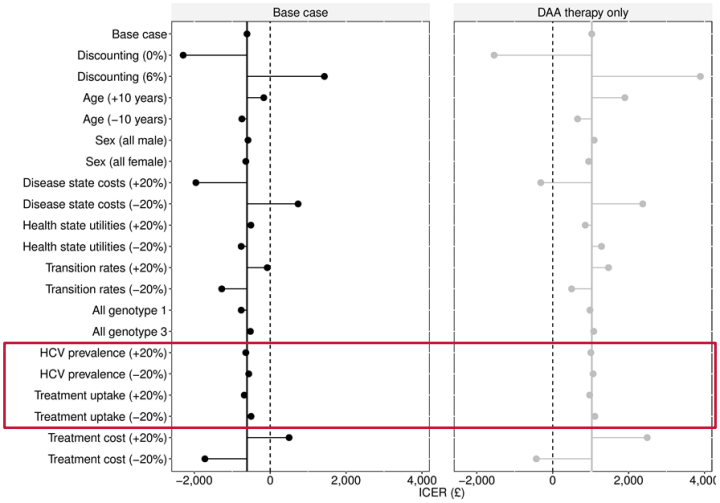

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Limitations of analysis

Study:

- Retrospective observational single centre study

Impact to healthcare:

- Modelling assumptions
  - Treatment (Costs, SVR)
  - Disease progression
  - Disease management

Impact to individuals:

- Difficulty quantifying subjective metrics
- No long-term follow up (so impact of reinfection not examined)
- Societal and productivity costs not included

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Conclusions

- Outreach screening and treatment of hepatitis C is demonstrably feasible in Drug Treatment Units with specialist care support
- High linkage to care, treatment uptake and rates of SVR
- This study demonstrates that an outreach screening and treatment programme is likely to offer a significantly cost-effective strategy
- Under base case assumptions the screening and treatment strategy is estimated to save £2,498 per patient with a QALY gain of 4.10 years over a lifetime, compared to no screening
- In a hypothetical scenario where all patients were treated with DAA only regimes, it is estimated that an incremental cost of £1,029 per QALY would be incurred

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Manuscript in Press

doi: 10.1111/liv.13240

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Acknowledgements

Imperial College Healthcare NHS Trust

Lorna Harrison
Liver and Antiviral unit staff

HEOR Health Economics and Outcomes Research Ltd.

Thomas Ward
Hayley Bennett Wilton
Samantha Webster
Professor Philip McEwan

Imperial College London

Professor Mark Thursz
Dr Nowlan Selvapatt

Central and North West London NHS Foundation Trust

Jody Lombardini

Imperial College London

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