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Hepatitis C disease transmission and treatment uptake: impact on the cost-effectiveness of new direct-acting antiviral therapies

Hayley Bennett[1] · Jason Gordon[1,2] · Beverley Jones[1] · Thomas Ward[1] ·
Samantha Webster[1] · Anupama Kalsekar[3] · Yong Yuan[3] · Michael Brenner[4] ·
Phil McEwan[1,5]

Abstract

Background Hepatitis C virus (HCV) treatment can reduce the incidence of future infections through removing opportunities for onward transmission. This benefit is not captured in conventional cost-effectiveness evaluations of treatment and is particularly relevant in patient groups with a high risk of transmission, such as those people who inject drugs (PWID), where the treatment rates have been historically low. This study aimed to quantify how reduced HCV transmission changes the cost-effectiveness of new direct-acting antiviral (DAA) regimens as a function of treatment uptake rates.

Methods An established model of HCV disease transmission and progression was used to quantify the impact of treatment uptake (10–100%), within the PWID population, on the cost-effectiveness of a DAA regimen versus pre-DAA standard of care, conducted using daclatasvir plus sofosbuvir in the UK setting as an illustrative example.

Results The consequences of reduced disease transmission due to treatment were associated with additional net monetary benefit of £24,304–£90,559 per patient treated at £20,000/QALY, when 10–100% of eligible patients receive treatment with 100% efficacy. Dependent on patient genotype, the cost-effectiveness of HCV treatment using daclatasvir plus sofosbuvir improved by 36–79% versus conventional analysis, at 10–100% treatment uptake in the PWID population.

Conclusions The estimated cost-effectiveness of HCV treatment was shown to improve as more patients are treated, suggesting that the value of DAA regimens to the NHS could be enhanced by improved treatment uptake rates among PWID. However, the challenge for the future will lie in achieving increased rates of treatment uptake, particularly in the PWID population.

Keywords Hepatitis C virus · Disease transmission · Cost-effectiveness · PWID

JEL Classification I1

✉ Hayley Bennett
hayley.bennettwilton@heor.co.uk

1 HEOR, Health Economics and Outcomes Research Ltd, 9 Oak Tree Court, Mulberry Drive, Cardiff Gate Business Park, Cardiff CF23 8RS, UK

2 Department of Public Health, University of Adelaide, Adelaide, Australia

3 World Wide Health Economics and Outcomes Research, Bristol-Myers Squibb Pharmaceuticals Ltd, Princeton, USA

4 UK HEOR, Bristol-Myers Squibb Pharmaceuticals Ltd, Uxbridge, UK

5 School of Human and Health Sciences, Swansea University, Swansea, UK

Introduction

Chronic hepatitis C virus (HCV) infection is a major cause of liver disease globally [1], and the associated mortality and morbidity is predicted to increase in many countries [2]. In the UK, the reported rate of deaths and hospital admissions associated with HCV-related end-stage liver disease (ESLD) and hepatocellular carcinoma (HCC) continues to rise, while it is acknowledged that national data underestimate the true scope of the problem [3].

An estimated 214,000 people in the UK are chronically infected with HCV, predominantly HCV genotypes 1 and 3. Injecting drug use continues to be the principal risk factor for HCV infection [3]; 90% of the 13,758 diagnosed cases of HCV infection in 2013 were estimated to be from injecting

drug use [4]. More generally, survey data suggest that approximately two in five people who inject drugs (PWID) are currently living with HCV infection in the UK [3, 4].

The established standard of care for HCV uses a pegylated interferon-alfa and ribavirin (PR) backbone, which is associated with efficacy and tolerability concerns, particularly in those with advanced disease [5, 6]. By contrast, newly available direct-acting antiviral (DAA) agents can be used as part of an oral-only, interferon-free regimen and are associated with improved tolerability and efficacy, shorter treatment durations and rates of sustained virologic response (SVR, an objective measure of cure [7]) approaching 100% [8–11]. However, these new therapies are also associated with considerable acquisition costs.

Economic evaluations of newly available DAA regimens have demonstrated that their use is largely cost-effective [12–14], due in part to the severe consequences of progression to ESLD [15, 16]. Within a UK context, the National Institute for Health and Care Excellence (NICE) has recommended for use several of the newly available DAA agents, including sofosbuvir, simeprevir, ledipasvir, and daclatasvir [17–21].

During the more recent of these appraisals, NICE recognized the importance of capturing the potential downstream benefits of cure for future disease transmission [22, 23]. By removing the opportunity of onward transmission, treatment has the potential to reduce the incidence of future infections [24]. Through modeling exercises, even modest increases in treatment uptake have been estimated to reduce disease transmission amongst high-risk populations, and in this way reduce the overall prevalence of HCV [25–31]. In line with this evidence, the European Association of the Study of the Liver (EASL) 2015 guidelines recommend prioritization of treatment for individuals at risk of transmitting HCV, including active injection drug users [7].

