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Assessing the Cost-effectiveness of Finding Cases of Hepatitis C Infection in UK Migrant Populations and the Value of Further Research

Running title: The economics of finding UK migrants with HCV

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ABSTRACT

Introduction

Hepatitis C (HCV) infection can cause cirrhosis, liver cancer and death in the absence of treatment. Many people living in the UK but born overseas are believed to be infected with HCV although many are unlikely to know they are infected. The aim of this study is to assess the potential for a case finding approach to be cost-effective and to estimate the value of further research.

Method

An economic evaluation and value of information analysis was undertaken by developing a model of HCV disease progression and by populating it with evidence from the published literature. They were performed from a UK National Health Services cost perspective and outcomes were expressed in terms of quality-adjusted life-years (QALYs). The comparator intervention was defined as the background rate of testing (ie. no intervention).

Results

The base case results generated an incremental cost-effectiveness ratio (ICER) of about £23,200 per additional QALY. However, the ICER was shown to be particularly sensitive to HCV seroprevalence, the intervention effect / cost and the probability of treatment uptake. The value of information analysis suggested that approximately £4 million should be spent on further research.

Discussion

This evaluation demonstrates that testing UK migrants for HCV could be cost-effective. However, further research, particularly to refine estimates of the probability of treatment uptake once identified, the utility associated with sustained virological response and the cost of the intervention, would help to increase the robustness of this conclusion.

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INTRODUCTION

Hepatitis C virus (HCV) is common with an estimated 150 million [1] people chronically infected worldwide. Infection causes progressive liver damage that, without treatment, may lead to cirrhosis, liver cancer and death [2]. Evidence suggests that antiviral treatment for hepatitis C (HCV) infection is highly cost-effective [3-5]. However, as disease progression is relatively slow, with approximately 20% of individuals progressing to cirrhosis within 20 years, many individuals remain unaware they are chronically infected [6].

In the UK, injecting drug use is the major risk factor for acquiring HCV, but mortality and morbidity from chronic HCV is rising disproportionately among people from migrant communities [7]. It has been estimated that 30,000 individuals born overseas but living in the UK will develop chronic HCV, of whom 5,000 may develop cirrhosis in the next 20 years if untreated [8]. A policy of screening for hepatitis infection in people born outside the UK was rejected by the National Screening Committee in 2011, partly because evidence-based assessments of the costs of identifying and inviting individuals for tests were lacking [9]. More recently, the UK's National Institute for Health and Care Excellence (NICE) has issued guidance relating to methods of increasing HCV case finding and treatment uptake within high risk and migrant communities [10]. However, the evidence base on which the recommendations were based was arguably weak and contained a number of important uncertainties [10]. The guidance is due to be considered for update in 2015.

In this study we update the economic evaluation of a HCV case finding intervention for UK migrant populations that underpinned some of NICEs recommendations and estimate the

value of conducting further research. The latter can be undertaken by incorporating a 'value of information' (VoI) analysis within the design of an economic evaluation. Full details of this technique are available elsewhere [11, 12], but its results – the expected value of perfect information (EVPI) - can be interpreted as the maximum amount a funder should be willing to pay for further research given a threshold value of the cost of an additional unit of health, such as a Quality-Adjusted Life-Year (QALY). A number of factors influence the EVPI, but the ability of research to change policy (ie. move a cost-effectiveness estimate to the opposite side of a threshold value such as £20,000 to £30,000 per additional QALY [13]) is central to it, as is the size of the population who could benefit from the research. The EVPI can either be reported for the entire decision problem reflecting the joint uncertainties in all the sampled parameters, or for subsets of them, such as utilities, costs and probabilities. The latter is referred to as the expected value of partially perfect information (EVPPI), and its advantage is that disaggregating the EVPI in this manner means that the main drivers of any decision uncertainty are more readily identifiable and that subsequent research can be more directed.

METHODS

The economic evaluation was undertaken using a Markov modelling approach, where individuals move between a set of discrete health states, in this instance on a 6-monthly basis [14]. Health outcomes were expressed in terms of QALYs. A UK's National Health Service's cost perspective was used and future costs and QALYs were discounted at 3.5% per annum. All results are displayed in £ 2010 prices and a lifetime horizon was used. Uncertainty in the results was examined using deterministic and probabilistic sensitivity analysis (PSA); distributions shown in the tables relate to the PSA analysis. . The PSA results were also analysed using analysis of covariance techniques (ANCOVA). The PSA / EVPI results were based on 1,000 sampled parameter values whereas the EVPPI results were based on 1,000 second order and 1,000 first order simulations. HCV

transmission was not included in the model as nearly all infections are believed to occur in UK migrant populations before entering the country [2].

