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Is antenatal screening for hepatitis C virus cost effective? A decade's experience at a London centre

b) Authors: Nowlan Selvapatt[1], Thomas Ward[2], Heather Bailey[3], Hayley Bennett[2], Claire Thorne[3], Lay-May See[4], Gareth Tudor-Williams[5], Mark Thursz[1,6], Phil McEwan[2,7], Ashley Brown[1]

c) Institutions:

1. Department of Hepatology, St Mary's Hospital, Imperial College Healthcare NHS Trust, London, UK
2. Health Economics and Outcomes Research Limited, Wales, UK
3. University College London Institute of Child Health, London, UK
4. Department of Gastroenterology and Hepatology, Kingston Hospital NHS Foundation Trust, UK
5. Department of Paediatrics, St Mary's Hospital Campus, Imperial College, UK
6. Department of Hepatology, St Mary's Hospital Campus, Imperial College, UK
7. Swansea Centre for Health Economics, Swansea University, Wales UK

d) Corresponding author contact details: Nowlan Selvapatt, Department of Hepatology, Imperial College, 10th Floor QEQM, St Mary's Hospital Campus, London, W2 1NY.

T: 0203 312 5701 F: 0207 402 2796 E: nowlan.selvapatt@imperial.nhs.uk

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g) **List of abbreviations**

HCV: hepatitis C virus

ESLD: end stage liver disease

HCC: hepatocellular carcinoma

DAA: direct acting antiviral

HBV: hepatitis B virus

REDCAP: research electronic data capture

MONARCH: modelling the natural history and cost effectiveness of hepatitis C

QALY: quality adjusted life year

SVR: sustained virologic response

eRVR: extended rapid virologic response

SA: sensitivity analysis

BC: base case

ICER: incremental cost effectiveness ratio

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Abstract

Background: This study aims to assess the cost-effectiveness of a routine universal antenatal hepatitis C virus (HCV) screening programme at a London centre.

Methods: Ten years' retrospective antenatal screening and outcome data informed a cost-effectiveness analysis using the previously validated MONARCH model. The cost and quality-of-life outcomes associated with the screening and treatment of newly identified hepatitis C cases were used to generate cost-effectiveness estimates for the screening programme.

Results: A total of 35,355 women were screened between 1st November 2003 and 1st March 2013; 136 women (0.38%) were found to be HCV antibody positive. Of 78 (0.22%) viraemic cases, 44 (0.12%) were newly diagnosed. In addition, the screening programme identified three (6.8%) vertical transmissions in children of newly diagnosed mothers. Of 16 newly diagnosed mothers biopsied, all were in the F0-F2 METAVIR disease stages, and 50% had HCV genotype 1. Postnatal treatment with pegylated interferon and ribavirin was initiated in 19 women, with 14 (74%) achieving sustained virologic response. The total cost of screening and confirmation of diagnoses was estimated to be £240,641. This translates to £5,469 per newly diagnosed individual. The incremental cost-effectiveness ratio of this screening and treatment strategy was £2,400 per QALY gained. Treatment with newer direct acting antiviral regimens would have a projected cost of £9,139 per QALY

gained, well below the £20,000-30,000/QALY gained willingness-to-pay threshold applied by policy advisory bodies.

Conclusions: This study demonstrates that an antenatal screening and treatment programme is feasible and effective, at a cost considered acceptable.

Introduction

Hepatitis C virus (HCV) is a blood borne virus with a chronic course in most infected individuals. It is usually asymptomatic in the early years, but persistent infection can lead to end-stage liver disease (ESLD) and hepatocellular carcinoma (HCC) [1]. In the UK, both hospital admissions and deaths from HCV-related ESLD and HCC are continuing to rise, and the number of transplants indicated due to HCV-related cirrhosis has more than quadrupled between 1996 and 2013 [2]. Previously published European antenatal data suggest an HCV prevalence of up to 0.6% in this population [3][4].

It is estimated that at least 40% of cases remain undiagnosed in the UK [2]. In 2012, birth cohort screening for HCV was recommended by the Centers for Disease Control and Prevention (CDC) [5]; however, outside the US, screening for HCV is generally only undertaken in high-risk populations. Risk based screening may not be effective for three main reasons: firstly, in the primary care setting, HCV risk factors are often not fully explored [6][7]; secondly, patients do not always report transient behaviours (e.g. injecting drug use) that occurred years or decades ago; thirdly, many acquire infection iatrogenically in their country of origin and are unaware of exposure risk. Other strategies for HCV case finding are therefore becoming increasingly pertinent, especially given the recent advances in treatments with the introduction of new generation direct acting antivirals (DAAs). Antenatal screening for several infectious diseases, including HIV and hepatitis B virus (HBV), is performed routinely in many countries including the UK [8]. This is

commonly motivated by the risk of perinatal transmission; this is estimated at 6% amongst HCV patients [9][10]. However, in the absence of interventions available to prevent HCV transmission, routine screening for HCV in pregnancy has not been recommended in most countries [11]. Successful identification and treatment of HCV-infected individuals is associated with improved long-term health, through the avoidance of ESLD, and increased life expectancy [12][13].

Previous studies have shown benefit in the adoption of a routine antenatal screening programme for HCV over risk based testing strategies [3][14]. These studies demonstrate that up to 75% of newly diagnosed mothers have no reported “high risk” behaviour. Whilst many of these women were born in countries with a higher prevalence and risk of infection, screening of migrants would potentially be stigmatising. Women screened and diagnosed with HCV during the antenatal period are generally healthy and motivated, with high rates of attendance to follow-up observed [3]. Given that testing for HCV antibodies can be carried out using the same laboratory samples taken for routine antenatal virology screening for HIV and HBV, minimal additional resource use is required. The costs of diagnostic confirmation and the treatment of newly identified patients pose potentially significant costs, but these may be offset against the potential future costs of late diagnosis and the treatment of complications, should these women be diagnosed only when the disease has progressed.

