Cost-effectiveness of Ledipasvir/Sofosbuvir for the Treatment of Chronic Hepatitis C in the UK: A Dynamic Transmission Modelling Approach

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BACKGROUND

- Several direct-acting antiviral treatments for chronic hepatitis C (CHC) have been deemed cost-effective in England, however economic evaluations have typically excluded reinfection or prevention benefits, a limitation highlighted by the healthcare payer[1].
- Due to concerns around budget and potential for reinfection, access to new and effective treatments is limited, especially for people who inject drugs (PWID), in many countries.
- A model including both reinfection and onward transmission is preferable to static alternatives that are often used (where reinfection and onward transmission are not modelled), as this would include the impact of treatment on the population as a whole as well as capturing any negative consequences of reinfection.

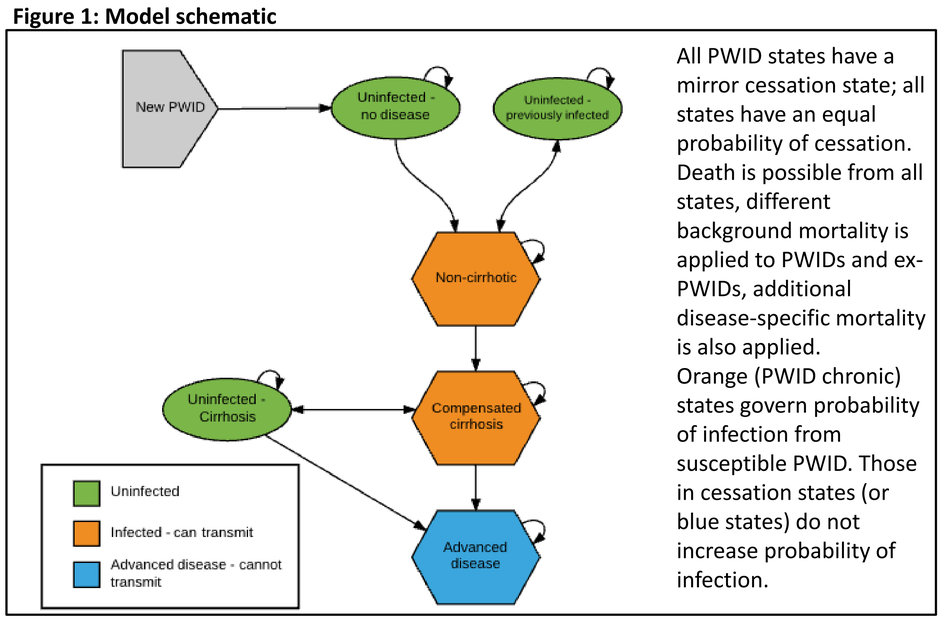
OBJECTIVES

- This study aimed to use a dynamic transmission model to determine the cost-effectiveness of ledipasvir/sofosbuvir with(out) ribavirin (LDV/SOF +/- RBV) versus no treatment in CHC, with the aim of evaluating:
  1. Cost-effectiveness compared with a static model
  2. How cost-effectiveness changes with treatment access
  3. Cost-effectiveness of treating PWID

METHODS

- A dynamic model of CHC transmission and progression among PWID and ex-PWID was built from the perspective of the National Health Service (NHS) and personal social services (PSS). The model structure was similar to that submitted by the manufacturer for LDV/SOF[1] (a Markov state transition model previously accepted by the healthcare payer in England), with additional states to simulate onward transmission and reinfection (see Figure 1); enabling a comparison with the original model [Objective 1]. The model captures those who are uninfected as well as the infected population.
- The model includes CHC genotypes 1-4. It was assumed that infection was mutually exclusive (i.e. infection with one genotype stopped infection with any other) and there was equal risk of primary infection and reinfection. At baseline, 37.5% of PWID have CHC (of any genotype).
- Active uninfected PWID may become infected within the model; the rate of infection was relative to the proportion of infected PWID. PWID may permanently cease injecting drugs, after an average of 11 years[2], after which they are no longer at risk of infection (or onward transmission if infected).
- In the base case, 3% of PWID and 7% of ex-PWID were treated with LDV/SOF in comparison to no treatment; a range of treatment coverage rates were then tested in scenario analyses [Objective 2].
- The key model inputs are described in Table 1.
- In order to address data gaps in the model inputs, a calibration exercise was undertaken. This involved systematically assessing the fit of the model to existing outcomes data, by adjusting the free (unmeasured) parameters (probabilities of infection with genotypes 1-4 and replacement rate of PWID) in order to predict future outcomes and then iteratively adjusting these free parameters to minimise the difference between the model outcomes and the real-world data. The model was fitted to match genotype prevalence data reported in a Public Health England (PHE) report[3] (presented in Table 2), assuming that no treatment was given, as well as an assumption that the total population size and ratio of PWID to ex-PWID remains constant over time.
- Costs, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICERs) were calculated for the total cohort and for PWID [Objective 3].