One recent economic evaluation assessed the cost-effectiveness of treating PWID in the UK when incorporating the downstream consequences of cure on future disease transmission, and demonstrated that this improved cost-effectiveness versus treatment in the non-PWID population [32]. The study also assessed competing treatment prioritization strategies and found that immediate treatment of PWID with chronic HCV in the UK would be prioritized ahead of patients with moderate HCV, after treating people with severe disease, due to the additional benefit of averting secondary infections. However, in order to avoid overt bias in the evaluation towards PWID treatment, the authors conservatively examined a very low treatment rate among PWID because HCV treatment rates among PWID are low in the UK and most other global settings [32]. Previous research has demonstrated that while improved SVR profiles led to reductions in modeled HCV

prevalence, increased treatment uptake was the key driver of future infections avoided, which results in fewer complications, significant cost savings, and QALY gains [33].

Given the proven clinical benefits of new DAA regimens, including improved tolerability and efficacy [8–11], an increase in treatment uptake is plausible, particularly in the context of low historical treatment rates. However, an assessment of the impact of increasing treatment uptake on the cost-effectiveness of DAAs in PWID has not been undertaken.

The aim of this study was to build on existing research, using an established model of HCV disease transmission and disease progression [33] to demonstrate how the cost-effectiveness of DAAs differs based on treatment uptake as a result of reduced disease transmission. As an example, treatment of the PWID population in the UK setting is presented, using daclatasvir plus sofosbuvir versus pre-DAA standard of care.

Methods

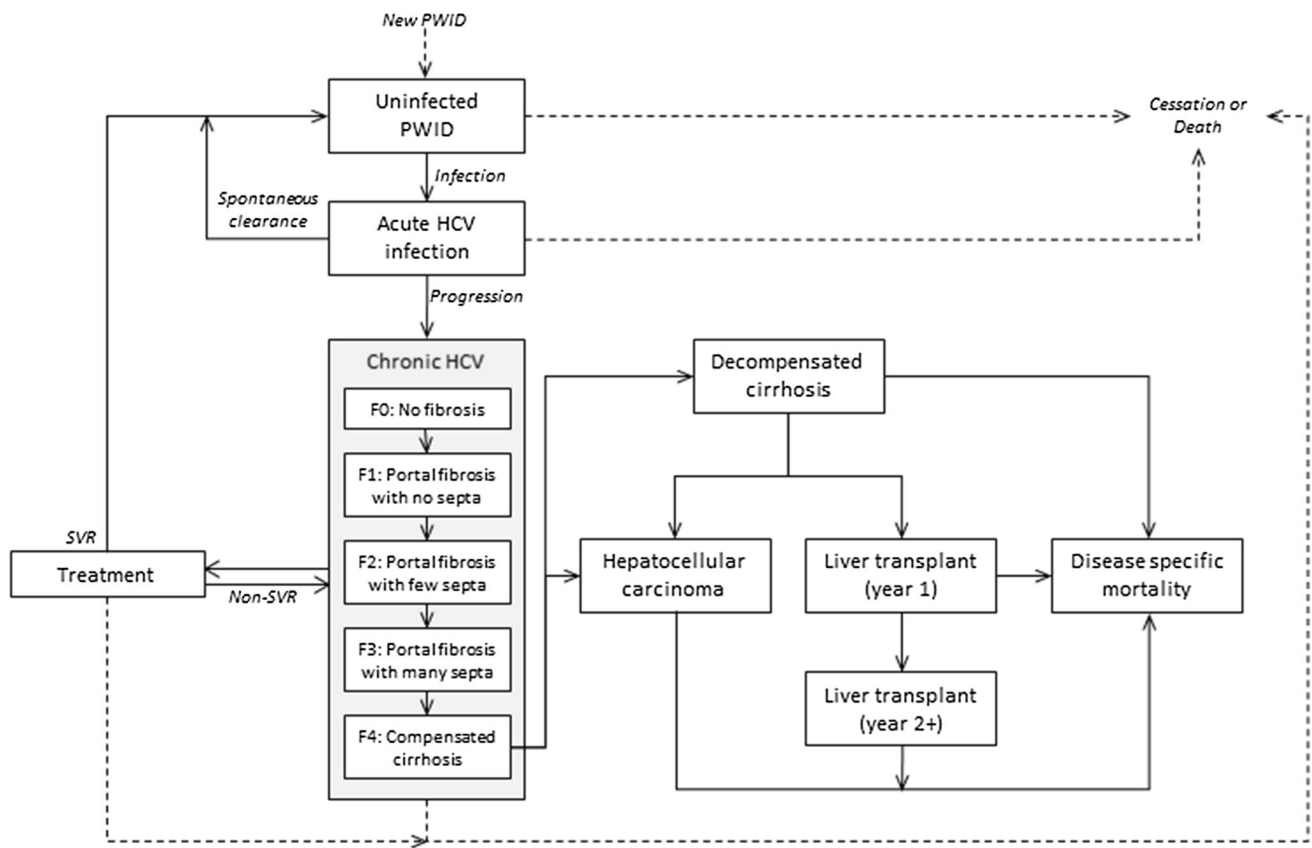### Combined HCV progression/transmission model

A previously published model was utilized [33], based on a combination of established HCV disease progression and disease transmission models [29, 33–37].