This study aims to evaluate the cost-effectiveness of routine screening for HCV antibodies in the antenatal population of a London hospital, based on data from a ten-year screening programme, using a previously published and validated simulation model of HCV.

Methods

Screening and treatment

Between 1st November 2003 and 1st March 2013, all pregnant women attending the antenatal clinics at St Mary's Hospital, Imperial College Healthcare NHS Trust, London for their "booking in" visit were offered HCV antibody testing as part of their screening. All positive results were directly reported from the virology lab to a specialist midwifery team trained in the management of patients with viral hepatitis. All mothers in which HCV antibodies were identified were referred to a named consultant hepatologist working closely with the antenatal team. Mothers with initial undetectable viral load results had a further viral load assessment after the pregnancy to confirm spontaneous resolver status, before being discharged from follow-up. Mothers with identified viraemia were counselled in the antenatal hepatology clinic and reviewed in a family clinic following delivery, with their child, by the same hepatologist and a paediatric consultant with specialist interest in infectious diseases. All children of infected mothers were tested serologically for HCV at 15 months. These mothers were then offered regular hepatology follow-up and worked up for treatment per standard practice.

Antenatal and medical records were reviewed to evaluate the service provided to these women over the last ten years and their outcomes. Individual patient data were anonymised. Data were managed using REDCap electronic data capture tools [15]. Information recorded included patient demographics, antenatal data, maternal HCV status and their risk factors, dates of hepatology appointments, outcomes of work up and, if relevant, treatment records and outcomes.

Cost-effectiveness model

The MONARCH (MOdelling the NAtural histoRy and Cost effectiveness of Hepatitis C) model is a previously published and validated HCV disease progression and cost-effectiveness model designed to progress a cohort of subjects in annual cycles through METAVIR fibrosis stages and potentially to ESLD complications and death [16][17]. Patients in METAVIR fibrosis stages F0–F4 incur an annual probability of all-cause mortality [18], whilst patients suffering from ESLD complications incur disease-specific mortality rates. Figure 1 shows the model flow diagram and Table S1 (supplementary data) reports the transition rates applied in the model. Disease progression is modelled over a lifetime assuming a maximum age of 100 years. Total costs, quality-adjusted life-years (QALYs), and numbers of predicted ESLD complications and deaths are estimated over the simulated period.

Fibrosis stage transition probabilities were informed by characteristics of the screened population with respect to age, sex, HCV genotype and source of infection (Table S1). Initially, patients' disease stage was reported as either

mild, moderate or severe. To inform the initial distribution of patients across fibrosis stages, it was assumed that mild and moderate disease corresponded to fibrosis stages F0–F1 and F2–F3, respectively.

The outcomes of the screening programme were used as the basis of a cost-effectiveness analysis using the MONARCH model. The additional costs of screening were compared to the benefits of identifying new cases and the opportunity for treating them, in terms of future quality of life, survival and cost implications of long-term HCV complications. The results of modelling were used to determine an upper threshold for the cost of screening. The UK advisory body, the National Institute of Health and Care Excellence (NICE), considers an intervention cost-effective at a threshold of £20,000 to £30,000 per QALY gained [19]; in the US, the threshold is $50,000 per QALY gained [20], and a previous European evaluation of an antenatal HCV screening programme applied a threshold of €20,000 to €50,000 [21].

A healthcare payer perspective was taken and only direct medical costs considered. Patient and societal costs, such as increased productivity among working adults, were not included. HCV-specific treatment and monitoring costs were derived from weekly estimated costs, accommodating duration of treatment by HCV genotype. Testing costs were based on cost tariffs at Imperial College Healthcare NHS Trust, as demonstrated in Table S2 (supplemental data). Costs associated with the screening programme included the costs of identifying patients through the use of both HCV antibody and confirmatory testing amongst all patients; those subsequently

identified as having HCV antibodies underwent RNA, genotype and baseline liver screening. Costs associated with liver biopsy were applied to the patients that underwent the procedure, whilst patients that were treated incurred antiviral therapy-related costs. All costs and health utility estimates (measured as QALYs), presented in Table 1, are independent of age and were discounted annually at a rate of 3.5%, to reflect their present value. All costs were inflated to 2013 values using the Health and Social Care index [22].

In the base case, the identification and treatment of patients was modelled as observed in the women in our study centre treated with pegylated-interferon alpha and ribavirin (IFN/RBV) only. It was assumed that patients infected with HCV genotypes 1 and 4 received 48 weeks of treatment, and those with HCV genotypes 2 and 3 received 24 weeks of therapy. Conservative assumptions around drug cost were made; it was assumed no patients ended treatment early due to discontinuation or extended rapid virologic response (eRVR). Any bias introduced by this assumption would be against the screening strategy. Amongst all treated patients, there was no evidence of significant anaemia or dose reduction and no blood or platelet transfusions; as such, the costs of treating any adverse events were not modelled. Therapy-specific disutility was applied to patients whilst receiving treatment, upon completion of treatment no further disutility was incurred.

Two additional scenarios were modelled relating to the introduction of new generation DAAs: as either the initial treatment option or as subsequent treatment for patients failing to achieve SVR with IFN/RBV; to illustrate this, a

treatment success rate (SVR) of 95% for 12 weeks of sofosbuvir triple therapy (SOF + IFN/RBV) was applied across all genotypes and fibrosis stages, estimated from results of recent phase 3 trials [23][24]. In these additional scenarios, the identification of patients for treatment was modelled as observed in the study centre.

