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Cost-effectiveness of HCV case-finding for people who inject drugs via dried blood spot testing in specialist addiction services and prisons

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ABSTRACT

Objectives: People who inject drugs (PWID) are at high risk for acquiring hepatitis C virus (HCV), but many are unaware of their infection. HCV dried blood spot (DBS) testing increases case-finding in addiction services and prisons. We determine the cost-effectiveness of increasing HCV case-finding among PWID by offering DBS testing in specialist addiction services or prisons as compared to using venepuncture.

Design: Cost-utility analysis using a dynamic HCV transmission model among PWID, including: disease progression, diagnosis, treatment, injecting status, incarceration and addition services contact.

Setting: UK.

Intervention: DBS testing in specialist addiction services or prisons. Intervention impact was determined by a meta-analysis of primary data.

Primary and secondary outcome measures: Costs (in UK £, £1=US$1.60) and utilities (quality-adjusted life years, QALYs) were attached to each state and the incremental cost effectiveness ratio (ICER) determined. Multivariate uncertainty and one-way sensitivity analyses were performed.

Results: For a £20 000 per QALY gained willingness-to-pay threshold, DBS testing in addiction services is cost-effective (ICER of £14 600 per QALY gained). Under the base-case assumption of no continuity of treatment/care when exiting/entering prison, DBS testing in prisons is not cost-effective (ICER of £59 400 per QALY gained). Results are robust to changes in HCV prevalence; increasing PWID treatment rates to those for ex-PWID considerably reduces ICER (£4500 and £30 000 per QALY gained for addiction services and prison, respectively). If continuity of care is >40%, the prison DBS ICER falls below £20 000 per QALY gained.

Conclusions: Despite low PWID treatment rates, increasing case-finding can be cost-effective in specialist addiction services, and in prisons if continuity of treatment/care is ensured.

ARTICLE SUMMARY

Article focus
- We performed a cost-utility analysis of increasing hepatitis C virus (HCV) case-finding among people who inject drugs (PWID) by offering dried blood spot testing in specialist addiction services or prisons.

Key messages
- Despite low PWID treatment rates, increasing case-finding for PWID can be cost-effective in specialist addiction services.
- In prisons, the cost-effectiveness of HCV case-finding depends on adequate continuity of treatment/care between prison and the community, as many treatments are discontinued due to the short incarceration times.

Strengths and limitations of this study
- We used a dynamic mathematical model of HCV transmission to capture the potential prevention benefits of treatment, which has been shown to increase the cost-effectiveness of HCV treatment for PWID.
- Key limitations are the limited empirical data on PWID health utilities, treatment rates and intervention impact.

drug use, with over 90% of new infections among people who inject drugs (PWID).[1] However, diagnosis rates are low, with only half of the infected PWID in the USA and the UK diagnosed.[2]

The majority of HCV testing performed in the USA and the UK is through venepuncture, which is available in virtually all prisons,[3] and addiction services (structured programmes providing pharmacological or non-pharmacological drug treatment in the community) either on site or by referral. However, testing opportunities among PWID may still be limited. This is because venous access can be poor and specialist staff (who

INTRODUCTION

In developed countries, the hepatitis C virus (HCV) is spread primarily through injecting

may not be available at all potential testing sites) are required to take blood, which if only available in hospital phlebotomy services can increase stigma.[4]

Dried blood spot (DBS) testing is non-invasive and can be performed by clinical and non-clinical staff. Two UK studies[5][6] showed that offering DBS testing within specialist addiction services and prisons led to a threefold to sixfold increase in HCV testing, and a recent systematic review identified DBS as the best available targeted intervention for increasing HCV case-finding among PWID.[7] Hence, DBS testing could be an important component of any strategy attempting to scale up treatment provision for PWID, for both care and prevention.[8]

We perform a cost-utility analysis of introducing DBS testing among current and former PWID in specialist addiction services and prisons in the UK.[5] Unlike previous economic evaluations of HCV testing in these settings,[9][10] we incorporate a dynamic mathematical model to capture the potential prevention benefits of treatment, which can substantially increase the cost-effectiveness of HCV treatment for PWID.[11] A dynamic model accounts for the individual and population benefits of treatment, as well as the dynamic nature of incarceration, especially among PWID. Our model is the first to explore the importance of continuity of care between prison and the community.