Figure 1 depicts the progression of an individual patient.

The disease transmission component was based on the HCV transmission model published by Martin et al. [25, 29], and is comparable with other published HCV transmission models [28]. The deterministic compartment model simulates susceptible PWID individuals who become acutely infected with HCV, and may either spontaneously clear the infection or progress to chronic HCV. The PWID population is stratified by transmission risk (low versus high risk) and receipt of opiate substitution therapy (OST); rates of onward transmission are controlled by relative risks of acquiring HCV in each subgroup (Table 1).

If individuals with chronic HCV infection receive treatment, they may achieve SVR and re-enter the uninfected state; uninfected patients can no longer transmit the virus to others, but become susceptible to reinfection. Patients who fail treatment remain chronically infected and at risk of passing infection to others, with no option to re-treat modeled following treatment failure.

The progression of new chronically infected patients was modeled from F0 (assuming age 20 years), through liver fibrosis stages, and from the F4 disease stage to decompensated cirrhosis, HCC, liver transplant, or death. Dynamic, fibrosis stage-specific transition rates from a meta-regression analysis from a multi-country, multi-

Fig. 1 Combined disease transmission and disease progression model schematic

center study using data from 33,121 individuals chronically infected with HCV were utilized [38]. Additional transition rates were obtained from Martin et al. [74]. Genotype 3-specific multipliers (relating to fibrosis stage progression and the progression from compensated cirrhosis and decompensated cirrhosis to HCC) were utilized [39].

Data and assumptions

A prevalent population of PWID was established according to historical data regarding treatment prior to 2015 as described previously [33], and the impact of new therapies was assessed thereafter. Data inputs were based upon the PWID population in Edinburgh (Table 1); the size of the modeled PWID population was assumed to be fixed.

Costs and utilities associated with HCV disease progression and treatment were based on a review of the published literature, and are in line with inputs reported by Townsend et al. [40]. Costs and utilities for health states, complications, and treatment regimens are described in Table 2; monitoring costs were obtained from a previous HCV economic analysis conducted within the UK [41]. In the absence of a published utility value for patients achieving SVR from fibrosis stage F4, it was assumed that utility following SVR was the same for patients in F3 and

F4 pre-treatment. This assumption was based on (1) SVR being accepted as a cure, and (2) cirrhosis has been shown to regress in up to 75% of patients achieving SVR [7, 42–44]. Where required, costs were inflated to 2013 values using the Hospital and Community Health Services (HCHS) Index [45].

Clinical data inputs [SVR, extended rapid virologic response (eRVR) and discontinuation rates] extracted for each of the assessed treatments are summarized in Table 3. Predominantly, clinical data were obtained from naive comparisons of daclatasvir + sofosbuvir with relevant treatment regimens. It was assumed that all discontinuations for the respective regimen occur in week 4 (the earliest point of discontinuation that the model allows).

Analysis

In order to quantify the health economic value of HCV treatment unaccounted for in conventional economic analyses, the cost offsets and quality-adjusted life-year (QALY) gains associated with reduced disease transmission following treatment (SVR rate 50–100%) in the PWID population were estimated versus no treatment; no costs of treatment were modeled. The predicted cost offsets and QALY gains were then combined to present the

Table 1 Summary of modeling data inputs, obtained from Martin et al. [25, 29]

