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Economic Evaluation

An Economic Evaluation of the Cost-Effectiveness of Opt-Out Hepatitis B and Hepatitis C Testing in an Emergency Department Setting in the United Kingdom

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ABSTRACT

Objectives: The prevalence of hepatitis is high in emergency department (ED) attendees in the United Kingdom, with a prevalence of up to 2% for hepatitis B (HBV) HBsAg, and 2.9% for hepatitis C (HCV) RNA. The aim of this paper is to perform an economic evaluation of opt-out ED-based HCV and HBV testing.

Methods: A Markov model was developed to analyze the cost-effectiveness of opt-out HCV and HBV testing in EDs in the UK. The model used data from UK studies of ED testing to parameterize the HCV and HBV prevalence (1.4% HCV RNA, 0.84% HBsAg), test costs, and intervention effects (contact rates and linkage to care). For HCV, we used an antibody test cost of £3.64 and RNA test cost of £68.38, and assumed direct-acting antiviral treatment costs of £10 000. For HBV, we used a combined HBsAg and confirmatory test cost of £5.79. We also modeled the minimum prevalence of HCV (RNA-positive) and HBV (HBsAg) required to make ED testing cost-effective at a £20 000 willingness to pay per quality-adjusted life-year threshold.

Results: In the base case, ED testing was highly cost-effective, with HCV and HBV testing costing £8019 and £9858 per quality-adjusted life-year gained, respectively. HCV and HBV ED testing remained cost-effective at 0.25% HCV RNA or HBsAg prevalence or higher.

Conclusions: Emergency department testing for HCV and HBV is highly likely to be cost-effective in many areas across the UK depending on their prevalence. Ongoing studies will help evaluate ED testing across different regions to inform testing guidelines.

Keywords: hepatitis B, hepatitis C, cost-benefit analysis, emergency service hospital, diagnostic tests, routine, mass screening.

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Introduction

Across Europe there are approximately 29 million people living with the hepatitis C virus (HCV) or hepatitis B virus (HBV).[1] These individuals are often asymptomatic in the early stages of infection, with disease progression leading to liver complications including cirrhosis, hepatocellular carcinoma, and liver failure, and eventually causing death.[2,3] Despite the United Kingdom having a lower estimated prevalence of HCV and HBV compared with the European average, there are approximately 210 000 individuals living with HCV (0.3% among the general population) despite curative direct-acting antiviral (DAA) treatments available, and an estimated 440 000 individuals living with HBV (0.7% among the general population), with only 19% diagnosed.[4–6]

The United Kingdom has adopted the World Health Organization targets to eliminate viral hepatitis as a major public health threat by 2030, which includes diagnosing 90% of cases and providing treatment to 80% of diagnosed individuals (where eligible).[7] Moreover, with DAA treatments for HCV achieving high cure rates (sustained virological response [SVR]) at decreasing prices, and generic HBV treatments now available, there is considerable scope for case-finding activities to be cost-effective.[7–9]

In Europe, current recommendations for HCV and HBV case-finding activities are largely risk-based, with routine testing limited to settings attended by high-risk populations, such as drug treatment services, prisons, and sexual health centres.[10,11] HBV testing is also routinely performed in antenatal services to prevent mother-to-child transmission.[11] Emerging UK evidence suggests an additional setting for HCV and HBV case-finding is emergency departments (EDs), as the prevalence of viral hepatitis tends to be higher among ED attendees (up to 2.9% HCV RNA, and 2% HBV HBsAg) compared with the general population, as a result of higher attendance rates among marginalized communities.[5,12–17] In 2019, 25.6 million people attended EDs in England, with

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approximately 40% receiving blood tests as part of their routine care, providing a valuable opportunity for bloodborne virus (BBV) testing.[14,15,18] The National Institute for Health and Care Excellence (NICE) currently recommends HIV testing in EDs for areas with prevalence of ≥0.2%.[19] Nevertheless, there is currently no equivalent UK guidance for HCV or HBV testing in EDs owing to a lack of cost-effectiveness evidence, although NICE did recently highlight ED testing as an area of interest for its next surveillance point.[20]

The aim of this article is to perform a cost-effectiveness analysis of opt-out ED-based HCV and HBV testing and linkage to care for all individuals over age 16, and to consider the prevalence thresholds above which this intervention may be cost-effective in the United Kingdom.