METHODS

Mathematical model

An existing dynamic, deterministic model of HCV transmission, progression and HCV treatment was adapted to project the impact of introducing DBS testing in prisons and addiction services.[11] See online supplementary appendix for details and model schematics. Briefly, the model stratifies by: injecting state (never PWID/PWID/ex-PWID); incarceration status (never/currently/formerly); contact with addiction services (in contact/not in contact); age ((15–19), (20–24), (25–29), (30–54), (55–64), (65–74), (75+)); HCV infection and disease progression (never infected, spontaneously cleared, mild HCV, moderate HCV, compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, liver transplant, post-transplant). HCV disease stages are further subdivided into undiagnosed or diagnosed, where those who are diagnosed can either be lost to follow-up, in referral (early/late), on antiviral treatment, sustained viral response (SVR) or non-SVR.

All PWID can acquire and transmit HCV, but imprisoned PWID only transmit HCV to other prisoners. We define ex-PWID as those who have permanently ceased injecting, and assume no ongoing transmission from non/ex-PWID. An individual's risk of acquiring HCV is proportional to the setting-specific HCV prevalence (prison/community). The model assumes a background rate of HCV testing for all PWID and ex-PWID in the community/prison, and in addiction services for PWID.

No UK data exist regarding continuity of care (treatment or referral) on prison entry/exit, but experts described difficulty in ensuring continuity on release (Eamonn O'Moore(Offender Health, UK Department of Health), Iain Brew(HMP Leeds) *personal communication*). Therefore, in our base case, we assume that those in treatment or referral become lost to follow-up upon entering/exiting prison, but can be retested/retreated.

Model fitting and base-case projections

For the probabilistic uncertainty analysis, 1000 parameter sets were sampled from each parameter uncertainty distribution in table 1 and online supplementary appendix tables 1 and 2. For the parameter set, the model was calibrated to UK epidemiological data on incarceration, injecting drug use, HCV prevalence and diagnosis. This was achieved through a multistep parameter sampling and model calibration process, utilising simplified models where possible to reduce computational time and to verify the full model predictions against simplified models. For details on the model calibration (including schematics and equations) and initialisation (see online supplementary appendix).

After calibration, for each of the 1000 parameter sets, the model was run with and without the intervention ('intervention' and 'baseline', respectively). We model an intervention of offering DBS testing in prison, compared to a baseline of current testing with venepuncture only. Additionally, we evaluate an intervention of offering DBS in specialist addiction services, compared to a baseline of current testing with venepuncture. The economic analysis was performed from a UK National Health Service perspective. Costs (in 2011 GBP, £1=US $1.55) and health utilities (in QALYs) were attached to each model compartment. Costs and QALYs were discounted at 3.5% per annum as per the National Institute for Health and Clinical Excellence guidelines, with a 100-year time horizon (to accrue individual and population benefits). The mean incremental cost-effectiveness ratio (ICER) was calculated and cost-effectiveness determined using the UK willingness-to-pay (WTP) threshold, estimated between £20 000 and £30 000 per QALY gained.[12] The cost-effectiveness acceptability curves were constructed and univariate sensitivity analyses undertaken. Analysis of covariance (ANCOVA) methods were used to summarise the proportion of the variability in the incremental costs and QALYs explained by the uncertainty in input parameters.[13]

Parameters

All parameters can be found in table 1 and the online supplementary appendix tables 1–4.

Health state utilities

Uninfected utility values were taken from the UK population norms for non-PWID, and a large cross-sectional study of injectors in Scotland[14] for current PWID. We

Table 1 Intervention parameters

	Mean value	Distribution	Units	References
Intervention effect (proportional change in testing rate)				
Addiction services	3.6 (2.3–5.8)	Lognormal (μ=1.285, σ=0.239)	–	5
Prison	2.6 (0.2–34.9)	Lognormal (μ=0.968, σ=1.317)	–	5
Intervention costs (addiction services)				
Organisation/coordination of training*	2005.71		Per health board	†
Training session‡	135		Per training session	†
Attendees time§	1620		Per training session	†
Travel reimbursement for training leader¶	90.86		Per training session	†
Total cost per addiction services training	3851.57		Per training session	†
Mean number tested	40.3		Per addiction service**	5
Total intervention cost per test	95.57	Uniform±50%	Per test	
Intervention costs (prison)				
Organisation/coordination of training††	7020		Per prison	†
Training session‡	135		Per prison	†
Attendees time‡‡	405		Per prison	†
Travel reimbursement for training leader§§	127.20		Per prison	†
Total cost per prison training	7687.20		Per prison	†
Mean number tested per prison	116		Per prison	5
Total intervention cost per test	66.27	Uniform±50%	Per test	