Sensitivity analysis

A series of sensitivity analyses (SA) were conducted, to evaluate the impact of uncertainty in the following areas on modelled base case results:

1) (a) Increasing and (b) decreasing the age at diagnosis by five years.
2) Adjusting SVR rates associated with IFN/RBV to reflect the consensus literature; i.e., 52% in HCV genotype 1 patients [25], 75% in HCV genotype 2 patients [26], 75% in HCV genotype 3 patients [26], and 48% in HCV genotype 4 patients [27].
3) Treatment of all newly diagnosed patients.
4) HCV prevalence amongst the screened population of (a) 0.1% and (b) 0.6%.

Results

Results of the screening and treatment programme

During the ten-year period evaluated, a total of 35,355 women underwent antenatal HCV screening at St Mary's Hospital. A total of 136 (0.38%) HCV antibody positive results were confirmed (figure 2). Overall, 44 women (0.12%) were newly diagnosed with chronic HCV. Of the remaining 92 women

with positive HCV antibody results, 34 had received prior diagnosis and 58 had sequential negative HCV viral loads, indicating spontaneous clearance of the virus.

Of the 44 newly diagnosed women, the majority were HCV genotypes 1 and 3 (figure 2), with a median age of 33 years (range 23–46) at diagnosis. None were co-infected with either HIV or HBV. Subsequently, a total of 19 women underwent treatment for HCV with IFN/RBV, of which 14 (74%) achieved SVR. Three additional women were treated and achieved SVR, one genotype 1 with IFN/RBV and boceprevir and two genotype 4 patients with DAAs as part of a clinical trial.

Of the 44 newly diagnosed women, 14 were born in the UK, 14 in Eastern Europe, 3 in Western Europe, 4 in Africa and 9 in Asia. The likely source of HCV infection was identified as blood transfusion for one mother, whilst 11 out of the 44 mothers had a prior history of injecting drug use. Of these 11 women, one spontaneously cleared the virus the year after diagnosis and two underwent treatment, with one successful SVR. On review of the reasons for not undertaking treatment, eight mothers did not attend clinic follow-up due to complex social factors.

Five (11%) children born to mothers newly diagnosed with HCV had evidence of HCV antibodies when tested. One child had a weak antibody response but never had detectable HCV RNA, and a second child who had a viral load of 7

$x10^6$ IU/mL at the age of 4 months had spontaneously cleared the virus by the

age of 12 months. Three children (6.8%) are under active follow-up with vertically acquired HCV, all with HCV genotype 3a, one of which is undergoing treatment with IFN/RBV at the time of writing. At least ten other cases were also identified as result of contact tracing as a consequence of mothers being diagnosed.

Cost-effectiveness results

The total cost of screening and confirmation of diagnoses was estimated to be £240,641. This translates to £6.81, £5,469 and £12,665 per individual screened, newly diagnosed and treated at the study centre, respectively.

Base case results are presented in Table 2 and compare a screening and treatment strategy to a no screening and no treatment strategy. These results were based on the 19 patients who were treated with IFN/RBV following screening at the study centre. When comparing treatment versus no treatment, the cost offsets associated with avoided HCV-related complications provide a relative cost-saving in patients with HCV genotypes 1, 2 and 3. Patients with genotype 4 infection incurred a greater cost, due to the relatively low observed rate of SVR, but remained cost-effective with an incremental cost-effectiveness ratio (ICER) of £4,054 per QALY gained. Across all treated patients, treatment is dominant over no treatment; that is treatment provides greater health benefits at a lower overall cost.

After factoring in the additional costs associated with screening, additional healthcare expenditure is incurred as a result of the total screening and

treatment strategy. However, when compared to the improvement in QALYs achieved in treated patients, the associated ICER of £2,400 (approximately €3,072/$3,840 USD) remains well below the accepted thresholds. Based upon screening this population of 35,355 women, it was estimated that the cost associated with screening each individual could be increased up to £31.04 and still remain cost-effective at the £20,000/QALY gained threshold.

Table 2 demonstrates the potential impact of DAA use upon the cost-effectiveness of a HCV screening programme. Whilst incurring increased therapy-related costs, the improved SVR rates associated with SOF+IFN/RBV generated significant increases in QALYs and life expectancy (DAA scenario 1). A similar relationship was observed when IFN/RBV treatment failure was followed by SOF+IFN/RBV treatment (DAA scenario 2). These scenarios resulted in ICERs of £9,139 (approximately €11,697/$14,622) and £3,105 (approximately €3,974/$4,968) respectively.

Sensitivity analysis

The screening strategy remained cost-effective under all sensitivity analyses performed, as presented in Table 3. The cost-effectiveness of screening was most significantly impacted by the prevalence of HCV infection amongst the screened women and the proportion of identified women treated. Compared to a screening cost threshold of approximately £31/person in the base case, varying the underlying HCV prevalence to 0.1% and 0.6% lead to thresholds

of £14.07 and £84.43, respectively. The most cost-effective measure is expected to be ensuring the treatment of all diagnosed viraemic patients. Results suggest that treating all identified patients within the screening programme would have been dominant over no screening. Furthermore, after adjusting the prevalence of HCV infection to 0.1% or 0.6%, treatment of all positively diagnosed women would remain a more cost-effective scenario than treating a proportion as in the base case.

Conversely, age and changes in SVR were less influential. Increasing the age at which patients were diagnosed, however, proved to decrease cost-effectiveness of the screening programme. Utilising alternative SVR rates had a minor impact on the cost-effectiveness of screening, increasing the estimated ICER to £3,922. A summary of ICER and screening cost threshold results are presented in Figure 3, where the dashed line represents the estimated cost per person screened incurred at the study centre.