Intervention and target population

A small number of hepatitis case finding methods have been studied in UK migrant populations [15-17], as identified in a recent systematic review [18]. This analysis, however, was based on a recent approach in which Pakistani/British Pakistani people registered at general practices (GPs) in London were written to and invited to 'opt out' of being tested for hepatitis B and C infection. Those who did not opt out were telephoned and asked to attend a clinic for a test. Although only an abstract was available, it was the most recent HCV-study to be identified and was UK-based [16]. The comparator programme was defined as the background likelihood of testing, or 'no intervention'. For the purposes of the VoI analysis, the population of interest was defined as migrants from the Indian subcontinent, primarily Bangladesh, India and Pakistan. Evidence suggests that net migration to the UK from this region is about +93,000 people per annum [19, 20].

Model structure

The Markov model included 12 main health states that were further subdivided according to whether or not HCV status was known; it is largely based on a previously used model structure (Figure 1) [3, 21]. Individuals were assumed to 'enter' the model in the uninfected, mild HCV, moderate HCV, and compensated cirrhosis (CC) heath states, all with unknown HCV Ab and RNA status.

Although varied in a sensitivity analysis, the HCV status of individuals who developed DC, hepatocellular cirrhosis (HCC) and those receiving a liver transplant was assumed to be known at all times due to the severity of the disease and likely presentation. Individuals were assumed to die from non-HCV related causes from all health states at an age adjusted rate. Individuals who were diagnosed HCV Ab+ / RNA+ were eligible for antiviral treatment if they had mild HCV, moderate HCV, or CC. In each case treatment was associated with a

chance of sustained viral response (SVR). A single probability (0.45) of being referred for specialist care, attending it, and starting treatment was included as it is understood some individuals who are identified as eligible for treatment do not receive it [22]. Individuals who achieve SVR were assumed not to experience further liver disease progression. Those who failed antiviral treatment (non-SVRs) were assumed to have the same disease progression as those who had not received treatment. Repeat treatment was not considered at any point. The basic model logic was that increased testing leads to more or earlier antiviral treatment in a proportion of individuals who require it.

Tests

The basic test for HCV was assumed to be an antibody test (Ab). Individuals who tested Ab+ were assumed to receive a PCR RNA test to confirm chronic infection. Twenty-six percent of individuals who tested Ab+ were assumed to have spontaneously cleared their infection, and therefore to test PCR RNA- [23]. Both tests were assumed to be 100% accurate.

Transition probabilities

Transition probabilities represent the chance of moving between health states over the 6 month cycle period. Model values were based on those reported in a 2007 UK Health Technology Assessment report [3] (Table 1~~Table 1~~). The probability of SVR was taken from studies using pegylated interferon [21, 24-27], and weighted according to genotype; evidence from the UK Health Protection Agency (HPA) suggests that people of South Asian or British Asian origin are 4 times more likely to have genotype 3 than genotype 1 [7]. The probability of SVR for people with CC was assumed to be lower than for people with mild or moderate HCV [28].

HCV seroprevalence

Recent UK HPA [7] data suggests that of 52,533 HCV tests undertaken by people with South / British Asian backgrounds, 1,658 were Ab+ (3.2%). Values of 1% and 5% were used in the sensitivity analysis.

The background rate of testing, in the absence of the intervention was also estimated using the HPA data. First, the total population of England and Wales is estimated to be 56.1 million of which 6.8% of people are estimated to be Bangladeshi, Pakistani or Indian. Second, HPA data suggests that in 2010, 52,533 of likely South-Asian descent were tested for HCV antibody; the data is thought to relate to about a third of all tests in England. Thus, the base case annual background rate of testing was estimated to be ([[1/0.333]*52,533]/[56.1 million*0.068]) = 0.041. A small study in six UK primary care practices also found that less than 5% of migrants were tested for HCV (Shivani Datta, paper in review).

A potential complication with this evaluation is that the costs and benefits of testing and treatment might not be fully realised from a UK NHS perspective since individuals could leave the country sometime after a diagnosis of chronic infection. This possibility was not included in the base case analysis, but was investigated in a sensitivity analysis by assuming 1% of people left the country every 6 months irrespective of HCV status.