All cost estimates assume a staff-nurse cost per hour of £36 (median estimate for band 5 general practice nurse[21]).
*1 Nurse 2 days/week for 6 months for seven health boards. One training session per health board.
†Noel Craine, personal communication.
‡1 Nurse, half day.
§12 Nurses, half day.
¶1200 miles (£0.53 per mile) for travel to seven health boards.
**Assumed 1 addiction service per health board.
††1 Nurse full time for five prisons (1 training session per prison).
‡‡3 Nurses per prison, half day.
§§1200 miles (£0.53 per mile) for five prisons.

assumed equal utilities for ex-PWID and non-PWID.[10] Utilities for the HCV disease and treatment stages came from the UK HCV trials and economic evaluations[15–17] and were used for ex-PWID. To derive PWID HCV utilities, non-PWID HCV utilities were rescaled by multiplying by the ratio of the uninfected PWID utility to the uninfected ex-PWID utility for the youngest age group. All states included disutilities with age.

No disutility was associated with testing in the base case. However, some evidence suggests that PWID may experience a disutility after positive HCV diagnosis.[14 18] We explored the impact of a disutility (0.09,[14] see online supplementary appendix) on diagnosis, which was fully regained with treatment SVR.

Health state and testing costs
Healthcare costs for HCV disease stages, antiviral treatment (pegylated interferon-α and ribavirin, pegIFN+RBV) and testing were taken from the UK economic analyses.[15 16 19 20] Data on the yield (proportion tests Ab+) and prevalence in each setting were used to calculate the number of non-PWID tested for each PWID/ex-PWID (see online supplementary appendix). Costs were inflated to 2011 GBP using the Health and Community Hospital Service pay and prices index.[21]

Additional PWID treatment delivery costs were applied.[11] We assumed that undiagnosed individuals would not incur HCV-related healthcare costs unless progressing to decompensated disease.[9]

HCV disease progression parameters
Transition rates between disease stages were taken from the UK economic evaluations.[15–17] Although estimates were not PWID-specific, a recent meta-analysis suggests little evidence for differences in progression between PWID and non-PWID.[22]

HCV prevalence
PWID HCV chronic prevalence was estimated from the HCV antibody prevalence among PWID in England (45% (41% to 49%, 95%CI)[23]). As one-quarter of acute infections spontaneously clear,[24] we assume three-quarters of those who are ever exposed (antibody positive) are chronically infected, resulting in 35% chronic infection among PWID.

Incarceration duration
Incarceration duration for non-PWID and ex-PWID was age-stratified, with a mean of 8 months.[25] However, PWID have shorter durations in custody than

non-PWID.[25–27] We used a 4-month PWID incarceration duration, based on an estimate for England and Wales.[25] A recent study in Scotland reported a median sentence of 7.1 months in PWID,[27] which, given that most prisoners serve approximately half their sentence,[28] would also equate to a duration of 4 months.

Testing rates

The overall baseline PWID testing rate (mean 12% undiagnosed PWID per year) was estimated through fitting the model to the current proportion of diagnosed PWID (approximately 50%[2]). Data on the proportion of tests from each setting (29% and 12% of tests originated from addiction services and prisons, respectively) were used in combination with the model projected annual numbers of PWID in contact with each setting to calculate setting-specific testing rates (0.5% and 2% per month of undiagnosed PWID in contact with addiction services and prisons, respectively, see online supplementary appendix). We assume that ex-PWID are tested at equal rates to PWID in prison and in general community settings. We assumed all diagnostic tests to be 100% accurate due to the high sensitivity and specificity of DBS (99.6% sensitivity, 100% specificity in a setting with 50% prevalence[29]) and venepuncture assays,[30] and because those who receive an initial positive test will receive additional tests before treatment.

Referral and treatment transition rates

The referral rate from testing services to secondary care (35%) was estimated from a UK study.[31] Those not referred or not attending referral were considered to be 'lost to follow-up'.