Methods

Model Analysis and Decision Problem

We developed a decision model to analyze opt-out HCV and HBV testing, performed for all individuals attending the ED and receiving a blood test (as part of routine care) who did not opt out of hepatitis testing. Emergency department testing for HCV and HBV was compared with no ED testing, which consisted of a background rate of hepatitis testing, occurring in other settings, only. Opting out of testing involved the patient declining testing when informed by the clinician that a viral hepatitis test would be performed. As there are no shared costs between the 2 tests, the model considered opt-out testing of HCV and HBV separately, both compared with no immediate testing. The decision model consists of a decision tree, with HBV and HCV testing options, which feed into 3 distinct state transition Markov models representing chronic HBV, chronic HCV, and no infection. We assumed all individuals started at an age of 45 years based on data of BBV testing in EDs from the UK.[14,15] For each Markov model, patients move between discrete health states using an annual cycle length. The analysis was performed from the perspective of the UK National Health Service (NHS), and all results are presented in pounds (£, GBP) for 2017. Outcomes were measured in quality-adjusted life-years (QALYs). A lifetime time horizon was used, and all costs and outcomes were discounted at 3.5%, as per NICE guidelines.[21] Results are presented as incremental cost effectiveness ratios (ICERs) per QALY gained.

Model Structure and Parameterization

To capture the impact of the intervention, we identified 3 UK studies of ED-based HCV and HBV testing and linkage to care. We included 2 studies that performed testing and reflex (ie, same sample) confirmatory testing, with ED-based linkage to care.[14,15] We did not include a study that performed ED testing without reflex confirmatory testing, because individuals from this study were required to return to a local sexual health service for confirmatory testing, before being linked to care.[22]

Model Structure

A decision tree was developed to determine the impact of the intervention on testing and subsequent linkage to care. It captured the following: outcome of test (HBsAg+, HCV RNA+, negative), diagnosis status (new diagnosis vs previously known diagnosis), proportion of patients contacted after a positive diagnosis, and the probability of attendance to referral. The proportion of patients receiving treatment was captured in the HCV model. For the HBV model, the model captures the proportion of individuals that engage in care, as not all individuals identified will require immediate treatment. The model structures are shown and described in Appendix Figures 1-4 in the Supplementary Materials found at https://doi.org/10.1016/j.jval.2020.03.014.

For individuals with HCV, an estimated 54.5% of new ED diagnoses that were successfully contacted were current- or ex-people who inject drugs (PWID).[14] Risk factor information was not available for patients who were not contacted. A lower proportion representing only current-PWIDs (27.3%) was also considered.[14] For HCV-infected PWIDs, the disease progression, reinfection rate, and background risk of mortality differed compared with non-PWIDs. We did not consider PWID status in the HBV model because this was not reported as a risk factor in the same ED study.[14] The model did not capture the benefit associated with reduced onward transmission after treatment. Nor did the model consider the potential for HCV/HBV coinfection to occur in patients, as this was rare across patients in both ED testing studies (<1% of those testing positive).[14,15]

Prevalence

The combined prevalence from the included studies was 1.4% HCV RNA prevalence (132/9423) and 0.84% HBsAg prevalence (80/9476).[14,15] One ED study reported HCV antigen prevalence; however, we assumed these would be RNA positive. These were varied in threshold sensitivity analyses to estimate the minimum prevalence thresholds at which the intervention remains cost-effective, since BBV prevalence varies geographically (ranging from 0.6%-2.9% for HCV and 0%-2% for HBV across UK studies).[14–17]

We also performed a sensitivity analysis of testing by age group (16-29, 30-49, 50-69, 70+) using stratified prevalence estimates.[14,15] Other model parameters were assumed to remain unchanged due to a lack of age-specific data (see Appendix Table 6 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.03.014).

Linkage to care

For individuals testing positive in the ED, from the 2 included studies we derived the proportion that were successfully contacted (*contact rate*), the proportion requiring linkage to care (defined as those not previously diagnosed, or those previously diagnosed but not currently linked to care), the proportion attending their referral after being contacted, and the proportion engaging in care.[14,15] Different linkage to care parameters were explored in sensitivity analyses.

