Cost-effectiveness of pharmacy-led versus conventionally delivered antiviral treatment for hepatitis C in patients receiving opioid substitution therapy: An economic evaluation alongside a pragmatic cluster randomised trial


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**ARTICLE INFO**

**Article history:**
Accepted 21 September 2022

**SUMMARY**

**Background:** Elimination targets for hepatitis C have been set across the world. In the UK almost 90% of infections are in people who inject drugs. Evidence shows community case-finding is effective at identifying and treating undiagnosed patients. The aim of this analysis was to assess, from a healthcare provider perspective, the cost-effectiveness of a new pharmacist-led test and treat pathway for hepatitis C in opioid agonist treatment (OAT) patients attending community pharmacies compared to conventional care.

**Methods:** In a cluster randomised controlled trial, pharmacies were randomised to the pharmacist-led or conventional care pathway. Mean cost per OAT patient and per patient initiating treatment was identified for each pathway. A Markov model tracking disease progression was developed, with a 50-year time horizon and 3%-5% time discount rate, to estimate the incremental cost-effectiveness ratio (ICER) per quality-adjusted life-year (QALY) gained and the probability of being cost-effective at a £30,000 per QALY willingness-to-pay threshold. Probabilistic sensitivity analysis was performed for a range of drug discounts, re-infection rates, and model assumptions.

**Findings:** Mean cost per OAT patient (£3,674 vs £1,965) and per patient initiating treatment (£863 vs £404) was higher in the pharmacist-led pathway, due to higher uptake of testing and pharmacist time requirements. Over a 50-year time horizon the ICER per QALY gained was £31,612 at NHS indicative price for treatment (£38,979 for 12 weeks) and 12,1/100 person-years re-infection rate, reducing to £21,027/£10,220/-£501 per QALY gained with 30%/60%/90% drug price discounts and £25,273/£21,738/£14,912 per QALY gained at re-infection rates of 8.5/2 per 100 person-years. At 30%/60%/90% drug discount rates, the pharmacist-led pathway had an 80%/98%/100% probability of being cost-effective.

**Interpretation:** The pharmacist-led pathway is effective at increasing testing and treatment uptake, with cost-effectiveness being highly dependent on drug price discounts.

**Funding:** Trial funding provided by the Scottish Government, Gilead Sciences, and Bristol-Myers Squibb.

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**Research in context**

**Evidence before the study**

Our SuperDOT-C cluster RCT demonstrated that compared to conventional hospital-based care in the UK, a pharmacist-led service resulted in higher uptake of both testing and...
treatment for HCV (Radley and colleagues, 2020). In 2019, we reported a systematic review in Cinahl, Embase, Medline, PsycINFO, PubMed and Google Scholar to December 2017 of community and primary-care-based hepatitis C testing and direct acting antiviral drug treatment services (Radley and colleagues 2019). It found two studies of services provided by pharmacists; the feasibility study for the SuperDOT-C trial (Radley and colleagues, 2017) and a non-randomised study of patients served by an American Indian/Alaskan Native tribal health system, which found that patients treated in pharmacist clinics achieved high rates of SVR similar to non-pharmacist clinics (David and colleagues, 2017). To the best of our knowledge, no economic evaluation of pharmacist-led hepatitis C testing and direct acting antiviral drug treatment services has been published. However, the cost-effectiveness of routine HCV screening and treatment has been shown in other settings, including by general practitioners and community hepatitis nurses in Australia and New Zealand (Palmer and colleagues, 2020).

Added value of this study

Our study shows that in addition to higher uptake of both testing and treatment for HCV, the pharmacist-led service can improve quality of life among people with hepatitis C who inject drugs and that the pathway was cost-effective having accounted for realistic drug discount rates.

Implications of all the available evidence

WHO hepatitis C elimination targets require improvement in both the identification and treatment in high-risk groups and reliance on conventional hospital-based care is suboptimal as high-risk groups including people who inject drugs are less likely to engage with these services. Our study has demonstrated that the pharmacist-led streamlining of the patient pathway can contribute to the called-for improvement and represents good value for money within the context of the UK health service.

Introduction

The World Health Organization (WHO) targets to eliminate hepatitis C virus (HCV) have been adopted and accelerated by England and Scotland with earlier deadlines of 2025 and 2024, respectively. HCV infection is often asymptomatic, but if not treated, can progress to liver cirrhosis and hepatocellular carcinoma. In the UK, almost 90% of infections are in people with an injecting history or people who inject drugs (PWID), with around half being infected. Therefore, finding and testing high-risk populations such as PWID is essential to reach elimination targets. While dried blood spot tests (DBSTs) screen for HCV antibodies with high diagnostic accuracy and direct-acting antivirals (DAAs) achieve an effective cure in over 90% of patients, almost half of PWID infected with HCV in England, Wales, and Northern Ireland are undiagnosed. Evidence suggests testing for HCV within community pharmacies can be effective at identifying undiagnosed individuals and increasing treatment rates, and be cost-effective. A streamlined pathway for testing and treatment, in which all care is provided within the community pharmacy where the individuals receive opioid agonist treatment (OAT), could increase testing and treatment uptake, by minimising stigma and interactions with unfamiliar health care professionals which is considered a barrier to treatment.