Parameter[a]	Value	References
Duration of injecting lifetime	11 years	Sweeting et al. [55]; Kimber et al. [56]
Overall mortality rate	1% per year	Hickman et al. [57]; Cornish et al. [58]
Proportion of PWID at high risk	33%	Health Protection Scotland [59]; Allen et al. [60]
Proportion of PWID on OST	57%	University of the West of Scotland [61], unpublished[b]
Duration on OST	8 months	Cornish et al. [58]
Duration at high risk	14 months	Vickerman et al. [62]; Kemp [63]
Proportion of patients genotype 1	53%	Innes et al. [64]
Chronic HCV prevalence among PWID in 2012	25%	University of the West of Scotland [61]
Proportion spontaneous clearance of acute infection	26%	Micallef et al. [65]
Duration of acute period	6 months	Mondelli et al. [66]
Relative risk for acquiring HCV while on OST	0.41	Turner et al. [67]
Relative risk for acquiring HCV for high risk	3.6	Allen et al. [60]; Turner et al. [67]
Baseline treatment rate per annum	8 per 1000 PWID	Innes [64], unpublished
Proportion of patients achieving SVR (treatments modeled prior to 2015)		
PR (genotype 1)	37%	Aspinall et al. [68]
PR (genotype 2/3)	67%	Aspinall et al. [68]
TVR/BOC +PR (genotype 1)	63%	Jacobson et al. [69]; Poordad et al. [70]
Treatment duration (treatments modeled prior to 2015)		
PR (genotype 1)—SVR	48 weeks	NICE TA106 [71]
PR (genotype 1)—non SVR	12 weeks	NICE TA106 [71]
PR (genotype 2/3)	24 weeks	NICE TA106 [71]
TVR/BOC +PR (genotype 1)	24 weeks	Jacobson et al. [69]; Poordad et al. [70]

BOC boceprevir, *HCV* hepatitis C virus, *NICE* National Institute for Health and Care Excellence, *OST* opiate substitution therapy, *PR* pegylated interferon-alfa + ribavirin, *PWID* people who inject drugs, *RBV* ribavirin, *SVR* sustained virologic response, *TVR* telaprevir

[a] All parameters utilized as reported in Martin et al. [25, 29]; full description of parameters and values may be found in original publication

[b] From 2008/2009 NESI survey, excluding those who attended a survey recruitment site for methadone

incremental net monetary benefit (iNMB), at a willingness-to-pay threshold of £20,000/QALY. In this context, iNMB may be interpreted as the maximum monetary investment that could be allocated to the new treatment (drug acquisition, administration, monitoring etc.) without exceeding the willingness-to-pay threshold.

Treatment uptake rates of 10–100% of chronically infected patients not previously treated were applied at the beginning of 2015, with no treatment over subsequent years. Treatment uptake was applied proportionally across all subgroups on or off OST, at high or low risk of transmission. Results were accumulated over a 50-year horizon (2015–2064) and presented per patient treated; due to the uncertainty in future dynamics of disease, shorter time horizons were assessed in sensitivity analyses.

To explore the impact of this underestimation of treatment benefit on cost-effectiveness estimates, a conventional cost-effectiveness evaluation of daclatasvir + sofosbuvir versus established standard of care in genotypes 1 and 3 was undertaken over a lifetime horizon (80 years), before adjusting for onward transmission. The population evaluated in the conventional analysis was aged 50 years, 67% male and distributed across fibrosis stages based on data reported in the hepatitis C in the UK: 2013 report (F0: 30.89%; F1: 30.89%; F2: 16.82%; F3: 16.82%; F4: 4.57%) [46, 47]. Age among treated PWID may be lower than the general population; any bias introduced by this limitation is likely to bias against the strategy to treat.

Treatment uptake rates of 10–100% were evaluated under the assumption that hypothetical cohorts were comprised of the specified genotype only. For patients infected with HCV genotype 1, established standard of care was modeled as PR, telaprevir + PR or no treatment. Established standard of care in patients with HCV genotype 3 was modeled as PR or no treatment.

The analysis was performed from the perspective of the UK NHS and Personal Social Services (PSS), and both costs and benefits were discounted annually at a rate of 3.5%, in line with UK guidelines [48].

Table 2 Summary of health state costs and utility inputs

Health state	Cost inputs (2013/2014 £)[a] Mean (SE)	Utility Mean (SE)	Source
F0–F4 fibrosis stages			
F0	187.59 (37.00)	0.77 (0.015)	Shepherd et al. [41]; Wright et al. [72]; Grieve et al. [73]; Martin et al. [74]
F1	187.59 (37.00)	0.77 (0.015)	
F2	974.68 (103.40)	0.66 (0.031)	
F3	974.68 (103.40)	0.66 (0.031)	
F4	1546.98 (314.25)	0.55 (0.054)	
SVR			
SVR from F0 to F1	352.08 (65.59)[b]	0.82 (0.043)	Shepherd et al. [41]; Wright et al. [72]; Grieve et al. [73]; Martin et al. [74]
SVR from F2 to F3	974.68 (103.40)[b]	0.72 (0.048)	
SVR from F4	1546.98 (314.25)[b]	0.72 (0.048)	Cost derived from Martin et al. [74]; Utility based on assumption
Complications			
Decompensated cirrhosis	12,398.93 (2065.55)	0.45 (0.031)	Shepherd et al. [41]; Wright et al. [72]; Grieve et al. [73]; Martin et al. [74]
HCC	11,047.70 (2596.18)	0.45 (0.031)	
Liver transplant (transplant cost)	37,151.92 (3921.53)	NA	
Liver transplant (cost of care: initial year)	12,857.04 (3463.66)	0.45 (0.031)	
Liver transplant (subsequent years)	1882.74 (482.61)	0.67 (0.066)	
Health state	Cost inputs (2013/2014 £)[a] Mean (SE)	Utility Mean (SE)	Utility source[c]
Treatment costs and disutilities			
DCV + SOF	2043.15 + 2915.25	0.035 (0.0035)[d]	AI444-040 [8]
TVR + PR	1866.50 + 124.40 + 66.95	0.102 (0.010)	TVR manufacturer submission to NICE [75]
PR	124.40 + 66.95	0.109 (0.010)	TVR manufacturer submission to NICE [75]