Intervention effect

The probability of testing in the intervention arm was based on the recent 'opt out' option described by Lewis et al [16]. Approximately 20% (223/1,134) of all eligible individuals were tested; many GP records did not contain up-to-date contact details largely explaining the modest uptake. This was assumed to be the intervention effect during the first model cycle, reverting to the background probability of testing after this time.

HCV treatment

In the base case individuals identified as HCV RNA+ were assumed to receive an average of 6 months treatment with pegylated interferon and ribavirin. The mean probabilities of SVR for people with mild / moderate disease or CC with genotype 2/3 infection were estimated to be 0.8 and 0.6 respectively [21, 24-26]. Both probabilities were assumed to lower for genotype 1 [28] infection and a sensitivity analysis was run in which treatment was assumed to include the addition of boceprevir / telaprevir.

Initial probabilities

Direct evidence on the numbers in each health state for the undiagnosed HCV chronically infected migrants could not be identified. Therefore this distribution was estimated based on the assumed seroprevalence of HCV and a modelling exercise to estimate baseline steady state distributions amongst current UK intravenous drug users (IDUs) [29]. However, as it is acknowledged that the uncertainty around these estimates is high, the probabilities were sampled. Not that the distribution is likely to underestimate the proportion of migrants in later disease stages, hence further deterministic sensitivity analysis was undertaken by assuming 10% of individuals had decompensated cirrhosis (DC) when testing HCV RNA+.

Utilities

Utility values can be viewed as the health-related quality-of-life associated with particular health states. The inputted values ~~; they~~ have been used in a number of UK technology assessment reports (eg Shepherd et al [3]) but were originally derived from ~~were taken from~~ a UK RCT of mild disease [4] and UK study enrolling individuals with latter stage disease [30]~~Shepherd [3]~~ (Table 2~~Table 2~~).

Costs

The costs of the intervention described above were not recorded. Moreover, determining the cost of a hepatitis case finding intervention from the literature is difficult, since reported interventions are idiosyncratic, often brief in their description and do not report resource use

in any detail. Therefore, for the purposes of the base case analysis, an intervention cost of £20 per eligible person was assumed, excluding the cost of any tests and treatments. Thus, if 100 individuals were eligible for testing, the total cost of the intervention was £2,000 irrespective of how many people subsequently attended for a test. The importance of this assumption was assessed in the sensitivity analysis and given the extent of uncertainty, a relatively high standard error was assumed for the probabilistic analysis (Table 3~~Table 3~~). The costs of antiviral treatment and health-state specific costs were taken from a number of well documented sources, inflated to 2010 £ where appropriated using the UKs Hospital and Community Health Services Pay and Prices Index [31] (Table 3~~Table 3~~).

RESULTS

The base case results produced mean per individual non-intervention and intervention costs of £373 and £425 respectively with associated QALYs of 17.759 and 17.762, producing an incremental cost-effectiveness ratio (ICER) of about £23,200 per additional QALY. The cost-effectiveness acceptability curve, however, showed a large degree of uncertainty around this result; the probability the intervention is cost-effective at a £20,000 to £30,000 per additional QALY threshold was between 35 and 71% (Figure 2~~Figure 2~~). The HCV seroprevalence required to generate incremental cost per QALYs of £20,000 or £30,000 were 4.4% or 2.1% respectively. The corresponding threshold values for the probability of testing (ie. the intervention effect) were 0.28 and 0.12 respectively.

ANCOVA

The ANCOVA results detail the contribution of each of the probabilistic input parameters in the PSA simulations to the incremental costs (mean £51.3; 95% 50.8, 51.8) and QALYs (mean 0.0022; 95% 0.00219, 0.00225) (Figure 3~~Figure 3~~). They show that 43% of the variation in incremental costs was attributable to the variation in the intervention cost. However, an even greater proportion of the variation (51%) was attributable to the background probability of testing. It was also responsible for the largest variation in the

incremental QALYs. None of transition probabilities representing the natural history of the disease accounted for a significant amount of the variation in the costs or QALYs.

One-way deterministic sensitivity analysis

The sensitivity analysis showed that the results were particularly affected by a number of variables, including HCV seroprevalence, the intervention effect / cost, the probability of treatment uptake and the probability of leaving the UK (Table 4~~Table 4~~). Increasing ~~T~~the cost of antiviral treatment or including the addition of boceprevir / telaprevir had little impact on the cost-effectiveness estimates.~~results.~~

EVP(P)I

Assuming the intervention remains a viable option for 10 years, it produces a total population EVPI of around £4 million over this period in the base case at a £30,000 QALY threshold (Table 5~~Table 5~~). However, the EVPPI analysis suggests that further research into the probability of treatment uptake, the utility associated with the SVR health states and the intervention cost would be of most value.