SuperDOT-C was a cluster randomised controlled trial (cRCT) to compare a community pharmacist-led pathway with a conventional care pathway of testing for HCV and treatment using DAAs in people receiving OAT. The trial aimed to investigate testing and treatment uptake, completion, and cure rates within the pathways to inform HCV elimination strategy. Within the conventional care pathway OAT patients who accepted the offer of a DBST and had a positive result or had been previously identified as having HCV antibodies, were referred to HCV treatment services within local drug treatment centres for assessment and treatment prescribing, then referred back to the pharmacy for treatment observation. Within the new pharmacist-led pathway all testing and treatment assessment, prescription and observation occurred solely within the pharmacy.

To inform HCV elimination policy decision making, this paper used data collected in the trial and assumptions about drug prices and HCV progression to explore whether the new pathway is a cost-effective strategy for HCV testing and treatment in OAT patients compared to conventional care.

Methods

The trial protocol (https://clinicaltrials.gov/ct2/show/NCT02706223) provides full details of eligibility criteria, recruitment, randomisation, treatment pathways and assessment methods. In brief, 55 community pharmacies within three Health Boards in Scotland (NHS Tayside, NHS Grampian, and NHS Greater Glasgow and Clyde) were recruited. Pharmacies were randomised to either the pharmacist-led intervention or the conventional care comparator. As knowledge of the testing and treatment pathway was essential to provide care, treatment blinded was not possible for pharmacists or patients. All patients attending the pharmacies for OAT, within the recruitment period of 9th December 2016 to 31st May 2018, were eligible to participate, yielding 2,718 total patients. Treatment eligibility criteria included: HCV PCR positive, HCV genotype 1 or 3, stable OAT dose for more than 12 weeks, Fibrotest-4 (FIB-4) score <3.25, no evidence of current or past decompensated liver disease, and willing to have a pharmacist supervise DAA administration. The primary outcome was to compare the rate of sustained virological response at 12 weeks (SVR12) calculated as the number of patients achieving SVR12 over the total number of eligible OAT patients for each pathway. Secondary outcomes include the comparison of the rates of DBST testing, DAA treatment initiation, DAA treatment completion, and SVR at 12 months.

Twenty-eight pharmacies with 1365 OAT patients were randomised to the pharmacist-led arm (see Supplementary Fig. S1). Twenty-eight pharmacies were initially randomised to the conventional care arm, however one pharmacy dropped out prior to patient enrolment resulting in 27 pharmacies with 1353 OAT patients. Five participants (two in the pharmacist-led arm and three in the conventional care arm) had Fib 4 >3.25 and were excluded from treatment; they were included in our analysis, but costs after referral were not applied as further information on resource use by these patients was not available. Individual-level data were collected from patients who consented to treatment, totalling 356 patients. As reported previously, in the pharmacist-led arm 219 patients consented to treatment compared to 137 in the conventional care arm, with 98 and 43 patients achieving SVR12, respectively. The pharmacist-led pathway achieved a higher rate of testing (18% vs 11%, p = 0.0594), treatment initiation (8% vs 5%, p = 0.0015), and SVR12 (7% vs 3%, p < 0.0001).

The pathways were mapped out through discussions with clinical members of the research team to identify the components of resource-use at each stage. Resources included: diagnostic tests (opportunistic screening DBST, blood samples for treatment assessment, SVR12 assessment DBST); drug treatment; staff time in the provision of the tests, treatment assessment, prescription, and monitoring. Within the pharmacist-led pathway, treatment assessment bloods were taken by a nurse visiting the pharmacy who was
booked in for a 2.5-h slot to assess six to eight patients when the need arose. For this analysis, costs were applied based on the nurse seeing seven patients per slot. Data were collected on case report forms completed by the pharmacists at each pharmacy and entered into a data management system by the trial management team.