DCV daclatasvir, *NA* not applicable, *NICE* National Institute for Health and Care Excellence, *NR* not reported, *PR* pegylated interferon-alfa + ribavirin, *SE* standard error, *SOF* sofosbuvir, *SVR* sustained virologic response, *TVR* telaprevir

[a] Costs inflated to 2013–2014 prices using the Hospital and Community Health Services inflation indices [76]

[b] Cost applied in year of SVR (year 1) only

[c] Weekly treatment acquisition costs based on Monthly Index of Medical Specialities (MIMS) [77]

[d] SE unavailable so assumed to be 10% of the mean value

Results

Underestimation of value of SVR in conventional health economic models

Figure 2 graphically illustrates the cost savings, QALY gains, and iNMB at a willingness-to-pay threshold of £20,000/QALY associated with the disease transmission consequences of HCV treatment, dependent on treatment uptake and SVR rate. In the modeled scenario, where all previously untreated patients were treated with an antiretroviral therapy with a 100% SVR rate, the predicted iNMB was estimated to be £90,559 per patient treated (cost

savings: £20,733, QALY gains: 3.49), as a result of reduced opportunity for future transmission of infection. In contrast, treating 10% of patients produced a lower iNMB of £29,188 per patient treated, at the same SVR rate (100%). Treating only 10% of patients using a less effective therapy (SVR 50%) further reduced the iNMB to £24,304 per treated patient.

Impact on cost-effectiveness of newly available DAA therapies

The conventional evaluation of daclatasvir + sofosbuvir versus no treatment in genotype 1 produces incremental

Table 3 Summary of clinical data inputs

Population	Treatment regimen	Duration (weeks)	SVR24 n (%)	Discontinuation rate	eRVR	Source(s)
Genotype 1	DCV + SOF	12	39/41 (95%)	0	–	AI444-040 [8, 78]
	TVR + PR	TVR: 12	271/363 (75%)	0.262	58%	ADVANCE [69]
		PR: 24–48				
	PR	48	142/271 (52%)[a]	0.264[b]	–	NV15942 [79]
Genotype 3	DCV + SOF	12	91/101 (90%)[c]	0	–	ALLY-3 [80]
	PR	24	110/176 (63%)[c]	0.222[b]	–	FISSION [9]

Rate of SVR and discontinuations based on treatment-naive patients

DCV daclatasvir, *eRVR* extended rapid viral response, *PR* pegylated interferon-alfa + ribavirin, *SOF* sofosbuvir, *SVR* sustained virologic response, *TVR* telaprevir

[a] SVR defined as undetectable serum HCV RNA level at the end of treatment, and during 12- to 24-week follow-up

[b] Rate of discontinuation in genotype-specific subgroup unavailable; data for overall treatment arm presented

[c] SVR 24 data unavailable; SVR12 data presented

benefits of 3.05 QALYs at an incremental cost of £36,764, corresponding to iNMB of £24,165 and an incremental cost-effectiveness ratio (ICER) of £12,068. The value associated with reduced disease transmission as a consequence of 95% of patients achieving SVR was estimated to be £81,652 at 100% treatment uptake. Adding this value to the conventional estimates increases iNMB (£105,817) and decreases the ICER (£2911) by a factor of approximately 4.

Figure 3 shows the impact of incorporating the estimated health and economic benefits associated with reduced onward transmission into the ICER calculations for the illustrative comparison of daclatasvir + sofosbuvir versus established comparators in genotype 1 and genotype 3 patients. The estimated cost-effectiveness of the daclatasvir-based regimens improves with the inclusion of future transmission consequences, and this improvement increases with greater treatment uptake. In patients with HCV genotype 1, ICERs associated with daclatasvir + sofosbuvir versus no treatment, PR, telaprevir + PR fell by £6812–£9157, £12,015–£19,208, and £13,846–£25,924, respectively, dependent on treatment uptake rate (10–100%), compared to the base case (conventional analysis, no benefit of reduced onward transmission); this corresponds to relative reductions of 36–76% in ICERs. Similarly, in the HCV genotype 3 scenario, base case ICERs associated with daclatasvir + sofosbuvir fell by £6314–£8334 and £18,016–£28,841 in comparisons against no treatment and PR, respectively, depending on treatment uptake rate (10–100%) corresponding to relative reductions of 41–79% in the ICER.