Approximately 50% of diagnosed ex-PWID in referral are treated within 2 years.[31–33] Since many delay treatment, we assume that after 2 years, 10% of those in referral initiate treatment annually. Within prison, treatment rates are lower than in the community,[31 34] although a recent UK prison audit found that 24% of those diagnosed were treated (Iain Brew(HMP Leeds), unpublished data). We therefore estimated halved treatment initiation rates in prison as compared to the community.

PWID treatment rates are unknown, but thought to be similarly low to other countries,[35 36] with an estimated <1% of PWID treated annually (Graham Foster (Consultant Hepatologist), personal communication). Hence, if we assume that 1% of infected PWID are treated within 2 years, this equates to treating approximately 5.5% of those who attend referral (35% of the 50% diagnosed) within 2 years. After 2 years, 1% of those in referral are treated annually thereafter.

Intervention

The effect of introducing DBS was modelled by assuming a 3.6-fold increase in testing (2.2 to 5.8 CI) in addiction services, and a 2.6-fold increase in testing (0.1 to 34.9 CI) in prison, based on two multicentre studies (table 1 and online supplementary appendix).

Intervention costs were determined from the study methods[5] and in consultation with the authors (table 1).

Sensitivity analyses

We performed one-way sensitivity analyses on: time horizon (50/200 years), discount rates (3.5% costs/1.5% QALYs), PWID treatment rates (increased in each setting), PWID SVR rates (reduced by 20%), PWID HCV chronic prevalence (20%/50%), antiviral treatment (telaprevir/boceprevir for genotype 1 patients, see online supplementary appendix) and continuity of care for treatment/referral on entry/exit from prison (varied from 0% to 100%). We also explored the effect of assuming no prevention benefit (but allowing for reinfection) by permanently fixing the force of infection.

RESULTS
Case finding in addiction services

The incremental cost effectiveness ratio (ICER) of increasing case-finding in addiction services, by introducing DBS testing, was an estimated £14 600 (US$22 630) per QALY gained in the base case (table 2). At a £20 000 or £30 000 WTP threshold, the intervention is likely to be cost-effective in 69% or 93%, respectively, of the simulations (figure 1A). Uncertainty in the intervention effect contributed to 86% and 58%, respectively, of the variation in incremental costs and QALYs. The remaining variation in incremental QALYs was mainly due to uncertainty in the treatment rates (22%) and health utilities (17%).

For most sensitivity analyses, the ICER remained below a £30 000 WTP threshold (figure 2A). Reducing the time horizon to 50 years increased the estimated ICER to £22 900 per QALY gained because fewer prevention benefits were accrued, whereas lengthening to 200 years increased the cost-effectiveness. Changing the discount rates to 3.5% costs/1.5% QALYs or no discounting decreased the estimated ICER to £5100 or £6700 per QALY gained, respectively. Variations in baseline HCV chronic prevalence had little effect (<10%). At lower prevalence (20%), identifying cases was more expensive but the prevention impact was greater due to the reduced reinfection risk, whereas the opposite occurred at higher prevalence (50%).

Increasing treatment rates increased the intervention's cost-effectiveness. If 50% (compared to 5.5% for base case) of PWID in referral initiated treatment within 2 years (a treatment rate achieved by one UK service,[37]) the ICER fell to £4500 per QALY gained. If SVR rates among PWID were 20% lower than in ex-PWID, the ICER increased by 14% (£16 700per QALY gained). Using telaprevir/boceprevir for genotype 1 patients minimally altered the ICER. Ignoring any prevention benefit doubled the ICER to £29 900 per QALY gained.

Only one sensitivity analysis substantially altered the cost-effectiveness conclusion. If a disutility was attached to diagnosis, the intervention resulted in negative

Table 2 Cost-effectiveness results from the base-case intervention analyses

Intervention location	Discounted costs (2011 £) (95% interval)	Discounted QALYs (95% interval)	Incremental costs (95% interval)	Incremental QALYs (95% interval)	ICER (£ per QALY gained)
Addiction services					
Baseline	37 181 582 (19 384 816 to 67 271 249)	5 354 331 (4 867 168 to 5 960 766)	–	–	–
Intervention	38 099 060 (20 140 578 to 68 378 488)	5 354 393 (4 867 206 to 5 960 853)	917 478 (481 174 to 1 664 430)	63 (19 to 153)	14 632
Prison					
Baseline	37 181 582 (19 384 816 to 67 271 249)	5 354 331 (4 867 168 to 5 960 766)	–	–	–
Intervention	38 245 293 (19 852 634 to 68 601 970)	5 354 349 (4 867 184 to 5 960 823)	1 063 710 (–225 101 to 6 060 267)	18 (–12 to 75)	59 418

incremental QALYs (due to low treatment rates) and was dominated (more expensive with fewer health benefits). However, even with this disutility, if treatment rates were increased to 50% of PWID in referral initiating treatment within 2 years, then the estimated ICER was £20 100 per QALY gained.