Additional analyses were undertaken relating to the most influential parameters for cost-effectiveness; i.e., the prevalence of HCV viraemia amongst the screened population and the uptake of treatment amongst those positively diagnosed. In each case, base case parameter values were utilised, whilst the prevalence of HCV or the rates of treatment uptake were contrasted over sensible ranges to investigate the effect upon cost-effectiveness. Results are presented in Figure 4, where the solid black line represents the £20,000/QALY threshold and the dashed black line represents the base case ICER of £2,400.

Discussion

Within the population of this study, addition of HCV screening and treatment was expected to be cost-effective. These findings are driven by the relatively low additional costs required to implement HCV antibody testing alongside existing antenatal screening tests. Overall, the incidence of newly diagnosed HCV was 0.12%, whilst seemingly low, it is comparable to the prevalence of new HBV (0.16%) and HIV (0.04%) diagnoses observed amongst antenatal screenings in England in 2013 [35]. This study has demonstrated that cost-effectiveness improves when the prevalence of HCV is increased assuming that costs and treatment uptake are comparable to those observed in this study. In countries, such as Egypt where antenatal HCV prevalence have been reported at up to 2.4% [36], the benefits of screening would potentially outweigh the additional cost incurred if the same assumptions were made. Furthermore, within that particular cohort, 90% of viraemic mothers were previously unaware of their infection and over 10% of infected patients would have been missed when undertaking screening based upon identification of risk factors. This supports the rationale for universal antenatal screening of HCV, akin to HBV and HIV. It provides the mother an opportunity to access treatment with a view of achieving SVR. At the time of writing, 22 of 44 newly diagnosed women are in position to have future pregnancies without risk of vertical transmission.

Amongst patients considered in the analysis, the observed effectiveness of conventional interferon-based dual therapy in the antenatal population with

HCV genotypes 1–3 compared favourably to historical data. However, sensitivity analyses showed cost-effectiveness results were robust to deviations from the observed SVR rates. Since the analysis in this study was undertaken, an additional three patients were treated and achieved SVR: one was treated with IFN/RBV and boceprevir for 28 weeks and two further patients were treated with interferon-free DAA regimens as part of clinical trials; potentially resulting in an underestimation of cost-effectiveness. The costs of identification and treatment of these chronically infected women were shown to be offset by the reduced risk of future sequelae of HCV-related disease. Women, and their children, who may have been identified at a later stage are more likely to be symptomatic, more difficult to treat and at increased risk of developing complications and incurring higher costs. Improved cost-effectiveness estimated in younger patients further highlights the importance of early detection. Consideration of societal costs or costs incurred by patients, such as lost productivity were not accounted for, potentially underestimating the benefits of this screening programme.

Screening strategies are receiving increasing emphasis, given the associated morbidity associated with HCV and the emergence of more efficacious treatments. Other focussed strategies, such as birth cohort screening, have been demonstrated to be cost-effective and have been implemented in the US to augment screening strategies in high risk patients [17]. This strategy offers screening to all Americans born between 1945 and 1965, a birth cohort that is estimated to contain 75% of unidentified HCV infected persons [5]; however, uptake rates for this programme have not yet been reported. Risk-based

screening strategies will inevitably miss cases, and by design the birth cohort-screening programme in the US is likely not to capture 25% of HCV infections. Antenatal screening may offer a highly cost-effective strategy to identify HCV infection amongst a population that is most likely to benefit from treatment, due to demonstrated high rates of efficacy and therapy adherence.

Urbanus et al. reported that screening for HCV in Amsterdam's antenatal population was not cost-effective [21]. Two aspects that differ between the Urbanus study and this study, are (a) the inclusion of relatively high costs associated with screening and treatment within the Dutch population, and (b) the inclusion of life-years within the ICER calculation rather than QALYs. Indeed, when sensitivity analyses were performed with lower treatment costs, the Dutch screening programme was shown to be cost-effective, at a threshold of €20,000/QALY gained. The derivation of ICERs utilising life-years underestimates the benefit of treatment in relation to improved quality of life. This study demonstrated that antenatal screening has the potential to provide morbidity benefits as a result of detecting HCV-infected women earlier than they would normally be and thus preventing complications of HCV in later life.

This study is subject to a number of limitations relating to both modelling assumptions and the underlying characteristics of the study centre and population. The study centre is based in London, and, as demonstrated in the patient demographics, may have an overrepresented migrant population. Further cost may be incurred to provide a comparable programme, although centres undertaking routine antenatal HBV screening will undoubtedly have

established infrastructure that would minimise costs of incorporating new HCV diagnoses too. When considering base case assumptions, it was estimated that an additional £856,890 could have been spent within this programme whilst maintaining cost-effectiveness at a threshold of £20,000 per QALY, when using base case assumptions.

Application of UK rates of alcohol consumption, in the absence of study-specific data, may have affected the derivation of fibrosis stage transition rates; however, this is unlikely to have made any significant difference to modelling results. Additionally, age-dependent health utility estimates were not considered within the modelling analysis; however, when considering the young age of the modelled cohort compared to the average UK HCV patient, and that health state utility estimates are representative of patients of differing ages, such an assumption is not likely to introduce significant bias. Given the relatively high rate of HCV antibody positive but PCR negative patients within our study population, 58 of 35,355 women (0.16%) would have experienced a brief negative impact on quality of life until their spontaneously cleared status was confirmed. Mothers that were given a new positive diagnosis in the antenatal period but were not offered treatment may also incur a decrement in quality of life. We suggest, however, that the overall gain associated with early diagnosis and improved treatment outcomes is likely to outweigh this. The assumption that in the absence of screening women would not be otherwise diagnosed or treated until symptomatic may lead to overestimations of the benefit of screening; however, given that the majority of identified patients

would likely not be screened due to their “low” risk status, and in the absence of additional supporting data, this is an appropriate assumption.