Reducing the time horizon over which disease transmission was assessed led to the capture of fewer transmissions and also fewer long-term ESLD complications among newly infected patients; as a result, the magnitude of estimated cost and QALY savings associated with reduced transmission and their consequent impact on cost-

effectiveness diminished in these scenarios. In genotype 1 patients, depending on treatment uptake rate, ICERs were subject to relative reductions of 0–4% over 10 years and 11–28% over 20 years (compared to 36–76% over 50 years). Similarly, in genotype 3 patients, ICERs were subject to reductions of 0–4% over 10 years and 14–24% over 20 years (compared to 41–79% over 50 years).

Discussion

Curing patients with HCV benefits both the incident population infected with HCV and wider society by reducing the opportunity for infected individuals to transmit infection to others [24]. Conventional cost-effectiveness evaluations in HCV typically account only for the former (in terms of reduced progression to ESLD) and thus likely underestimate the cost-effectiveness of treatment, particularly amongst patient subgroups subject to high transmission risk, such as PWID. In people undertaking risky behavior, the value of cure is to some extent independent of the individual's disease stage; unfortunately, the proportion of the prevalent HCV population who are active PWID is uncertain.

This study is the first attempt to quantify the impact of reduced HCV transmission on the cost-effectiveness of DAA regimens as a function of increased treatment uptake, applying daclatasvir plus sofosbuvir for treatment of the high-risk PWID population in a UK setting as an example. The presented data support previously published research demonstrating that the cost-effectiveness of DAA treatment improves with the inclusion of future transmission consequences in the PWID population (compared to ex/non-PWID) [32]. However, this analysis also demonstrated that improvements in estimated cost-effectiveness were directly related to increased treatment uptake, due to increased cost offsets and QALY gains associated with the
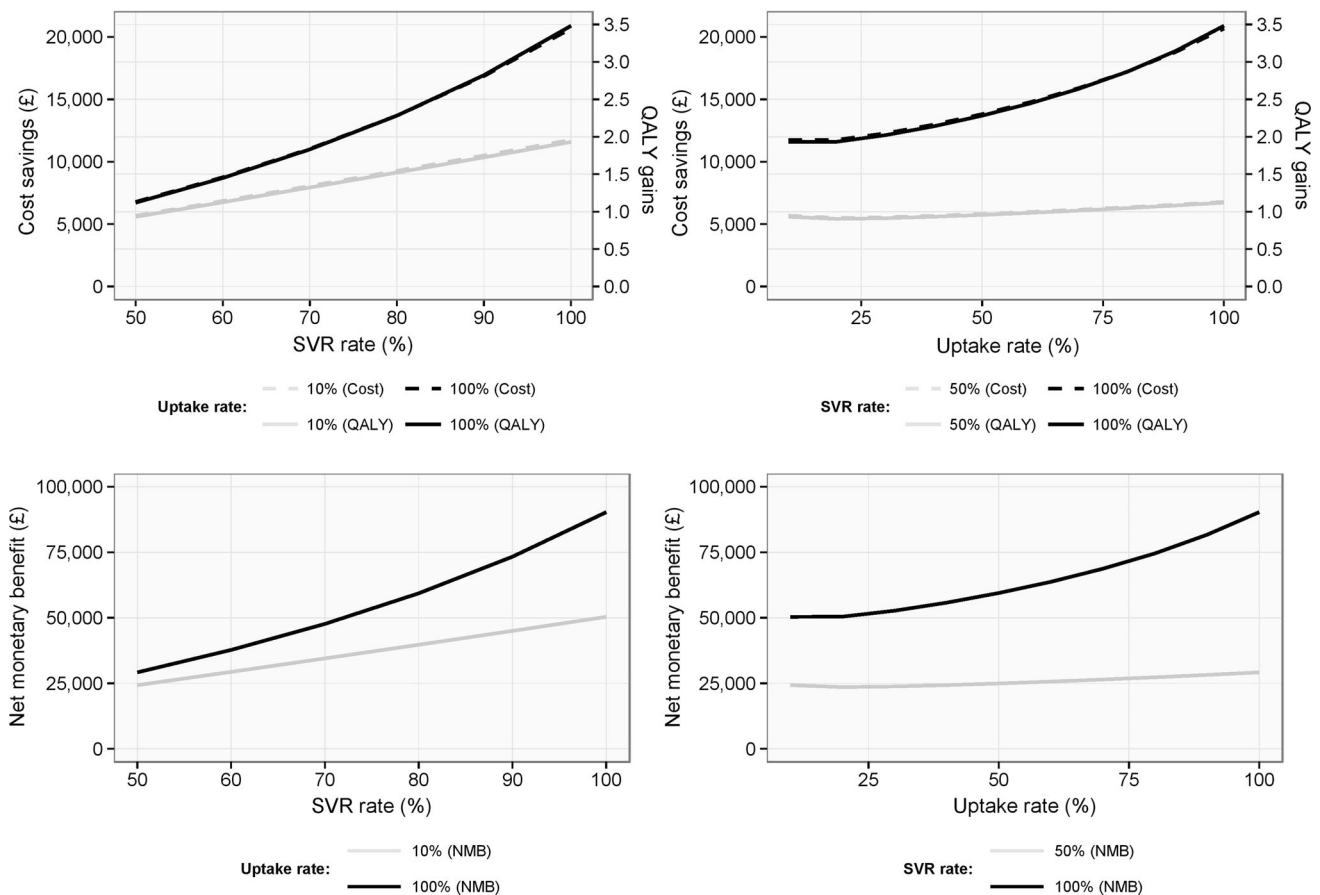
Fig. 2 Cost offsets, QALY gains, and incremental net monetary benefit associated with increased HCV treatment uptake and SVR. The effect of varying HCV treatment uptake and SVR is graphically illustrated (*light grey lines* represent low uptake/SVR; *dashed lines* in **a** and **b** represent costs, while *solid lines* represent QALYs). The effect of improving treatment uptake (10–100%) causes greater