Costing of the pathways was performed at the cluster/pharmacy level. Unit costs (Supplementary Table S1) of diagnostic tests were provided by NHS Tayside, staff costs from the Unit Costs of Health and Social Care 2019,13 and the cost of sofosbuvir/ledipasvir treatment from the British National Formulary.14 Sofosbuvir/daclatasvir treatment was also used within the trial for the treatment of genotype 3 infection, however as daclatasvir has since been discontinued all treatment was costed as sofosbuvir/ledipasvir which is approved for treatment of both genotype 1 and 3 infections. Other panenotypic drugs approved for the treatment of both genotypes 1 and 3 are available, most having similar NHS indicative prices as sofosbuvir/ledipasvir meaning costs reported in this analysis are applicable to alternative treatment regimens. At the time of the study, treatment duration differed by genotype (typically 8 weeks for genotype 1, 12 weeks for genotype 3). However, an equal treatment duration of 12 weeks for both genotypes was assumed for estimating drug costs in this analysis, which is the length of most current panenotypic treatment regimens. Typical staff time spent on each pathway stage was determined through discussion with clinical members of the research team. As data on the number of treatment assessment PCR tests were recorded in each pathway, but not for each pharmacy, a pathway-specific average cost (number of tests taken in pathway x unit cost/number eligible for DAA treatment in pathway) was applied to patients treated with DAA in each pharmacy. All costs are presented in pound sterling at 2019 prices, inflated where necessary using a UK government GDP deflator.15

**Within trial period economic analysis**

The trial period economic analysis was conducted using pharmacy-level testing data and individual patient-level treatment data collected prospectively within the trial, from a healthcare provider perspective. The mean cost per OAT patient and per patient initiating treatment for each pathway was identified. The cost-effectiveness of the pharmacist-led pathway within the trial period, assessed based on the incremental mean cost per patient achieving SVR12, was analysed using bootstrapping methods.16 Sensitivity of the findings to reductions in drug prices was assessed. It is standard practice for the NHS in the UK and healthcare services in many countries to negotiate discounts from the published list price of patented drugs. The actual price paid is commercially confidential and reflects volume discounts and competition. Therefore, we performed the analysis with a range of discounts (30%/60%/90%) from the list price that represent the true range of the actual cost to health services.

**Long-term analysis**

To evaluate cost-effectiveness of the intervention over a longer-term, a closed cohort Markov model of chronic HCV infection, disease progression, testing and treatment, and reinfection was developed (see details in Supplementary Figs. S2 and S3). The model assumed the higher treatment rate in the pharmacist-led (32.8% of estimated infected) versus conventional care (18.0% of estimated infected) pathway from the trial12 in the first year, with these rates reduced from the second year onwards to background treatment uptake rates (7% for Scotland) as they were prior to the SuperDOT-C trial, based on data from the 2015-2016 Needle Exchange Surveillance Initiative (NESI) (Supplementary Table S3). We modelled the entire cohort following either the pharmacist-led pathway or the conventional care pathway and compared them. Disease progression transition probabilities were taken from published literature (Supplementary Table S3). Testing and treatment costs were taken from our costing analysis, while HCV-related disease management costs and quality of life utility indices for chronic HCV infection were taken from UK-based studies (Supplementary Table S4). Model parameters were sampled probabilistically from their respective uncertainty distributions. Outcomes and costs for each pathway were tracked over a 50-year time horizon and compared, using a 3.5% yearly discount rate. We ran 1000 model simulations and calculated the incremental cost-effectiveness ratio (ICER) of the pharmacy-led pathway compared to the conventional pathway as the median cost per QALY gained. The probability of the pharmacy-led pathway being cost-effective at a UK willingness-to-pay (WTP) threshold of £30,000 was also estimated.

Sensitivity analyses were conducted on varying the 12-1/100py base case re-infection rate17 (8/100py, 5/100py, and 2/100py) and DAA drug price (30, 60, and 90% discount) to see how these affected the ICER. A threshold analysis was performed to determine what reduction in DAA drug price would be needed for the pharmacist-led pathway to have a 50% or 80% probability of being cost-effective at a £30,000 WTP threshold, and 80% probability of being cost-saving. Further sensitivity analyses were also conducted to test assumptions on: background treatment rate of 7% (none or double the baseline rate), average cohort age of 40 years (20 younger or 10 years older), injecting duration of 11.5 years (5 or 30 years), healthcare management costs (no costs pre-cirrhosis or double all healthcare costs), and 3.5% discount rate (none or double the baseline rate). Model results are presented as the median and 95% uncertainty interval (UI) of 1000 model simulations. All model analyses were performed in MATLAB (version 2021a).

**Role of the funding source**

Funders had no role in the study design; collection, analysis, or interpretation of data; the writing of this report; or the decision to submit for publication.