DISCUSSION

There are over 1.4 million people from the Indian subcontinent living in the UK with a net of over +90,000 long term migrants arriving each year. As HCV is endemic in parts of this region, many will be infected although unaware of their status. The UK does not currently have a national policy of screening migrants for HCV, partly because of lack of evidence on cost-effectiveness [9]. However, the results from this economic evaluation suggest that an opt-out GP case finding intervention could be cost-effective but that there is a large degree of uncertainty around this conclusion and value in conducting further research.

The major strength of this study is that it is based on an established model of HCV disease progression. Its major limitations are that a number of parameters and associated uncertainty bounds lacked empirical evidence and were based on opinion. Moreover, the

evaluation did not incorporate the possibility of simultaneously testing for hepatitis B (HBV) infection which is also thought to be endemic in many parts of the Indian subcontinent [2]. However, if it had, then logic dictates the cost-effectiveness estimate would improve since the costs of detection are effectively divided across two infections and treatment for HBV infection has been shown to be cost-effective [32, 33]. It would also mean that the EVPI would decrease since an improvement in cost-effectiveness would lessen the potential impact of further information.

An important issue is that we have evaluated the potential costs and effects of a particular 'one off' case finding intervention [16]. However, the results from two other much less effective interventions are also reported in the same abstract. Thus, while the cost-effectiveness of the GP intervention appears to be reasonable given the base case input assumptions, the likelihood that other case finding approaches are cost-effective is much less clear.

The EVPI analysis showed that the total value of further research into the costs and effects of the case finding intervention should not exceed £4 million over the next 10-years if HCV seroprevalence is thought to be around 3.2% at a cost per additional QALY threshold of £20,000. However, the EVPPI analysis suggests that most of the uncertainty is being driven by the intervention cost (£0.43 million), the probability of treatment uptake (£0.21 million) and the utility associated with the SVR health states (£0.87 million). ~~in this order.~~ Thus, improving the accuracy of these parameters should be the priority if the aim is to generate more certain cost-effectiveness estimates in the future.

The value of further research into the effectiveness of case finding, in terms of an increased probability of testing as a result of the case finding intervention, was noticeably small. This finding appears counterintuitive but is firstly explained by the large population size in the Lewis study (n=1,134), meaning the level of uncertainty in the parameter was already relatively low. Secondly, the lowest sampled probability of testing following the intervention

was 0.16; at this level the intervention is already cost-effective. Indeed, this illustrates the advantage of EVPI analysis over more traditional sensitivity analysis techniques, as its value reflects the ability of research to alter policy decisions rather than merely reflecting the impact of different parameter values on the actual cost-effectiveness estimate.

While there have been a number of economic evaluations of HCV case finding interventions in former or current (IDUs) [34], and others relating to HBV, only one could be found that evaluated an intervention to find HCV cases that was at least in part aimed at migrant populations [35]. This Dutch study evaluated the outcomes of a national intervention to increase awareness of possible HCV infection in all high risk groups and a support programme that provided training sessions for GPs. The base case ICER was approximately €12,000 per additional QALY. While this value is somewhat lower than our own, the QALYs were discounted at 1.5% rather than 3.5% per annum which would bring the results approximately into line.

There are reasons to believe the EVPI and EVPPI values could be conservative. First, the population projections are based on net rather than total immigration figures, the latter is nearer 120,000 per annum). Second, the population projections were based on figures from the Indian subcontinent while people migrating from other countries might also benefit from additional research. Third, the assessment was based on 10-year projections but immigration from HCV endemic countries is likely to continue past this time. Fourth, while we have sampled 'parameter' uncertainty, we have not allowed for the fact that the study from which the effectiveness estimate is derived is a single large non-controlled study. Thus we may have undervalued the uncertainty in effectiveness estimate and as a consequence, the benefits of further research into the accuracy of this parameter. Last, an interesting moral / ethical issue is whether or not to account for, and to exclude, the potential downstream costs and QALYs relating to people who leave the UK after being tested. In the base case analysis we chose not to include these outcomes, but we note that while their

exclusion would decrease the mean cost-effectiveness estimate, the EVPI would increase since the ICER is pushed neared to a £30,000 per additional QALY threshold.