The study did not evaluate the costs or benefits of the testing and treatment of children perinatally exposed. Three vertical transmissions from 44 newly diagnosed mothers were observed. There is little information available relating to the modelling of perinatally acquired HCV. Contact cases were not incorporated within the analysis, as the patient records could not be reliably used to assess contact tracing and treatment outcomes. Whilst not considered from an economic point of view, the detection of these cases has potentially allowed for appropriate and timely management preventing further morbidity and possibly further transmission.

To date, HCV screening is reserved for individuals with elevated risks of infection, such as injecting drug use and presence of other blood borne viruses. Despite higher prevalence rates in such groups treatment uptake is suboptimal and is of limited cost efficiency [37][38][39]. Due to complex social factors eight mothers did not attend clinic follow up and thus did not undertake treatment. This highlights an area in which service development can be optimised further.

Antenatal screening policies for HCV require reconsideration, given the positive outcomes following identification of infected women at an early stage of their disease. This study shows that, despite increased treatment costs of DAAs, associated improvements in SVR rates are expected to make their

inclusion in antenatal screening and treatment strategies cost-effective. The improved tolerability and shorter duration of newer HCV regimens may also further increase the uptake of therapy following diagnosis of HCV. It is hoped that committees responsible for national antenatal screening programmes will re-evaluate the need for HCV screening in the light of the evidence provided by this study.

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Figure 1: Flow diagram of the MONARCH model. Annual transition probabilities control progression through disease states.

Table 1: Cost and health utility parameters

Figure 2: Flow diagram showing the results of the numbers tested and the number of new diagnoses of HCV based on antenatal screening and outcomes of treatment within the cohort.

Table 2: Base case (BC) cost-effectiveness results (per treated patient)

Figure 3: Incremental cost-effectiveness ratios and estimated maximum cost per patient screened, assuming a maximum cost-effectiveness threshold of £20,000/QALY. The dashed line represents the estimated cost per person screened incurred at the study centre

Figure 4: The relationship between the cost-effectiveness of screening: and the prevalence of HCV amongst screened patients; and the treatment uptake amongst those newly identified as HCV positive. The solid black line represents the £20,000/QALY threshold and the dashed black line represents the base case ICER of £2,400.

Table 3: Sensitivity analysis results (per treated patient)

Table S1: Annual disease progression rates, distribution types and parameters used in the model

Table S2: Unit costs and resource use of screening cost components

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Table 1

	Cost parameters			Health utility parameters		
	Mean	SE	Source	Mean	SE	Source
Disease State (annual)						
F0/F1	£177.47	£35.01	[28]	0.77	0.015	[30]
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	
Treatments						
IFN/RBV	£191.35/week	NA	[29]	0.109*	0.010	[33]
SOF+IFN/RBV	£1,519.81/week	NA		0.148*	0.010	[34]

*These values represent therapy-specific disutilities.

DC, decompensated cirrhosis; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; IFN/RBV, pegylated interferon α and ribavirin; LTx, liver transplant; RNA, ribonucleic acid; SOF, sofosbuvir; SVR, sustained virologic respons

Table 2

	Base case: IFN/RBV	DAA scenario 1: All SOF+IFN/RBV	DAA scenario 2: SOF+IFN/RBV in IFN/RBV failures
No treatment			
Total cost (£)	20,749	20,749	20,749
Total QALYs	15.39	15.39	15.39
Total life years	22.13	22.13	22.13
Treatment			
Total cost (£)	14,233	38,630	18,723
Total QALYs	17.95	18.73	18.82
Total life years	23.07	23.33	23.37
Cost-effectiveness results of treatment versus no treatment			
Δ Cost (£)	-6,516	17,881	-2,027
Δ QALY	2.56	3.34	3.43
Δ Life years	0.94	1.19	1.24
ICER (£/QALY)	**Dominant**	**£5,350**	**Dominant**
Cost-effectiveness of screening programme			
Δ Cost (£)	6,149	30,546	10,639
Δ QALY	2.56	3.34	3.43
ICER (£/QALY)	**2,400**	**9,139**	**3,105**
Maximum cost of screening program to remain cost-effective at £20,000/QALY (£)			
Total	1,097,531	930,390	1,340,402
Per screening	31.04	26.32	37.91

DAA, direct acting antiviral, ICER, incremental cost-effectiveness ratio; IFN/RBV, pegylated interferon α and ribavirin; QALY, quality-adjusted life year; SOF, sofosbuvir.

Table 3

Lifetime cost-effectiveness	Base case (BC)	SA 1a: Age 28	SA 1b: Age 38	SA 2: Historical SVR %	SA 3: Treat all	SA 4a: 0.1% HCV		SA 4b: 0.6% HCV	
						Treat BC %	Treat all	Treat BC %	Treat all
No treatment									
Total cost (£)	20,749	21,440	19,840	21,749	20,837	20,749	20,837	20,749	20,837
Total QALYs	15.39	15.90	14.80	15.39	15.38	15.39	15.38	15.39	15.38
Total life years	22.13	22.89	21.25	22.13	22.13	22.13	22.13	22.13	22.13
Treatment									
Total cost (£)	14,233	14,417	13,993	16,604	14,152	14,233	14,152	14,233	14,152
Total QALYs	17.95	18.63	17.17	17.56	17.96	17.95	17.96	17.95	17.96
Total life years	23.07	23.95	22.06	22.92	23.08	23.07	23.08	23.07	23.08
Cost-effectiveness of treatment versus no treatment									
Δ Cost (£)	-6,516	-7,024	-5,847	-4,146	-6,685	-6,516	-6,685	-6,516	-6,685
Δ QALY	2.56	2.73	2.37	2.17	2.59	2.56	2.59	2.56	2.59
Δ Life years	0.94	1.05	0.81	0.79	0.95	0.94	0.95	0.94	0.95
ICER (£/QALY)	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant
Cost-effectiveness of screening programme									
Δ Cost (£)	6,149	5,642	6,818	8,520	-1,216	19,198	4,419	-124	-3,925
Δ QALY	2.56	2.73	2.37	2.17	2.59	2.56	2.59	2.56	2.59
ICER (£/QALY)	2,400	2,065	2,881	3,922	Dominant	7,492	1,707	Dominant	Dominant
Maximum cost of screening to remain cost-effective at £20,000/QALY (£)									
Total	1,097,531	1,171,480	1,010,514	904,304	2,572,019	497,477	1,165,817	2,984,863	6,994,903
Per patient	31.04	33.13	28.58	25.58	72.75	14.07	32.97	84.43	197.85