For those testing HCV RNA positive, it was estimated that 49.5% would require linkage to care (new diagnoses, or known diagnoses disengaged with care), of which 64.7% would be successfully contacted. Of those contacted, 90.3% would attend at least 1 clinic appointment, of which 85.7% would engage in care. We assumed that all HCV patients engaged in care would receive DAA treatment.

Of those testing HBsAg positive, it was estimated that 52.4% would require linkage to care, of which 64.7% would be successfully contacted. Of those contacted, 90.3% would attend at least 1 clinic appointment, of which 85.7% would engage in care. Patients engaged in care were assumed to receive treatment if indicated, (ie, in active disease or cirrhotic health states).

Treatment and outcomes

For HCV, individuals received DAA treatment, with SVR rates (91%-93%) derived from a UK national cohort.[23] There were no treatment restrictions for PWID, as per current NHS policy. We assumed those not achieving SVR with their first treatment would be re-treated once.

For HBV, treatment was assumed to be provided to those presenting with active disease, and all patients with cirrhosis,

based on NICE guidelines.[24] Various clinical studies informed the treatment outcomes for HBV, and NICE guidelines informed treatment stopping rules (based on HBeAg status and cirrhosis), with full details provided in the Appendix in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.03.014.[24–29] In summary, individuals were assumed to be treated with peginterferon alfa-2a (PegIFNα) and tenofovir disoproxil fumarate (TDF), and 13% of HBeAg-positive and 1% of HBeAg-negative individuals received emtricitabine alongside TDF, based on 1 clinical study used in our analysis.[26] Treatment aims to achieve HBsAg seroconversion, or HBeAg seroconversion (for HBeAg-positive individuals) or inactive disease (for HBeAg-negative individuals). We also performed a sensitivity analysis in which TDF was the first and only treatment used, without PegIFNα. We modeled the likelihood that some HBV patients will disengage from treatment over time as has been observed in long-term studies of patients on HBV treatment (Table 1). This is to remain conservative regarding the benefit associated with identifying new HBV patients, as was assessed in a sensitivity analysis.

Transition probabilities

Transition probabilities capturing disease progression from early disease health states up to the compensated cirrhosis health state were derived from a meta-regression of HCV progression rates.[30] Equivalent transitions for those identified as PWIDs with HCV were derived from a study estimating PWID disease progression.[31] For compensated cirrhosis and more advanced states, a previous health technology assessment (HTA) was used for transitions between health states.[32]

For HBV, HBeAg status-specific transition probabilities were derived from a previous HTA performed in the United Kingdom, and have been used for previous economic models.[33,34] For all individuals in the model receiving treatment, there was no risk of HBV-related mortality (until they progressed beyond compensated cirrhosis), as mortality is comparable to the general population.[35] Details on HBV transition probabilities are available in the Appendix Tables 2 and 3 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.03.014.

For both models, a background rate of mortality derived from UK life tables was applied to all health states, in addition to mortality associated with disease progression.[36] For PWIDs, a standardized mortality ratio of 7.8 was applied to background mortality, with injecting drug use assumed to cease after 11 years (Table 1).[37,38]

Background rate of testing

The annual background probability of testing was derived from Public Health England sentinel surveillance of BBV laboratory diagnoses, with 40% estimated coverage in the population, estimated from UK national population data.[36,39] The annual HCV testing probability (considering testing from all settings) was calculated as 1.9%, whereas the annual HBV testing probability, derived from non-antenatal screening tests, was 2%.

The probability of testing is likely to be higher for those currently infected, since the yield of positive tests across the UK observed in national statistics (1.4% for HCV and 1% for HBV) differs from prevalence among testers in the ED setting.[39] We adjusted the prevalence yield among background testing to account for the higher likelihood of testing in infected versus uninfected individuals to match the prevalence observed in national statistics.

For patients receiving background testing, it was assumed that the probability of referral and engaging in care was the same as for those individuals successfully contacted as part of the intervention.