Case finding in prison

The ICER of increasing case-finding in prison, by introducing DBS testing, was estimated at £59 400 (US $92 070) per QALY gained (21% likely to be cost-effective at a £30 000 WTP threshold) in the base case (table 2 and figure 1B). Uncertainty in the intervention effect contributed to most (>85%) of the variation in incremental costs and QALYs.

The base-case conclusion was robust to most one-way sensitivity analyses (figure 2B)—including time horizon, discount rates, HCV prevalence and use of new treatments. If 50% of PWID in referral initiated treatment within 2 years, the ICER would be halved to just below £30 000 per QALY gained.

Introducing continuity of care (which measures the proportion of initiated treatments/referrals that are continued when entering/exiting prison) led to an increase in cost-effectiveness: from an ICER of £59 400 per QALY gained with 0% continuity to £10 400 per QALY gained with 100% continuity (figure 3). The ICER fell below £20 000 when >40% continuity of care was ensured; at 40% continuity, the intervention was 57% and 83% likely to be cost-effective at the £20 000 and £30 000 WTP thresholds, respectively. The level of continuity required for prison case-finding to be cost-effective also depended on the treatment rates. If the prison treatment rates were increased to equal those in the community (50%/5.5% of ex-PWID/PWID treated within 2 years of referral), then 35% of the continuity results in an ICER would be just below £20 000 per QALY gained. Increasing treatment rates further so that 50% of all referred prisoners initiate treatment within 2 years lowers the required continuity to 20% for an ICER below £20 000.

DISCUSSION
Main findings

Our results indicate that the introduction of dried blood spot testing for HCV case-finding is likely to be cost-effective under commonly used willingness-to-pay thresholds in the UK (£20 000–£30 000/QALY gained[12]) and the USA ($50 000/QALY gained[38]) in addiction services, but not in prison, unless a minimum level of continuity of care in treatment or referral between prison and the community can be ensured. Ignoring the prevention benefit doubles the ICER of the intervention in addiction services. In the base case, most PWID treatments initiated in prison were interrupted due to the lack of continuity of care and short PWID incarceration times (~4 months) in the UK.[25][27] Consequently, little