Figure 1

Figure 1

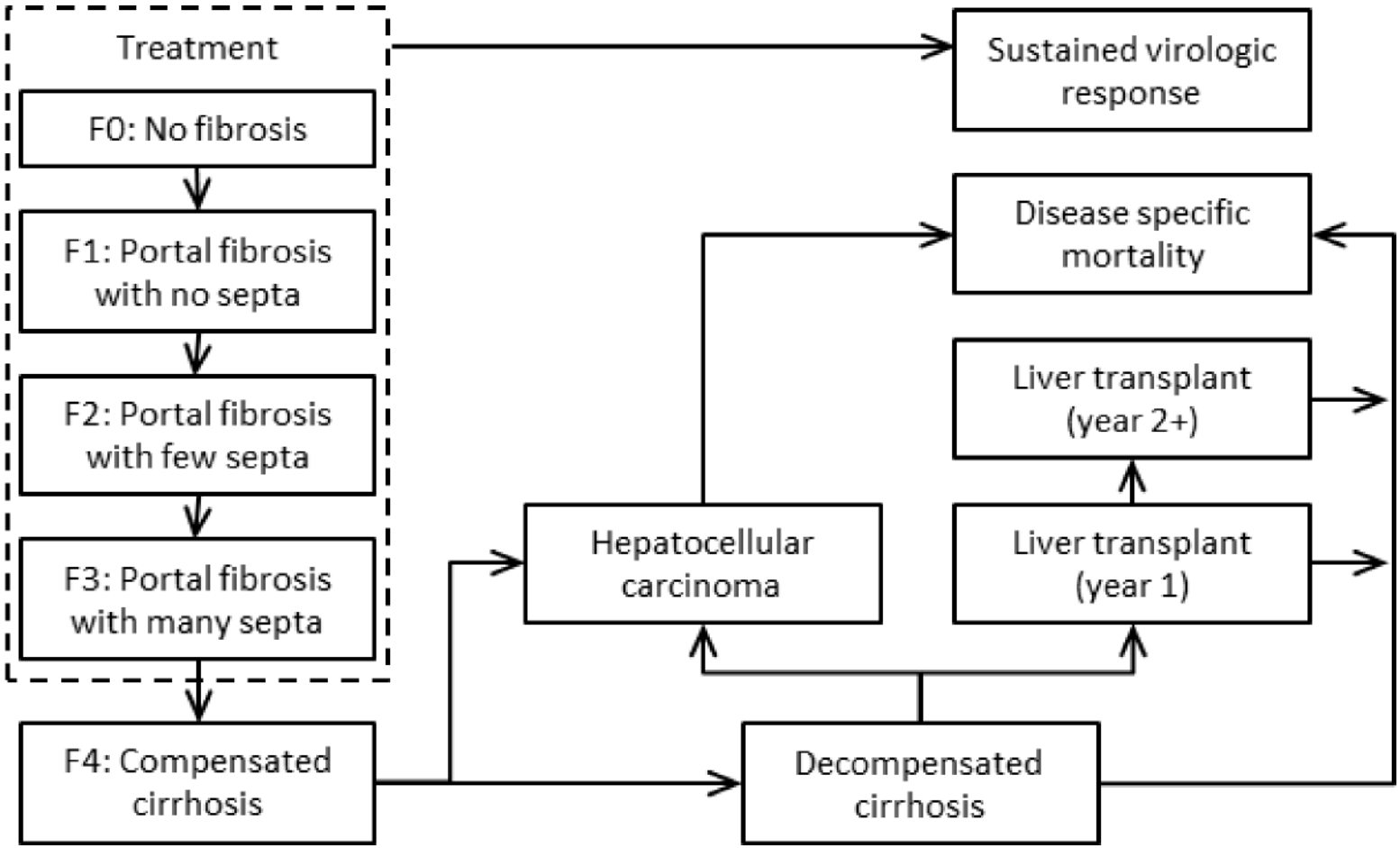
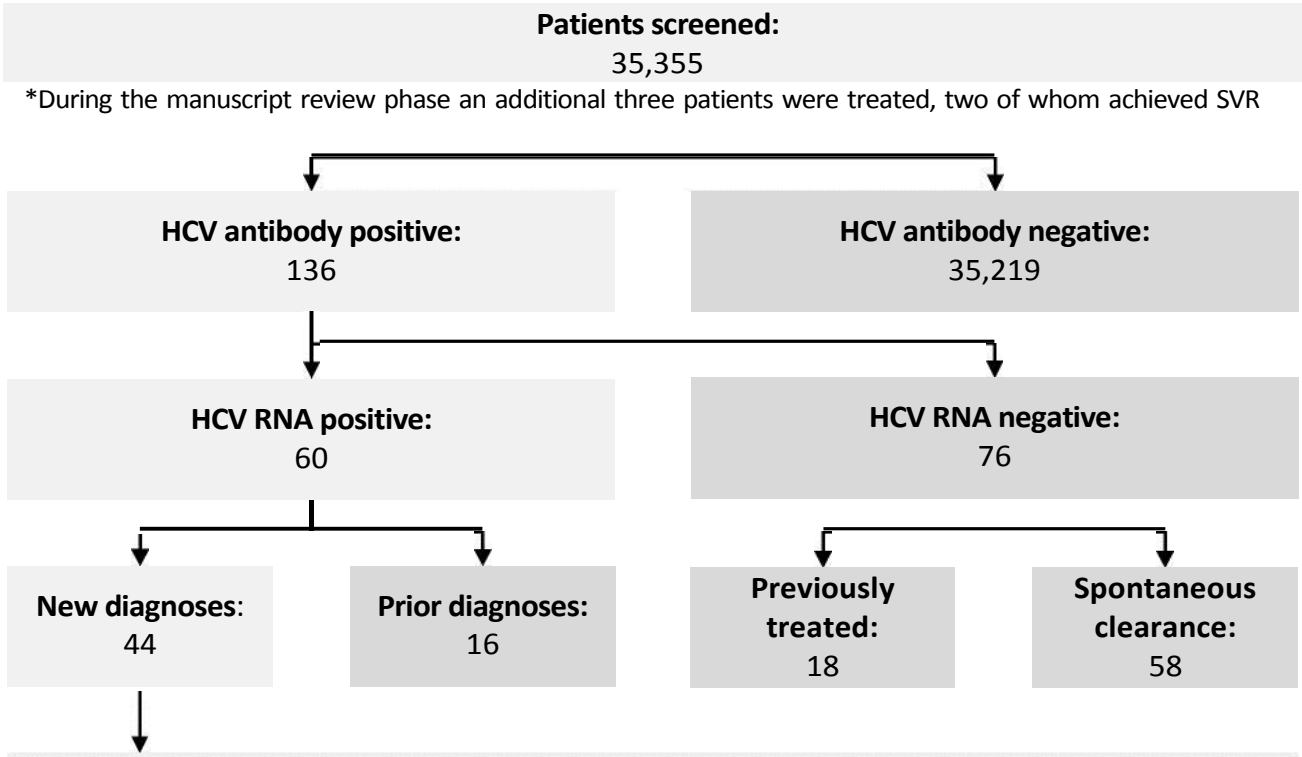