Utilities

For HCV, utility values for fibrosis and cirrhosis were derived from a UK RCT.[40] Pre-cirrhotic HBV utility values were derived from a previous economic evaluation, and subsequently used in a UK HTA.[34,41] Hepatitis B virus cirrhosis utility was assumed to be the same as HCV cirrhosis.[40] Utility values for advanced liver disease, for both HBV and HCV, were derived from a UK study of transplant patients.[42] A sensitivity analysis was performed considering a lower utility for PWIDs, using an alternative data source (maximum utility of 0.57, and therefore no utility benefit associated with achieving SVR).[43,44]

Costs

Hepatitis C virus test costs were derived from another ED testing study from London.[22] Both included studies performed an initial antibody test (£3.64), but confirmatory testing differed; one used a reflex RNA test[14], wheras the other performed a reflex HCV antigen test.[15] The model assumed confirmatory RNA testing (£68.38) was performed for those testing antibody positive.[22] For HBV, we assumed a HBsAg test was initially performed, followed by a confirmatory reflex HBsAg neutralization assay, with a combined cost of £5.79, derived from a London hospital (Guy's and St Thomas' NHS Trust, personal email communication, November 2017). We assumed the same test costs for individuals receiving background testing. Because tests were performed on routinely collected blood samples, costs for retrieving blood were not included. The model assumes all diagnostic and confirmatory tests were 100% accurate.

The time required to contact patients was reported by one ED study to be 15.7 minutes for HCV and 6.7 minutes for HBV, and we assumed an additional 10 minutes for administration activities.[14] We assumed this was performed by a hospital nurse.[45] The contact costs were applied to all individuals testing positive. Background testing could occur in various settings but was assumed to be the cost of a general practitioner appointment (£31).[45] A lower hypothetical cost (£10) was also considered, since testing could occur in other healthcare settings, with lower costs compared with a general practitioner appointment.

National Health Service DAA treatment costs are confidential, but may be as low as £5000 per course of treatment.[8] Due to uncertainty, we assumed costs of £10 ,000 for DAA treatment, and £15 000 for re-treatment, incurred only upon SVR, as per NHS policy.[46] Hospital outpatient visits prior to treatment and outpatient treatment monitoring costs were applied (Table 2).[47] We show results across DAA costs of £0 to £35,000 in a sensitivity analysis (see Appendix Figure 7 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.03.014).

Hepatitis B virus treatment costs were derived from the British National Formulary. The cost of 48 weeks of PegIFNα was £3672, assumed for 1 annual cycle.[48] The NHS is using generic TDF, with an estimated annual cost of £578.[9,48,49] For those receiving TDF with emtricitabine, the annual cost was £1299.[26,48] Treatment monitoring costs for HBV were assumed to be captured in health state costs.

Health state costs were derived from previous HTAs for HBV and HCV.[32,33,45] Individuals who were undiagnosed or diagnosed but not engaged in care were assumed to not accrue health state costs until they are diagnosed or reach decompensated cirrhosis or hepatocellular carcinoma health states.

Table 1. Base case decision parameters for intervention effects.

Base case probabilities	Mean value	Distribution	Source
HCV parameters			
Prevalence (RNA+)	1.4%	Beta (α = 132, β = 9291)	14,15
Proportion of Ab+ testing RNA+ on reflex test	62.9%	Beta (α = 132, β = 78)	14,15
Proportion of diagnoses requiring linkage to care*	49.5%	Beta (α = 55, β = 56)	14,15
Proportion contacted	61.8%	Beta (α = 47, β = 29)	14,15
Proportion attending referral	85.1%	Beta (α = 40, β = 7)	14,15
Proportion receiving treatment, post-referral	62.5%	Beta (α = 25, β = 15)	14,15
Background testing probability (annual)	1.9%	Beta (α = 347 440, β = 17 645 144)	36,39
Background testing yield (RNA+ prevalence among testers)	1.4%	Beta (α = 4982, β = 342 458)	39
Proportion F0	22.7%	Dirichlet (F0,F1,F2,F3,cirrhotic)‡	14
Proportion F1	22.7%	Dirichlet (F0,F1,F2,F3,cirrhotic)‡	14
Proportion F2	22.7%	Dirichlet (F0,F1,F2,F3,cirrhotic)‡	14
Proportion F3	15.9%	Dirichlet (F0,F1,F2,F3,cirrhotic)†	14
Proportion cirrhotic (F4)	15.9%	Dirichlet (F0,F1,F2,F3,cirrhotic)†	14
Proportion current PWID	54.5%	Beta (α = 6, β = 11)	14
Standard mortality ratio for IDU (while currently injecting)	7.8	Normal (95% CI = 5.4-10.8)	37
Duration of injecting (years)	11	Uniform (6, 16)	38
Annual probability of reinfection among PWIDs	19.3%	Beta (α = 15, β = 62)‡	51
HBV parameters			
Prevalence (HBsAg)	0.84%	Beta (α = 80, β = 9396)	14,15
Proportion of diagnoses requiring linkage to care†	52.4%	Beta (α = 33, β = 30)	14,15
Proportion contacted	64.7%	Beta (α = 33, β = 18)	14,15
Proportion attending referral	90.3%	Beta (α = 28, β = 3)	14,15
Proportion accepting treatment, post-referral (if indicated)	85.7%	Beta (α = 24, β = 4)	14,15
Background testing probability (annual)	2%	Beta (α = 355 585, β = 17 636 999)	36,39
Background testing yield (HBsAg prevalence among testers)	1%	Beta (α = 3543, β = 352 042)	39
Proportion with inactive disease (HBeAg+ seroconverted or HBeAg- inactive disease)	80%	Beta (α = 80, β = 20)	52
Proportion HBeAg+	14.5%	Beta (α = 71, β = 419)	52
Proportion cirrhotic (of those with active disease)	12%	Beta (α = 3, β = 22)	14
Annual loss to follow-up from treatment	3.3%	Uniform (1.7%, 5.0%)	28