Figure 1 Base-case cost-effectiveness acceptability curves for the dried blood spot intervention. Results shown for the (A) addiction services and (B) prison interventions for various willingness-to-pay thresholds.
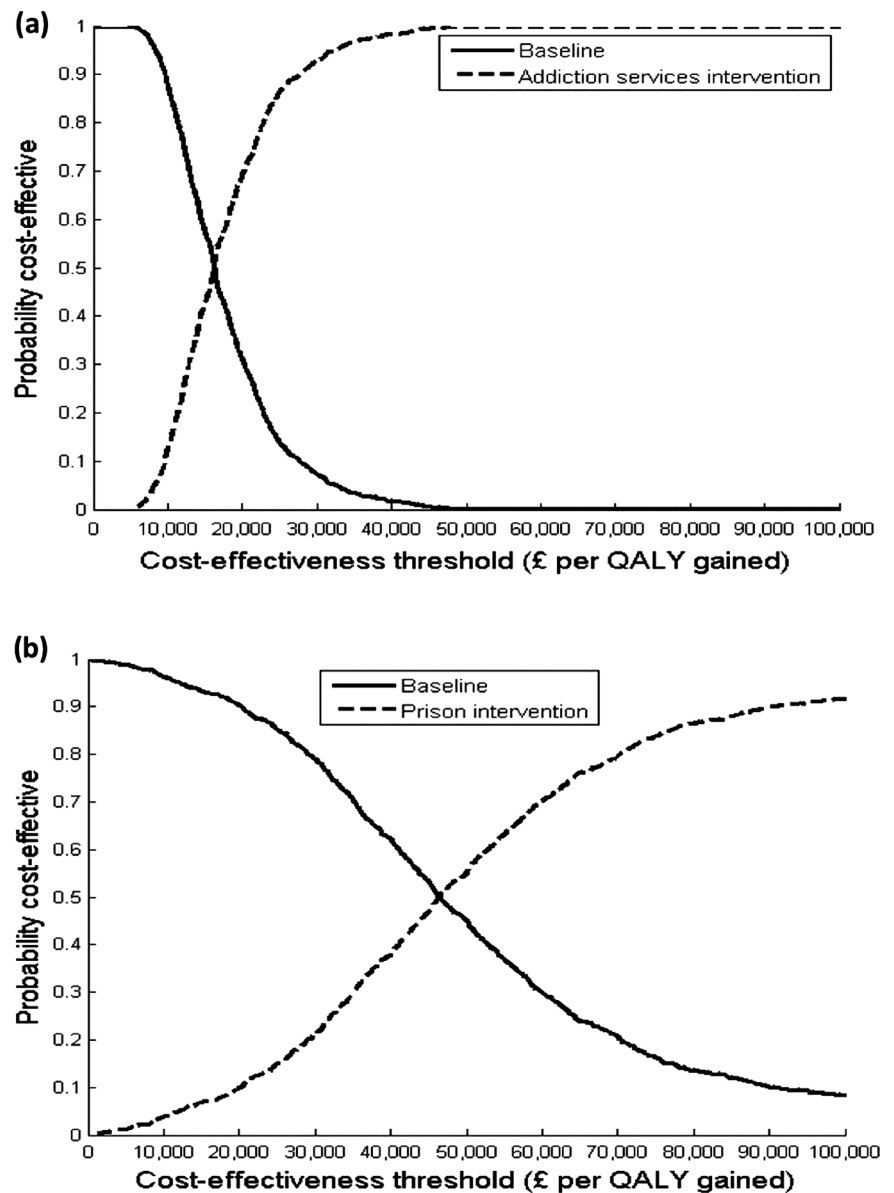
prevention benefit was achieved from the prison intervention, with the results approaching the 'static' model. With the low base-case PWID treatment rates, the continuity required for DBS to be cost-effective was approximately 35–40% of the estimated treatment/referral rates, but if the treatment/referral rates increased, then lower levels of continuity would be cost-effective. Crucially, not all treatments need to be initiated or completed in prison, as only maintaining treatment or referral contact is necessary. Finally, both interventions are most cost-effective at higher treatment rates.

Strengths and limitations
The key strength of this analysis is that the model is dynamic, therefore capturing the prevention impact of case-finding and treatment. The main limitations are concerned with parameter uncertainty and lack of model heterogeneity. First, we based our increase in case-finding on the DBS intervention which, though empirically

founded, was informed by relatively small UK studies, resulting in wide uncertainty around the effect estimates.

Second, the base case assumed comparatively low treatment rates for PWID, partly because the UK data on PWID treatment numbers are not available. This information is critical, as higher treatment rates increase the cost-effectiveness. This is especially important for prisons where treatment completion information was unavailable, yet strongly influenced cost-effectiveness. Additionally, even if treatment is interrupted, some may benefit from shortened treatment, which we did not incorporate.

Third, more data are needed to quantify PWID health utilities, which can be below the general population.[39] Especially important is whether any transient or permanent disutility on HCV diagnosis occurs, as current data are weak and not based on prospective studies. Our projections indicate that if a disutility occurs, then higher treatment rates are required for case-finding to be cost-effective.

Figure 2 Univariate sensitivity analyses on the mean incremental cost-effectiveness ratio (ICER). Results shown for the dried blood spot intervention in (A) addiction services and (B) prison. Vertical line represents the base-case ICER, estimated at (A) £14 600 per QALY gained and (B) £59 400 per QALY gained.
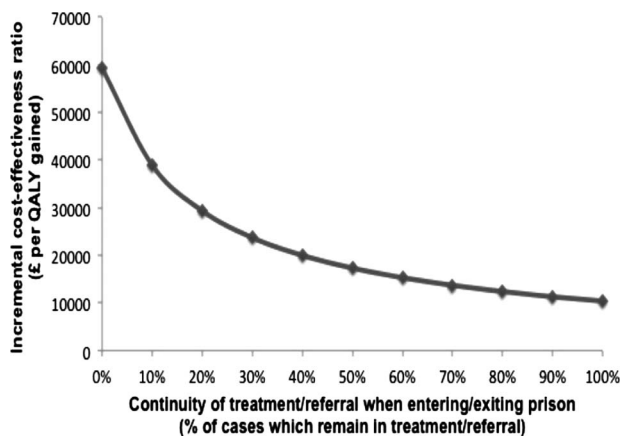

Figure 3 Incremental cost-effectiveness ratios for the prison intervention with varying continuity of care assumptions. Base-case scenario assumed 0% continuity.