QALY gains, cost offsets, and net monetary benefit (**a**, **b**), and this is dependent on SVR rate. Similarly, improving SVR rate (from 50–100%) causes greater QALY gains, cost offsets, and net monetary benefit (**b**, **d**), which can be elevated further by increasing treatment uptake

avoidance of greater numbers of future chronic infections. Assuming an optimal treatment uptake (all patients receiving immediate therapy), base-case ICERs associated with daclatasvir + sofosbuvir were reduced by up to 79% compared to standard of care.

Several assessments of the cost-effectiveness of new DAA regimens have been undertaken, focusing solely on benefits for individual patients without assessment of potential downstream benefits of reduced transmission [13, 14] and often demonstrating that it is more cost-effective to treat those with severe liver disease [49, 50]. This conclusion was supported by a recent evaluation that incorporated the consequences of HCV transmission, which found that treatment of ex/non-PWID with mild HCV was not cost-effective in contrast to delaying treatment [32]. By contrast, in the PWID population, there were substantial benefits in most scenarios for treating patients with mild disease due to the onward disease transmission and prevention benefits [32]. This conclusion is supported

by the evidence presented within this analysis, which has demonstrated that the benefits of HCV treatment associated with onward disease transmission can be maximized by improving treatment uptake in high-risk populations such as PWID.

The evidence presented here demonstrates that when a small treatment uptake is applied, there is limited impact on onward HCV transmission dynamics even within a high-risk population, such as PWID. Thus, the economic benefit of HCV treatment that could be realized in clinical practice is likely to be only slightly underestimated by exclusion of onward disease transmission from evaluations focused on individual patient-level benefit, such as those conducted by NICE. However, increasing treatment uptake improves the cost-effectiveness of DAAs, and hence value to the NHS would be maximized when treatment rates are improved.

Within the context of historical low treatment rates and reluctance to treat PWID [51, 52], an increase in treatment