CI indicates confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; IDU, injecting drug user; PWID, people who inject drugs.
*New diagnosis or known diagnosis not currently engaged in care.
†Sample size of 44, Dirichlet(10,10,10,7,7).
‡Annual probability calculated from 0.906 years mean follow-up (per person).

Sensitivity Analyses

We performed probabilistic sensitivity analysis with values for each parameter sampled simultaneously from their distributions, and 10 000 individual simulations being performed (distributions available in Tables 1-2, and Appendix Tables 1-5 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.03.014). Lastly, threshold analyses were undertaken to determine the minimum prevalence at which the intervention is cost-effective at a willingness-to-pay (WTP) threshold of £20 000 per QALY. We also performed threshold analyses for the prevalence required for cost-effectiveness across a range of patient contact rates and test costs (see Appendix Figure 8 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.03.014).

Results

Base-Case Analysis

Under the base-case settings, testing for HCV and HBV were both highly cost-effective. The ICER for HCV testing was £8019 per QALY, and for HBV testing was £9858 per QALY (Table 3). At a WTP of £20 000 per QALY, the threshold analysis suggested testing for both HCV and HBV would be cost-effective at 0.25% or higher (Fig. 1). For both HCV and HBV, the ICER reduced and then plateaued at higher prevalence estimates, although was never cost saving.

Deterministic Sensitivity Analyses

Hepatitis C virus and HBV testing remained cost-effective under all deterministic analyses, with the maximum ICER less than £12 000 per QALY (Fig. 2). For HCV, the ICER was sensitive to the cost of DAA treatment, the proportion of individuals tested that are current PWIDs, and the utility values for PWIDs. For both HCV and HBV testing, the results were also sensitive to the cost of the diagnostic test used, and the proportion of individuals requiring linkage to care. The results were somewhat sensitive to the proportion accepting treatment once referred and the proportion of diagnosed patients successfully contacted. The cost of contacting patients and the cost of background appointments had very little impact on the ICER for either HCV or HBV.

When considering ED testing by age, testing was highly cost-effective for those aged 16 to 69, but most cost-effective in those aged 30 to 69, with ICERs below £10 000 for both testing strategies. For those aged over 70 years (assuming a mean age of 80), the ICERs increased to £21 569 per QALY for HCV testing and £18 766 per QALY for HBV testing.

Table 2. Intervention and linkage to care costs.

Costs	Mean cost	Distribution	Reference
HCV			
HCV antibody test	£3.64	Uniform (£2.91, £4.37)	22
HCV RNA test	£68.38	Uniform (£54.70, £82.06)	22
DAA treatment	£10 000	N/A	8
DAA retreatment	£15 000	N/A	8/assumption
Outpatient evaluation	£238	Uniform (£190.40, £285.60)	47
Further outpatient evaluation	£262	Uniform (£209.60, £314.40)	47
DAA treatment monitoring	£1310	Uniform (£1048, £1572)	47
HBV			
HBsAg test (and confirmatory neutralization assay for HBsAg+)	£5.79	Varied by test cost multiplier	Guy's and St Thomas' NHS Trust, personal email communication, November 2017.
PegIFNα (annual)	£3672	N/A	48
TDF (annual)	£578	N/A	48
TDF + emtricitabine (annual)	£1299	N/A	48
Outpatient evaluation	£238	Uniform (£190.40, £285.60)	47
Further outpatient evaluation	£262	Uniform (£209.60, £314.40)	47
Contact costs (HBV and HCV)			
Cost per HCV contact*	£15.85	Uniform (£7.92, £23.77)	14,45
Cost per HBV contact*	£10.30	Uniform (£5.15, £15.45)	14,45
Cost of appointment (background testing)	£31.30	Uniform (£15.65, £46.95)	45