Figure 1: Model schematic



All PWID states have a mirror cessation state; all states have an equal probability of cessation. Death is possible from all states, different background mortality is applied to PWIDs and ex-PWIDs, additional disease-specific mortality is also applied. Orange (PWID chronic) states govern probability of infection from susceptible PWID. Those in cessation states (or blue states) do not increase probability of infection.

Table 1: Key inputs of the cost-effectiveness model

Model parameters	Used in model	Source
Time horizon	60 years	Aligned with previous submission[1]
Discount Rate	3.5% costs and QALYs	Aligned with previous submission[1]
Average age (years)	25 (PWID), 55 (ex-PWID)	Assumption
Ratio PWID:Ex-PWID	1:5 (5 ex-PWID for each PWID)	Assumption
GT1/2/3/4 at baseline	16.1%/1.7%/18.7%/1.1%	PHE report[3]

Table 2: Health state costs and utilities used in the cost-effectiveness model[1]

Health state	Cost per year (GBP)	Utility
Uninfected, no cirrhosis	£0	0.86 (ex-PWID no prev. inf.)[4] 0.79 (PWID, ex-PWID prev. inf.)
Non-cirrhotic disease	£363	0.75
Compensated cirrhosis	£1,540	0.55
Uninfected, with cirrhosis	£506	0.59
Decompensated cirrhosis	£12,339	0.45
Hepatocellular carcinoma	£10,994	0.45
Liver transplant	£111,017 (event + Year 1 follow-up)	0.45 (Year 1)
	£4,111 (Year 2+ follow-up)	0.67 (Year 2+)

RESULTS

- In the base case, treatment with LDV/SOF +/- RBV incurred an additional cost of £4,928 versus no treatment and generated 0.53 additional QALYs. The ICER was £9,249/QALY.
- This was similar to the weighted average ICER (weighted by genotype prevalence) for treatment-naïve patients from the manufacturer's cost-effectiveness submission (£9,518/QALY) [Objective 1].
- However, increased treatment rates improved cost-effectiveness (Figure 2), e.g. when treatment rates were quadrupled (PWID: 12%/year; ex-PWID: 28%/year), the ICER decreased to £6,096/QALY [Objective 2].
- Treatment of PWID was particularly cost-effective: if only PWID are treated (3% treated/year), the ICER decreased to £5,391/QALY [Objective 3].

Figure 2: Cost-effectiveness of LDV/SOF +/- RBV vs no treatment over a range of treatment coverage rates