Cost-effectiveness of DCV+SOF, by treatment uptake rate
(F0-F4 treatment naive)
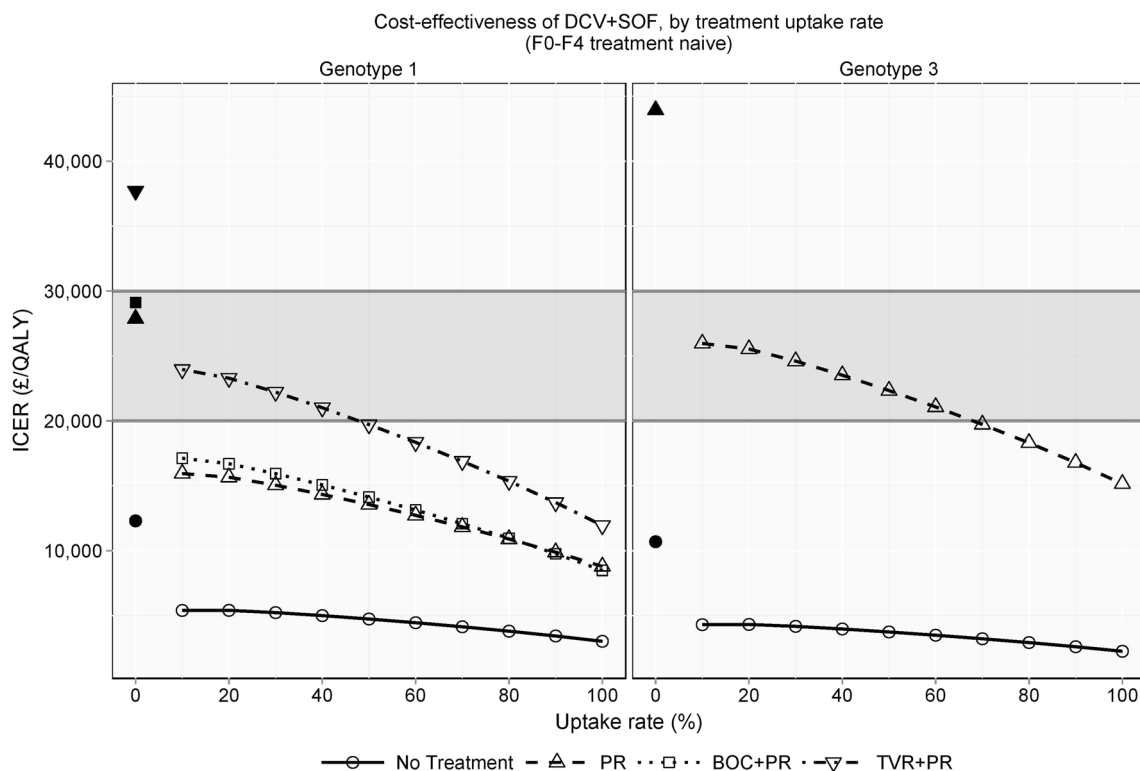
Fig. 3 Effect of accounting for 100% treatment uptake rate within a cost-effectiveness evaluation of daclatasvir + sofosbuvir versus established standard of care, contrasted with a conventional analysis (no inclusion of onward transmission, illustrated as *solid markers* at 0% uptake). Willingness-to-pay thresholds of £20,000 and £30,000 per QALY are represented (*grey boundaries*). Incremental cost-effectiveness ratios for daclatasvir + sofosbuvir versus standard of care for patients with HCV genotypes 1 or 3 are improved when accounting for the downstream benefits of increasing treatment uptake, resulting in ratios below the willingness-to-pay thresholds of £20,000 and £30,000 per QALY

uptake may be plausible given the proven clinical benefits of new DAA regimens, including the improved tolerability and efficacy [8–11]. However, modeling the associated service implications and the affordability of treating more patients with antiviral therapies were beyond the scope of this analysis. Increased uptake of treatment would inevitably place additional financial pressure on existing healthcare budgets with respect to access and delivery of care to a larger number of PWID, in addition to considerable drug acquisition costs. Although the costs of treating PWID patients should be weighed against the benefits of reduced onward HCV transmission to society, these long-term benefits will not offset the financial burden of increased treatment uptake on healthcare budgets fully or in the short term.

One possible approach to address concerns around affordability would be to prioritize, or target, treatment among patients with HCV with highest unmet medical need. Such patients would include those at greatest risk of progressing to advanced liver disease, and most likely to transmit their infection to others [53]. The aim of targeted therapy in this context would be to address areas of high unmet medical need, while obtaining the maximum

economic benefits (i.e., avoided infections) with the minimum expenditure (number of patients treated).

Although the relationship between cost-effectiveness and treatment uptake (and efficacy) may be generalized to other settings, this analysis evaluated a PWID population from a UK perspective, which is limited by the available epidemiological and behavioral data for the PWID population, with inputs derived from previous studies in the UK setting by Martin et al. [25, 29]. The analysis also focused on HCV genotype 1 and 3 only, since these genotypes have the highest prevalence within PWID [54]. As such, the generalizability of this research to other settings and patient groups should be considered within this context; indeed, previous research demonstrated that the cost-effectiveness of treatment strategies may differ in settings with a high HCV prevalence (>60%) among PWIDs [32].

In conclusion, using daclatasvir plus sofosbuvir for treatment of the high-risk PWID population in the UK setting to illustrate, this study is the first to demonstrate the relationship between the cost-effectiveness of HCV treatment and rate of treatment uptake. Cost-effectiveness of DAA treatment was shown to improve with increased treatment uptake, due to increased cost offsets and health

gains associated with the avoidance of greater numbers of future chronic infections. Indeed, a reimbursement decision could be substantially influenced by incorporating the potential benefits of increased treatment uptake and the resulting reduced onward transmission. Further, if treatment uptake rates in high-risk populations could be increased, DAAs would represent better value for money in clinical practice. The challenge for the future will lie in achieving increased rates of treatment uptake among high-risk populations.

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