DAA indicates direct-acting antiviral; HBV, hepatitis B virus; HCV, hepatitis C virus; N/A, not applicable; PegIFNα, peginterferon alfa-2a; TDF, tenofovir disoproxil fumarate.
*Cost of both successful and unsuccessful contacts.

Probabilistic Sensitivity Analyses

In the base-case analysis, HCV testing was 99.1% likely to be cost-effective, and HBV testing 98.4% likely to be cost-effective, at a WTP of £20 000 per QALY.

We also evaluated the probability that the intervention is cost-effective at different HCV and HBV prevalence. At HCV RNA and HBsAg prevalence of 0.5%, testing remained highly likely to be cost-effective for both, with HCV testing 94% likely, and HBV testing 95% likely to be cost-effective. At a prevalence of 0.3%, testing remained likely to be cost-effective for both strategies, but with less certainty (70% and 71% likely cost-effective for HCV and HBV testing, respectively). At a lower 0.2% prevalence, testing was unlikely to be cost-effective for either strategy, with a HCV testing 23% likely to be cost-effective, and HCV testing 24% likely to be cost-effective. Cost-effectiveness acceptability curves showing the probability of cost-effectiveness across a range of WTP thresholds, with base case and lower prevalence scenarios for HCV and HBV available in Appendix Figure 5 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.03.014.

Discussion

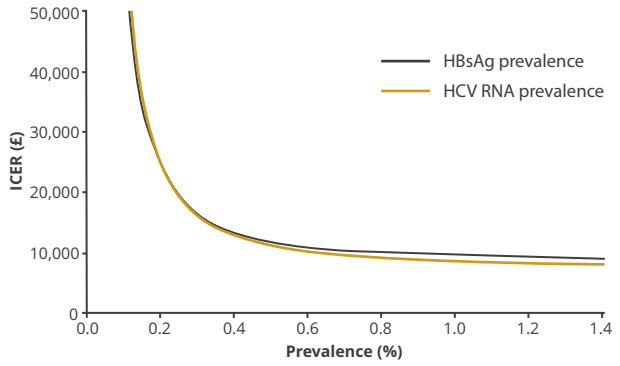
To our knowledge, this is the first economic evaluation of ED testing for HCV and HBV in the United Kingdom and adds to previous work demonstrating EDs are a viable setting for HCV and HBV testing in many areas of the United Kingdom.[14,15,22] At our base-case prevalence of 1.4% and 0.8% for HCV (RNA) and HBV (HBsAg), both testing strategies were highly cost-effective with ICERs below £10 000 per QALY, and the ICER did not increase above £12 000 for either testing strategy in any of the deterministic sensitivity analyses examined. While our analysis is an early economic evaluation in the absence of long-term testing data, the results of our probabilistic analysis suggest that testing remains highly likely to be cost-effective at 0.5% prevalence for both HCV and HBV. This compares favorably to the prevalence observed in recent ED testing studies across the United Kingdom. A recent study across 4 UK sites reported a pooled prevalence of 1.69% HCV RNA (range: 0.6%-2.9%), and 0.95% HBsAg (range: 0%-2%),[16] whereas other studies in London EDs have reported HCV RNA or antigen prevalence of 0.9% to 1.6% and HBsAg prevalence of 0.8% to

Table 3. Cost-effectiveness results for HCV and HBV screening per individual tested.