While the precise level of HCV seroprevalence is likely to vary by community setting [2], it is an important determinant of the cost-effectiveness of identification strategies, the ICER increased to £45,000 when 1% was assumed. However, if it is thought to be 2% or higher within any given population, then based on current evidence, we believe there is every possibility the GP-based intervention described herein is cost-effective at a £30,000 per additional QALY threshold.

NICE has recently concluded that migrants from HCV endemic countries should be tested for active infection, and case finding is recommended [10]. The UKs National Institute for Health Research has recently commissioned research on finding cases of hepatitis infection in UK migrant populations, at a cost of approximately £2 million (RP-PG-1209-10038) [36]. We broadly agree with NICEs recommendation and the funding decision for further research, but emphasise the importance of collecting information on parameters such as the background probability of testing and the intervention cost, not just the immediate intervention effect.

Disclosures

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Table 1: Base case probability inputs (suggested online supplementary material)

Parameter	Mean	Distribution	Source
Transition probabilities			
Mild to moderate*	0.025	Beta~(38.086, 1485.316)	Shepherd, Martin [3, 21]
Moderate to CC*	0.04	Beta~(26.905 700.2582)	Shepherd, Martin [3, 21]
CC to DC*	0.053	Beta~(14.617, 260.1732)	Shepherd, Martin [3, 21]
CC to HCC*	0.014	Beta~(1.9326, 136.1074)	Shepherd, Martin [3, 21]
DC to HCC*	0.014	Beta~(1.9326, 136.1074)	Shepherd, Martin [3, 21]
DC to death*	0.13	Beta~(147.03, 983.97)	Shepherd, Martin [3, 21]
DC to liver transplant (LT)*	0.03	Beta~(6.5256, 210.9945)	Shepherd, Martin [3, 21]
HCC to death*	0.43	Beta~(117.1, 155.23)	Shepherd, Martin [3, 21]
1st 6 months post LT to death*	0.21	Beta~(16.276, 61.2294)	Shepherd, Martin [3, 21]
>6 months post LT to death*	0.057	Beta~(22.902, 378.8825)	Shepherd, Martin [3, 21]
% Sustained viral response**			
Mild / mod. genotype 1	0.45	Uniform~(0.40, 0.50)	Martin and others [21, 24-28]
Mild / mod. genotype 2/3	0.80	Uniform~(0.75, 0.85)	Martin and others [21, 24-27]
CC genotype 1	0.25	Uniform~(0.20, 0.25)	Martin and others [21, 24-28]
CC genotype 2/3	0.60	Uniform~(0.55, 0.65)	Martin and others [21, 24-27]
Proportion with genotype 1	0.20	Fixed	UK HPA [7]
Intervention effect (1st cycle only, absolute probability of testing)	0.20	Beta~(n=1,134, r=223)	Lewis et al [16]
Probability of referral, attendance and treatment	0.45	Beta~(n=56, r=25)	Irving et al [22]
Background testing	0.041	Uniform~(0.001,0.081)	HPA [7] and assumptions
Proportion of HCV Ab+ who are RNA-	0.26	Beta~(156.9, 446.5)	Micallef et al [23]
Initial probabilities			
Uninfected	1-seroprevalence		-
HCV Ab+ / PCR-	pAbPCR+ *seroprevalence		-
Mild HCV	0.63*(1-pAvPCR)	Dirichlet(0.63,0.24,0.17)	Martin [21] and assumptions

Moderate HCV	0.24*(1-pAvPCR)	Dirichlet(0.63,0.24,0.17)	Martin [21] and assumptions
CC	0.17*(1-pAvPCR)	Dirichlet(0.63,0.24,0.17)	Martin [21] and assumptions
HCV seroprevalence	3.2%	-	HPA [7] and assumptions

*probabilities are annual, converted to 6 monthly probabilities in the model using 1-(1-prob)^0.5; Residual equals one minus the sum of the other related probabilities; **based on a combination therapy of pegylated interferon plus ribavirin; “where prevalence indicates HCV seroprevalence

Table 2: Base case utility values, all taken from Wright [4] which are repeated in Shepherd [3] unless otherwise indicated (suggested online supplementary material)