Figure 2



	Genotype 1	Genotype 2	Genotype 3	Genotype 4	Unknown
Total:	21	4	11	6	2
F0-F1	5	2	4	2	0
F2-F3	2	0		0	0
Unknown	14	2	1	4	2
Treated with IFN/RBV*	9	2	5	3	0
Achieved SVR:	7	2	4	1	0

through use of unlicensed therapies and one through the use of boceprevir combined with IFN/RBV. These patients have not been incorporated within the analysis.

Figure 3

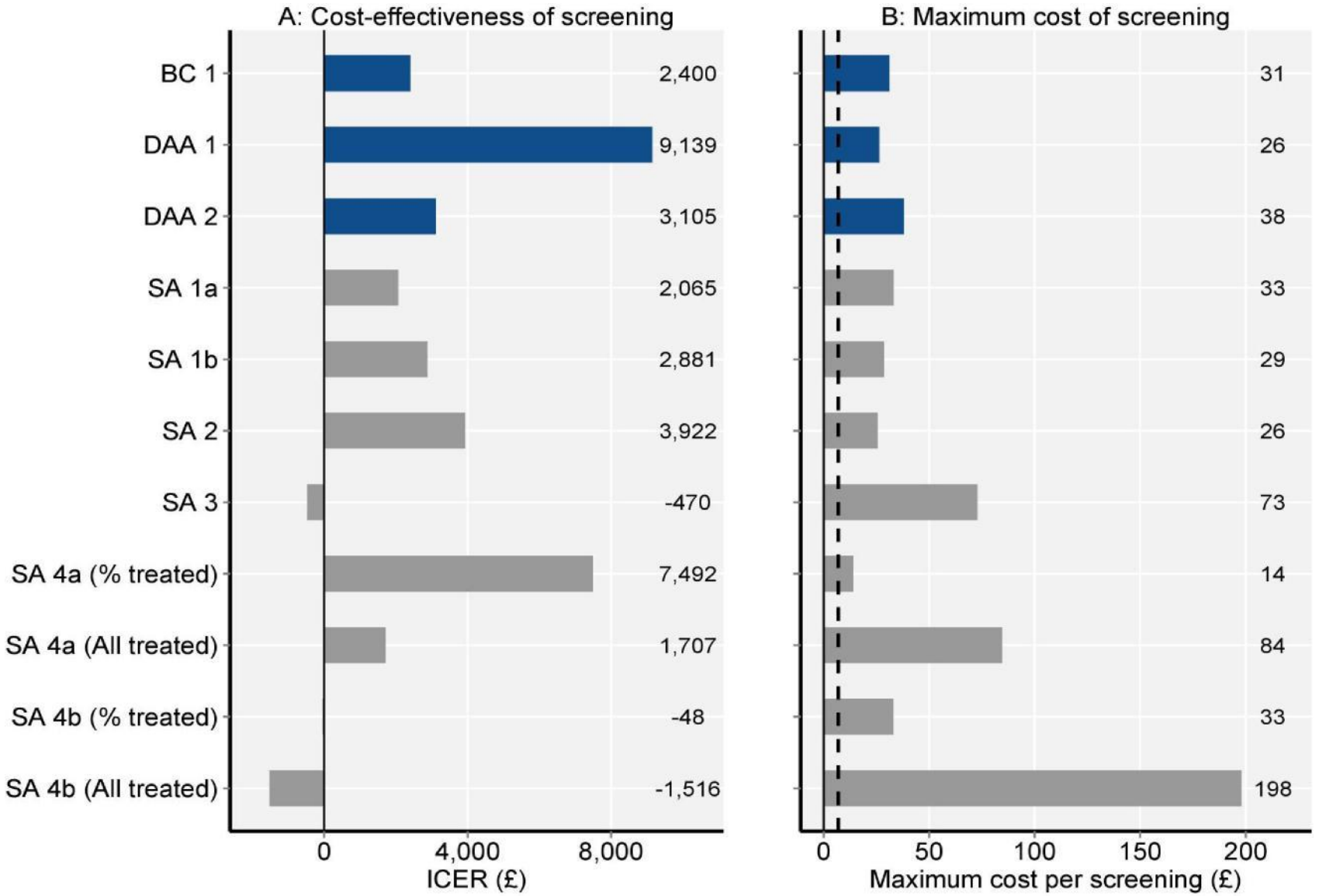
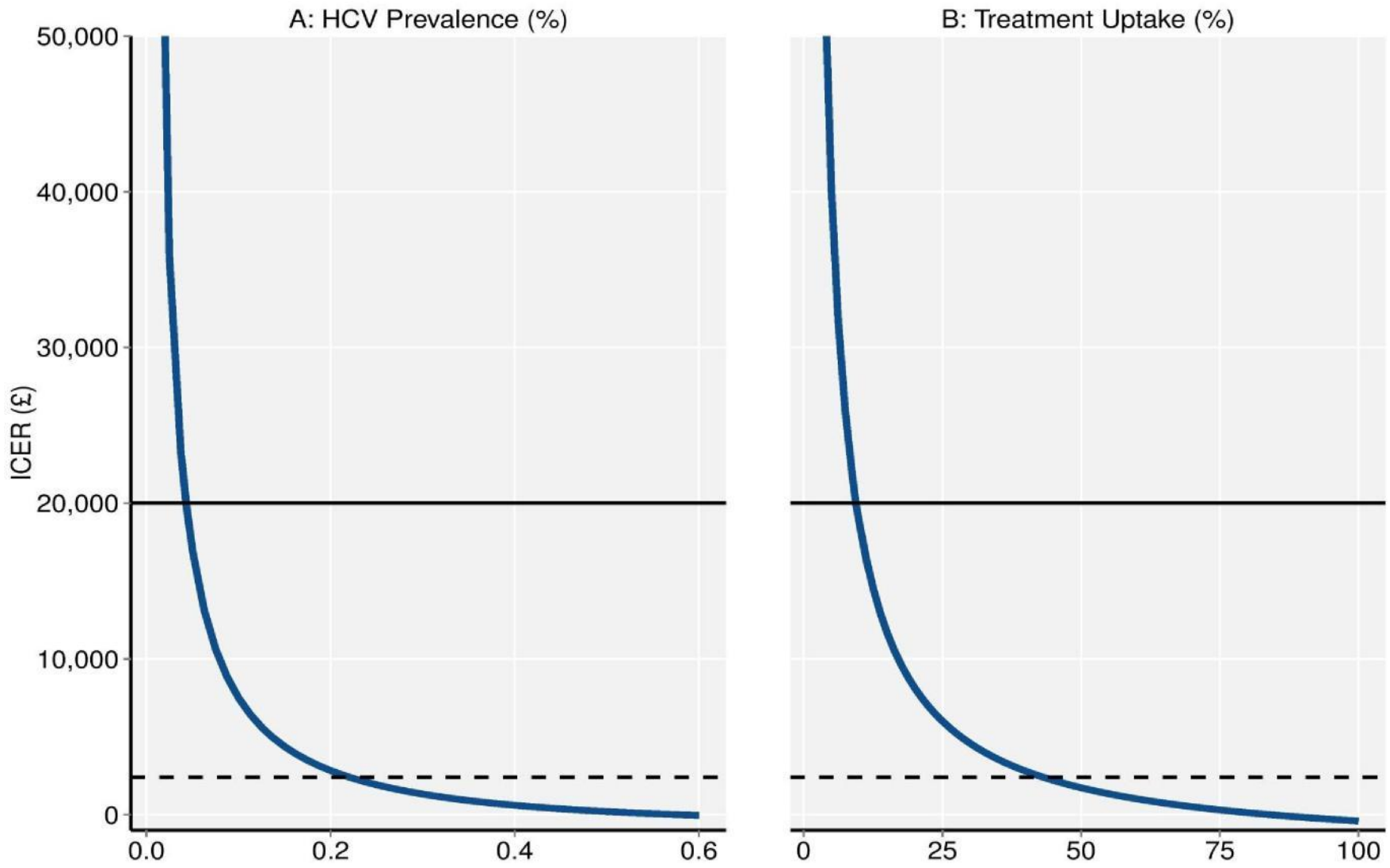

A: Cost-effectiveness of screening
BC 1
DAA 1
DAA 2
SA 1a
SA 1b
SA 2
SA 3
SA 4a (% treated)
SA 4a (All treated)
SA 4b (% treated)
SA 4b (All treated)
2,400
9,139
3,105
2,065
2,881
3,922
-470
7,492
1,707
-48
-1,516
0
4,000
8,000
ICER (£)
B: Maximum cost of screening
31
26
38
33
29
26
73
14
84
33
198
0
50
100
150
200
Maximum cost per screening (£)

Figure 4


A: HCV Prevalence (%)
B: Treatment Uptake (%)
ICER (£)
50,000
40,000
30,000
20,000
10,000
0
0.0
0.2
0.4
0.6
0
25
50
75
100