Testing	Testing option	Total costs	Total QALYs	Incr. costs	Incr. QALYs	ICER
HCV	No screening	£160.68	16.4879			
	ED screening	£184.47	16.4908	£23.79	0.0030	£8019
HBV	No screening	£90.66	16.5497			
	ED screening	£114.66	16.5522	£24.00	0.0024	£9858

ED indicates emergency department; HBV, hepatitis B virus; HCV, hepatitis C virus; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

Figure 1. Incremental cost-effectiveness ratio (ICER) by HCV RNA and HBsAg prevalence achieved during testing in an ED setting.

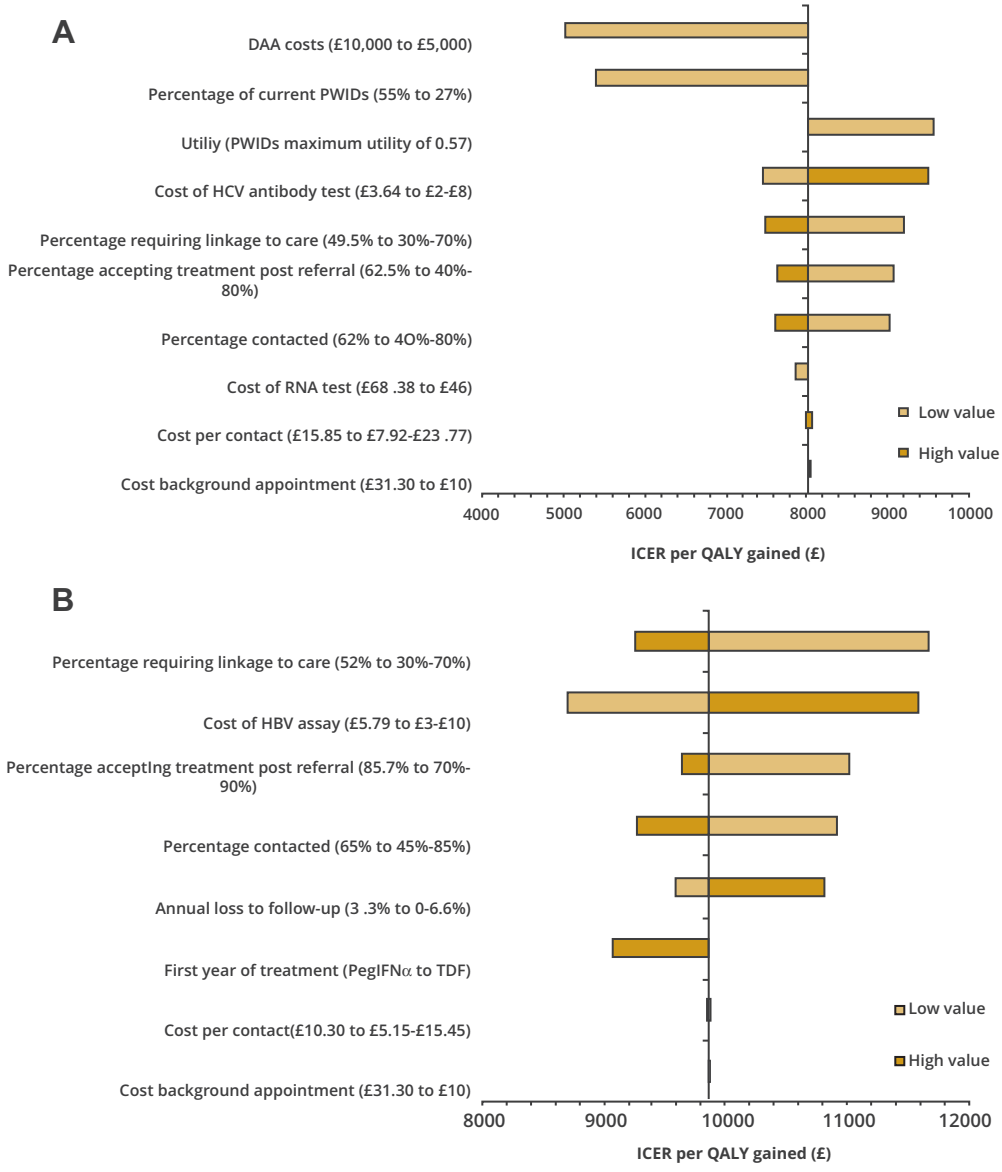


HCV indicates hepatitis C virus.