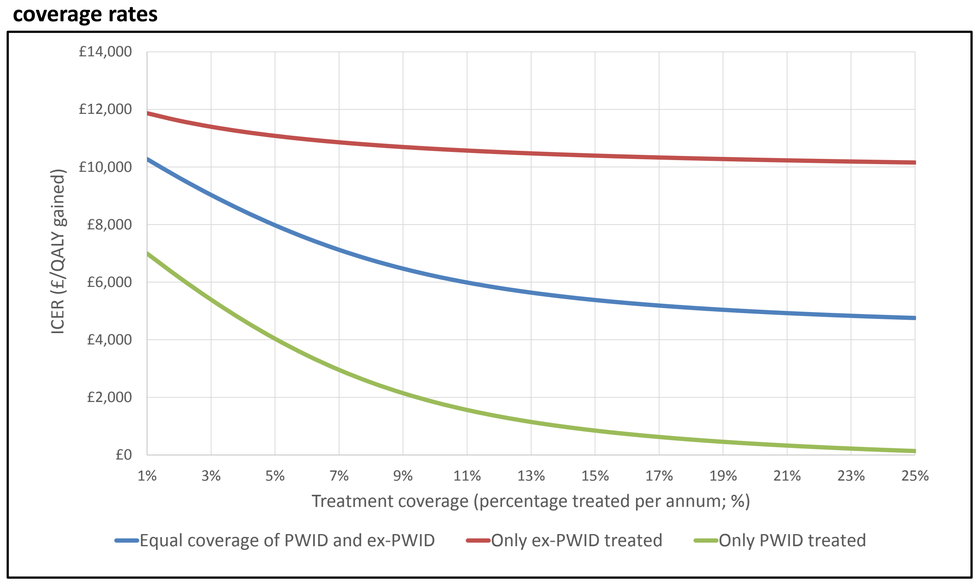


Figure 3: Prevalence of CHC in PWID over time (base case treatment)

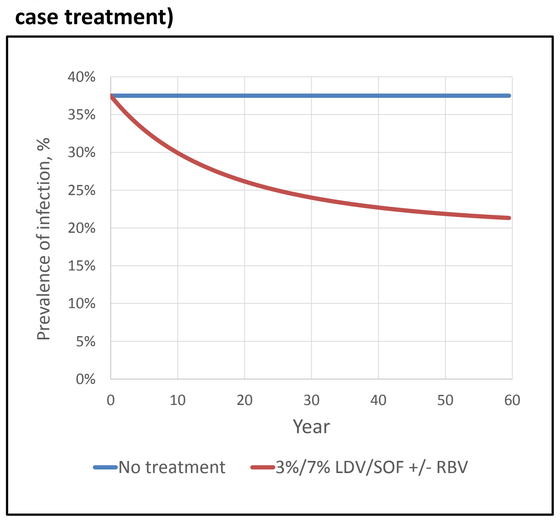
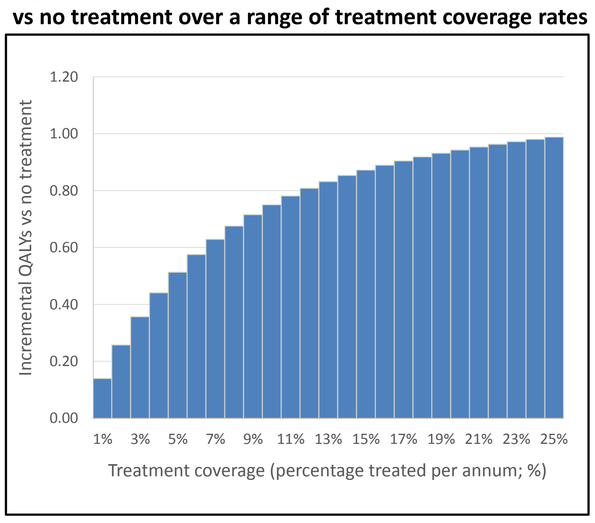


Figure 4: Incremental QALYs accrued by LDV/SOF +/- RBV vs no treatment over a range of treatment coverage rates



DISCUSSION & CONCLUSIONS

- Treatment rates in CHC are generally low, particularly in PWID, often driven by concerns regarding reinfection and cost.
- There is considerable unmet need amongst the PWID population, characterised by the low treatment rates in this group.
- If treatment rates among PWID are low, the cost-effectiveness of LDV/SOF from a dynamic model is similar to a static model without reinfection or onward transmission effects. However, treatment scale-up for those at risk of transmitting disease (i.e. PWID) will improve cost-effectiveness as benefits of avoiding onward transmission outweigh reinfection risk in the UK.
- This study suggests that successful strategies to treat PWID can deliver population-wide benefits. Increases in treatment coverage, particularly among PWID, improve both the population health and the cost-effectiveness of treatment.
- Furthermore, this study shows that population prevention benefits can impact cost-effectiveness conclusions – an understanding of the effects of treatment on the wider population is crucial for the evaluation of cost-effectiveness.

REFERENCES

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Study funded by Gilead Sciences

6th International Symposium on Hepatitis Care in Substance Users, New York, 6-8 September 2017

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