Utility value	Mean	Distribution
Uninfected		
Age 0-44 years	0.91	-
Age 45-54 years	0.85	-
Age 55-64 years	0.80	-
Age 65-74 years	0.78	-
Age 75+	0.73	
Mild HCV	0.77	Beta~(521.238, 155.6943)
Mild HCV SVR	0.82	Beta~(65.8678, 14.4588)
Moderate HCV	0.66	Beta~(168.246, 86.6723)
Moderate HCV SVR	0.72	Beta~(58.0608, 22.5792)
Compensated cirrhosis	0.55	Beta~(47.1021, 38.5381)
Compensated cirrhosis SVR	0.61	Beta~(58.0476, 37.1124)
Decompensated cirrhosis [30]	0.45	Beta~(123.75, 151.25)
Hepatocellular carcinoma [30]	0.45	Beta~(123.75, 151.25)
Liver transplant (1st year) [30]	0.45	Beta~(123.75, 151.25)
Liver transplant (subsequent years) [30]	0.66	Beta~(32, 16)

Utilities were calculated by multiplying the HCV uninfected age adjusted value by the relevant health state. For example, the utility of a 76 year old person with mild HCV = 0.73 x 0.77 = 0.56

Table 3: Base case cost inputs in 2010 prices unless otherwise stated (suggested online supplementary material)

Cost	Mean (£)	Distribution	Source
Health State*			
Annual mild HCV	138	Gamma~(25.7, 0.1862)	Martin, Shepherd [3, 29]
Annual moderate HCV	717	Gamma~(88.85, 0.1239)	Martin, Shepherd [3, 29]
Annual compensated cirrhosis	1,138	Gamma~(24.234, 0.0213)	Martin, Shepherd [3, 29]
Annual decompensated cirrhosis	9,120	Gamma~(36.0249, 0.004)	Martin, Shepherd [3, 29]
Annual hepatocellular carcinoma	8,127	Gamma~(18.108, 0.0022)	Martin, Shepherd [3, 29]
Liver transplant (per transplant)	27,330	Gamma~(89.7536, 0.0033)	Martin, Shepherd [3, 29]
Year following transplant	9,458	Gamma~(13.7788, 0.0015)	Martin, Shepherd [3, 29]
Annual post transplant	1,385	Gamma~(15.2189, 0.011)	Martin, Shepherd [3, 29]
Annual mild SVR	259	Gamma~(28.8141, 0.10)	Martin, Shepherd [3, 29]
Annual moderate SVR	717	Gamma~(89.004, 0.124)	Martin, Shepherd [3, 29]
Annual cirrhosis SVR	1138	Gamma~(25.81, 0.0227)	Martin, Shepherd [3, 29]
Antiviral treatment (for 6 months)⁺	5,612	Uniform~(4,806, 6,418)	Martin and BNF [21, 37]
PCR test (per test)	70	-	Martin [21]
HCV antibody test (per test)	10	-	Assumption
Nurse (GP practice, per test)	9.75	-	Curtis [38]
Intervention (per eligible person)**	20	Gamma~(4, 0.22)	Assumption

*All health state costs are stated in 2003/4 prices and are inflated to 2010 prices in the analysis ** Excludes the costs of the test itself; ⁺treatment is with pegylated interferon and ribavirin

Table 4: One way sensitivity analysis

Parameter	Base case value	ICER (£)
Base case		**23,200**
HCV Ab+ prevalence	3.2%	
1%		45,700
5%		19,300
Intervention cost per eligible person	£20*	
£10		18,300
£30		27,700
Intervention effect (absolute probability of testing in first 6 months)	0.197*	
0.1		34,500
0.3		19,500
Treatment referral and attendance (probability of treatment uptake)	0.45*	
0.33		31,000
0.66		15,600
Antiviral treatment costs – pegylated interferon and ribavirin	£5,612*	
£7,500		23,900
Addition of boceprevir / telaprevir for genotype 1		
£19,000 additional cost, probability SVR 0.63 (mild / moderates) and probability SVR 0.45 for compensated cirrhosis		23,740
Initial probability of having decompensated cirrhosis	0	
0.10		26,700
6 Monthly probability of permanently leaving the UK**	0	
0.01		32,500

*mean distribution value; **taken to be equivalent to no further costs or QALYs after 'exit'

Table 5: Expected value of perfect (EVPI) and partial (EVPPI) information results at a willingness to pay (WTP) of £30,000 per QALY and base case assumptions

Parameter	Population EVP(P)I (million)
Overall decision level	£3.80
WTP £20,000 per additional QALY	£4.07
1% HCV Ab+ seroprevalence	£1.13
1% HCV Ab+ seroprevalence and WTP £20,000	£0.10
Intervention effect (absolute probability of testing)	Negligible
Probability of treatment uptake	£0.21
Background probability of testing	Negligible
Utilities	£1.07
SVR health states	£0.87
Intervention cost	£0.43
Disease costs	Negligible
Transition probabilities	£0.02
Initial distribution across HCV disease states	Negligible