1.1%.[14,15,17] Thus, our study suggests ED testing is likely to be cost-effective in most UK settings. Furthermore, since the general population prevalence of HCV and HBV across Europe (1.1% and 0.9%, respectively) is similar to the base-case ED prevalence used in our analysis, ED testing could be cost-effective in other European settings, and also in other high-income countries with a HCV and HBV prevalence similar to or higher than the United Kingdom.[6]

Our prevalence threshold analysis suggests that ED testing would remain cost-effective even at low HCV RNA and HBsAg prevalence among ED attendees (0.25% or higher for both). These thresholds are similar to NICE recommendations for HIV testing in EDs in the United Kingdom (≥0.2%).[19] Nevertheless, there is no current NICE recommendation for ED testing for HCV and HBV, citing the absence of effectiveness or cost-effectiveness evidence for hepatitis testing in this setting in their 2017 review.[11] While the European Centre for Disease Prevention and Control

Figure 2. One-way deterministic sensitivity analysis (DSA) for A) HCV and B) HBV testing.



HBV indicates hepatitis B virus; HCV, hepatitis C virus.

guidelines recommend HCV and HBV testing in EDs with intermediate or high prevalence (≥2%), they do not cite any evidence for these much higher prevalence thresholds compared to our estimates.[10] While our prevalence threshold estimates provide guidance for the cost-effectiveness of ED-based HBV and HCV testing and linkage to care, further studies of ED testing would be of value to reduce the uncertainty at these thresholds, particularly as they will be sensitive to other model parameters that may differ from those used in our base-case analysis.

Our results also suggested that the cost-effectiveness of testing those aged 70 and above is uncertain, due to lower prevalence and lower life expectancy from the point of treatment. Nevertheless, further analyses are required to assess this in more detail owing to the limitations of the data available for this analysis.

Limitations

Our analysis is based on 2 non-controlled, observational studies from the United Kingdom, which have considerable limitations. The studies were either short in duration, or with a low uptake of hepatitis testing among eligible blood samples. Evans et al undertook 6 weeks of testing, with 56% testing uptake, whereas Parry et al undertook 9 months of testing, but with only 25% testing uptake. For this reason, our analysis does not evaluate how long testing should be implemented. The prevalence threshold results estimate the minimum prevalence required for the intervention to remain cost-effective, although this assumes that other parameters remain constant.

In addition to prevalence, early evidence suggests other parameters included in our model differ across ED departments, such as the type and sequence of tests performed and their costs, the proportion of individuals in the population that require linkage to care, and the effectiveness of contacting those testing positive.[50] These parameters influenced the estimated ICERs, and while they did not change the base case cost-effectiveness, they are likely to influence the prevalence thresholds for cost-effectiveness. Another limitation was the lack of detailed cost data relating to the intervention. Although the results of the sensitivity analyses showed this had little impact upon our results, we did not include staff training costs or incentives to increase testing rates that have been previously reported.[22] The intervention consists of a number of individual parts, including the initial test, informing the patient of the result, and linking individuals to care following a positive diagnosis. Although the model incorporates all of these components, we acknowledge that they are separate factors and that there are many ways in which they could be individually optimized.

Lastly, our model did not capture the potential prevention benefit associated with a reduction in onward transmission among PWIDs with HCV who achieve SVR, and thus likely underestimates the impact of HCV testing.

Conclusion

Although there is uncertainty regarding many of the parameters, our results suggest that ED-based HCV and HBV testing and linkage to care is highly cost-effective at our base-case prevalence. Moreover, the sensitivity analyses strongly suggest that this conclusion is robust. At a lower 0.5% prevalence, HCV and HBV testing remained highly likely to be cost-effective. This suggests the introduction of ED testing is likely to be cost-effective for many areas of the United Kingdom, since most ED-based HCV and HBV prevalence estimates from the United Kingdom exceed this.[14–16] Nevertheless, there is uncertainty around the prevalence thresholds at which HCV and HBV testing becomes cost-effective, although our analysis shows it is likely to be low.

Although our results suggest implementation of ED testing should be performed even in areas with a relatively low prevalence, interventions should be evaluated at a local level, using local data to inform key parameters and identify which of these context-specific parameters influence cost-effectiveness. Lastly, budget impact analyses using local data will be helpful for planning in areas introducing ED testing. These analyses will help reduce the uncertainty in our results and provide data to inform local healthcare decision-making bodies.

Supplemental Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2020.03.014.

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