Fourth, the model did not incorporate other interventions or behaviours that may influence HCV risk or treatment uptake. However, modelling work has shown introducing risk heterogeneity does not substantially reduce intervention impact if PWID circulate between risk states,[40] which is likely to occur as individuals move in/out of drug treatment and prison.

Fifth, the model was parameterised to the UK data, so our results are not necessarily applicable to other settings. However, our conclusions are robust to changes in HCV prevalence. Continuity of care could also be an issue in Australia, where PWID incarceration duration is similar to the UK.[41] However, sentences are longer in the USA,[42] so fewer treatments may be interrupted, and therefore case-finding in US prisons could be more cost-effective than our results indicate.

Our modelled UK treatment and HCV healthcare costs are within the range of those presented by recent US studies,[43 44] with the exception of approximately threefold higher liver transplantation costs, which would increase the cost-effectiveness of case-finding in the USA. Testing costs were taken from UK economic evaluations; however, it is possible that a streamlined and experienced testing service could lower costs associated with staff time, thus increasing cost-effectiveness.

Sixth, we were unable to evaluate future interferon-free direct-acting antiviral therapies as information on treatment costs and health utilities is unavailable. These treatments will most likely have increased SVR (90% for all genotypes), shorter treatment durations (12–24 weeks), lower toxicity and simpler dosing regimes.[45] Therapies with a shorter duration could not only increase the impact of testing and treatment in prison as more patients will be able to complete therapy prior to release, but also could potentially be more cost-effective depending on the ratio of additional costs to incremental impact.

Comparison with other studies

Two publications evaluated the cost-effectiveness of testing ex-PWID in prison, with ICERs varying from about £20 000[10] to £55 000[9] per QALY gained. Our results are consistent with Sutton *et al*,[9] who used the same discount rates as our study did. However, we included the possible prevention impact of treating PWID, and unlike the previous studies, show how continuity of care between prison and the community can make case-finding cost-effective.

Three papers evaluated testing PWID in drug services.[10 20 46] Differences in baseline assumptions led to varying ICERs from £28 100[20] to £17 500[10 46] per QALY gained. Our results for addiction services support those found in the latter studies.[10 46] However, the intervention examined in these studies[10 20 46] was one-off testing using a cohort model (with no evidence-based intervention effect) and neglected any prevention benefit.

Several US studies examined birth cohort screening for all people born in 1945–1965[44 47] or in 1946–1970[43] as compared to risk-based screening, reporting ICERs of $38 000 per QALY gained with direct-acting antivirals[43 44] and $5 400–16 000 per QALY gained with pegIFN +RBV.[44 47] Critically, the cost-effectiveness varies substantially by HCV prevalence,[47] and the estimated US prevalence is higher than that of many other developed countries. Additionally, ICERs were generated given assumptions of higher treatment rates, as well as greater utility gains with SVR than we had considered. Importantly, our intervention targets PWID with a risk of transmitting infection to others, whereas birth cohort screening is likely to identify infections among ex-injectors and non-injecting populations, which will have little primary prevention impact.

Implications

Our cost-effectiveness work indicates that increasing HCV case-finding in addiction services can be cost-effective. However, the cost-effectiveness of prison case-finding interventions depends on adequate continuity of care with the community. Few settings have developed comprehensive strategies to address this issue, though New York recently initiated the Hepatitis C Continuity Program.[48] In all settings, treatment uptake is critical: higher treatment rates prevent more disease transmission and increase the cost-effectiveness of case-finding interventions. If a disutility on

diagnosis occurs, higher treatment rates would be necessary to ensure cost-effectiveness. Further empirical data are required on treatment uptake and changes in utilities following diagnosis and treatment in order to compare targeted case-finding with cohort models.

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