List of Figures

References

1. World Health Organisation. *Hepatitis C Fact sheet N°164*. 2012; Available from: http://www.who.int/mediacentre/factsheets/fs164/en/index.html.
2. Uddin, G., Shoeb, D., Solaiman, S., et al. *Prevalence of chronic viral hepatitis in people of south Asian ethnicity living in England: the prevalence cannot necessarily be predicted from the prevalence in the country of origin.* Journal of Viral Hepatitis, 2010. **17**: p. 327-335.
3. Shepherd, J., Jones, J., Hartwell, D., Davidson, P., Price, A. and Waugh, N. *Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of mild chronic hepatitis C: a systematic review and economic evaluation.* Health Technology Assessment, 2007. **11**(11).
4. Wright, M., Grieve, R., Roberts, J., Main, J. and Thomas, H.C. *Health benefits of antiviral therapy for mild chronic hepatitis C: randomised controlled trial and economic evaluation.* Health Technol Assess, 2006. **10**(21): p. 1-113.
5. Sroczynski, G., Esteban, E., Conrads-Frank, A., et al. *Long-term effectiveness and cost-effectiveness of antiviral treatment in hepatitis C.* Journal of Viral Hepatitis, 2010. **17**(1): p. 34-50.
6. Rosen, H.R. *Chronic Hepatitis C Infection.* New England Journal of Medicine, 2011. **364**: p. 2429-38.
7. Health Protection Agency, *Sentinel Surveillance of Hepatitis Testing in England - Hepatitis C testing 2010 Report - Analyses of HCV testing data between 2007 and 2010 Health*, 2011: Collindale, UK.
8. Allaby, M., *Screening for Hepatitis B and Hepatitis C among ethnic minorities born outside the UK: A report for the National Screening Committee*, 2010, Solutions for Public Health.
9. National Screening Committee, *Screening for Hepatitis B and Hepatitis C among ethnic minorities born outside the UK Policy Position Statement*, 2011.
10. National Institute for Health and Clinical Excellence. *Hepatitis B and C - ways to promote and offer testing*. 2012; Available from: http://publications.nice.org.uk/hepatitis-b-and-c-ways-to-promote-and-offer-testing-to-people-at-increased-risk-of-infection-ph43.
11. Claxton, K., Ginnelly, L., Sculpher, M.J., Philips, Z. and Palmer, S. *A pilot study on the use of decision theory and value of information analysis as part of the National Health Service Health Technology Assessment Programme.* Health Technology Assessment, 2004. **8**(31): p. 1-118.
12. Briggs, A., Sculpher, M. and Claxton, K., *Decision modelling for health economic evaluation*. Handbooks in health economic evaluation series, ed. A. Gray and A. Briggs2006, Oxford: Oxford University Press.
13. National Institute for Health and Care Excellence, *Guide to the methods of technology appraisal*, 2013.
14. Beck, J.R. and Pauker, S.G. *The Markov process in medical prognosis.* Medical Decision Making, 1983. **3**(4): p. 419-458.
15. McPherson, S., Valappil, M., Moses, S., et al. *CHASE-B (Chinese hepatitis awareness, surveillance, and education): A pilot of targeted case finding for hepatitis B virus (HBV) in the British-Chinese community.* Gut, 2010. **60**.
16. Lewis, H., Burke, K., Begum, S., Ushiro-Limb, I. and Foster, G.R. *What is the best method of case finding for chronic viral hepatitis in migrant communities?* Gut, 2011. **Vol 60 Suppl 2**: p. A26.
17. Jafferbhoy, H., Miller, M., McIntyre, P., Mcleod, S. and Dillon, J.F. *Outreach community testing for hepatitis C in an ethnic population* Gut, 2010. **59**: p. A13.
18. Jones, L., Bates, G., McCoy, E., Beynon, C., McVeigh, J. and Bellis, M. *A systematic review of the effectiveness & cost-effectiveness of interventions aimed at raising awareness and engaging with groups who are at an increased risk of hepatitis B and C infection*. 2011; Available from: http://www.nice.org.uk/nicemedia/live/11957/59546/59546.pdf.

19. Office for National Statistics. *Population by Country of birth and Nationality July 2010 to June 2011*. 2012; Available from: http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-256033.
20. Office for National Statistics. *3.04 IPS Country of Birth by Sex, 1975-2011*. 2011; Available from: http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-280889.
21. Martin, N., Vickerman, P., Miners, A., Foster, G.R., Hutchinson, S.J., Goldberg, D.J. and Hickman, M. *Cost-effectiveness of hepatitis C virus antiviral treatment for injection drug user populations.* Hepatology, 2011: p. In press.
22. Irving, W.L., Smith, S., Cater, R., et al. *Clinical pathways for patients with newly diagnosed hepatitis C - what actually happens.* Journal of viral hepatitis, 2006. **13**(4): p. 264-71.
23. Micallef, J., Kaldor, J. and Dore, G. *Spontaneous viral clearance following hepatitis C infection: a systematic review of longitudinal studies. .* Journal of Viral Hepatitis, 2006. **13**: p. 34-41.
24. Hadziyannis, S.J., Sette, J.H., Morgan, T.R., et al. *Peginterferon-α2a and Ribavirin Combination Therapy in Chronic Hepatitis CA Randomized Study of Treatment Duration and Ribavirin Dose.* Annals of Internal Medicine, 2004. **140**(5): p. 346-355.
25. McHutchison, J.G., Lawitz, E.J., Shiffman, M.L., et al. *Peginterferon Alfa-2b or Alfa-2a with Ribavirin for Treatment of Hepatitis C Infection.* New England Journal of Medicine, 2009. **361**(6): p. 580-593.
26. Shiffman, M.L., Suter, F., Bacon, B.R., et al. *Peginterferon Alfa-2a and Ribavirin for 16 or 24 Weeks in HCV Genotype 2 or 3.* New England Journal of Medicine, 2007. **357**(2): p. 124-134.
27. National Institute for Health and Clinical Excellence, *Peginterferon alfa and ribavirin for the treatment of mild chronic hepatitis C*, 2006.
28. Bruno, S., Shiffman, M.L., Roberts, S.K., Gane, E.J., Messinger, D., Hadziyannis, S.J. and Marcellin, P. *Efficacy and safety of peginterferon alfa-2a (40KD) plus ribavirin in hepatitis C patients with advanced fibrosis and cirrhosis.* Hepatology, 2010. **51**(2): p. 388-397.
29. Martin, N., Miners, A. and Vickerman, P., *Assessing the cost-effectiveness of interventions to increase hepatitis C testing among injecting drug users: An economic modeling report*, 2012, London School of Hygiene and Tropical Medicine and University of Bristol.
30. Ratcliffe, J., Longworth, L., Young, T., Bryan, S., Burroughs, A. and Buxton, M. *Assessing health-related quality of life pre- and post-liver transplantation: a prospective multicenter study.* Liver Transpl, 2002. **8**(3): p. 263-70.
31. Curtis, L., *Unit costs of health & social care* 2010, Personal Social Services Research Unit, University of Kent.
32. Shepherd, J., Jones, J., Takeda, A., Davidson, P. and Price, A. *Adefovir dipivoxil and pegylated interferon alfa-2a for the treatment of chronic hepatitis B: a systematic review and economic evaluation.* Health Technology Assessment, 2006. **10**(28).
33. Dakin, H., Bentley, A. and Dusheiko, G. *Cost–utility analysis of tenofovir disoproxil fumarate in the treatment of chronic hepatitis B.* Value in Health, 2010. **13**: p. 922-923.
34. Thompson Coon, J., Castelnuovoa, E., Pitt, M., Cramp, M., Siebert, U. and Stein, K. *Case finding for hepatitis C in primary care: a cost utility analysis.* Family Practice, 2006. **23**(4): p. 393-406.
35. Veldhuijzen, I.K., Toy, M., Hahné, S.J.M., De Wit, G.A., Schalm, S.W., de Man, R.A. and Richardus, J.H. *Screening and Early Treatment of Migrants for Chronic Hepatitis B Virus Infection Is Cost-Effective.* Gastroenterology, 2010. **138**(2): p. 522-530.
36. National Institute for Health Research. *Chronic viral hepatitis in ethnic minorities. Strategies to prevent the predicted increase in mortality*. 2012 [cited 2012 1/10/2012]; Available from: http://www.ccf.nihr.ac.uk/PGfAR/about/Pages/FundedProgrammesOld.aspx.
37. British Medical Association and Royal Pharmaceutical Society of Great Britain, *British National Formulary No. 62.* 2011.

38. Curtis, L., *Unit costs of health and social care*, 2011, PSSRU, University of Kent: Canterbury, UK.