**Results**

**Within trial period analysis**

The mean total cost of testing and treatment per pharmacy was higher in the pharmacist-led arm (£153,847) than the conventional care arm (£82,565) (Supplementary Table S2). Costs incurred varied considerably between pharmacies within each pathway. At the pharmacy level, mean testing/assessment costs per pharmacy were £138, £335, and £53 for opportunistic DBST, assessment bloods, and SVR12 DBST, respectively, in the pharmacist-led arm and £87, £167, and £25 in the conventional care arm, with the increase in cost per pharmacy being a result of higher testing rates. The mean cost of pharmacist time per pharmacy was £2,567 in the pharmacist-led arm and £1,322 in the conventional care arm, the higher cost being due to higher testing rates and the pharmacist’s role in treatment assessment in the pharmacist-led arm. The mean cost per OAT patient was £3,674 in the pharmacist-led arm and £1,965 in the conventional care arm. The mean cost per patient initiating treatment was £863 in the pharmacist-led arm and £404 in the conventional care arm.

Total pathway costs were dominated by drug treatment costs at a mean cost per pharmacy of £150,580 and £80,858 for the pharmacist-led and conventional care arms respectively. The major factor causing this difference is that more OAT patients agreed to testing and treatment in the pharmacist-led arm.

The estimated incremental mean cost per OAT patient achieving SVR12 was £39,094 (95% CI: £22,733, £50,330). Sensitivity analy-
Table 1
Projected costs and QALYs from the Markov model for the pharmacist-led intervention and convention care pathways. Costs and outcomes are discounted at 3.5% per annum.

<table>
<thead>
<tr>
<th>Drug list price</th>
<th>Costs (£ millions)</th>
<th>QALYs</th>
<th>ICER</th>
<th>Probability cost-effective</th>
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<td>7450.0</td>
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<td>£31,612</td>
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<td></td>
<td></td>
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<td>–</td>
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<td>260.9</td>
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</table>

Fig. 1. Varying re-infection rate. Probabilistic sensitivity analyses showing the effects on (A) the cost-effectiveness plane, and (B) the cost-effectiveness acceptability curve (CEAC) of varying the re-infection rate. Plots show: (i) base case (12.1 per 100 person-years [py]), (ii) 8 per 100py, (iii) 5 per 100py, and (iv) 2 per 100py. Costs and QALYs are discounted at a rate of 3.5% per annum. Time horizon is 50 years. Results are for 1000 model simulations.

Long-term analysis

Over a 50-year time horizon, assuming list treatment drug price and high re-infection rates, the pharmacist-led pathway had an ICER of £31,612 per QALY gained, with a 44.3% probability of being cost-effective at a £30,000 willingness-to-pay threshold (Table 1). However, HCV drugs in the UK and many other countries are not provided at list price. Sensitivity analyses varying re-infection rates suggest that lower rates improve the ICER, with rates of 8/100py, 5/100py, and 2/100py lowering the ICER to £25,373, £18,917, and £12,881 per QALY gained with a 70.9, 90.6, and 98.6% probability of being cost-effective (Fig. 1). Sensitivity analyses considering realistic discounts on drug price led to substantial reductions in the ICER and increases in the probability of being cost-effective. While a 30%/60% discount improves the ICER to £21,027/£10,220 per QALY gained with a 79.5%/98.3% probability of being cost-effective, a 90% discount in drug price results in a negative ICER of £501 per QALY gained which has a 100% probability of being cost-effective at the £30,000 willingness-to-pay threshold and a 62.3% probability of being cost-saving (Fig. 2). Threshold analyses suggest that the pharmacist-led pathway has a 50% and 80% probability of being cost-effective if DAA drug prices are discounted by 4.9% (£37,100 for 12-weeks) and 30.8% (£27,000 for 12-weeks), respectively, and an 80% probability of being cost-saving if DAA drug prices are discounted by 92.3% (£3,000 for 12-weeks) (Fig. 3).

Additional sensitivity analyses (Fig. 4) suggest that a bigger time discount rate (7% instead of 3.5%) and shorter time horizon (25 years instead of 50 years) cause a large increase in the ICER for the pharmacist-led pathway compared to the conventional pathway, to £60,524 and £53,550 per QALY gained, respectively. Moderate increases in the ICER are associated with assuming longer injecting duration (30 years instead of 11-5 years), older age of the cohort (10 years older), not including healthcare management costs, and no background treatment rate after the first year. Conversely, no discount rate reduces the ICER to £16,058 per QALY gained, while smaller decreases in the ICER occurred for a shorter injecting duration, younger cohort age, higher healthcare management costs, and higher background treatment rate.
Discussion

Key findings

This study highlighted the impact alternative strategies of testing and treatment can have on both uptake and costs. The implementation of the pharmacist-led pathway resulted in higher uptake of testing and treatment for HCV, and thus costs incurred. Our analysis suggests that the pharmacist-led pathway could be cost-effective with moderate reductions in drug price (achieved in many countries and existing contracts). Reductions in HCV re-infection rates – that were high during the trial – would also improve cost-effectiveness. The critical success factor was the increased diagnoses and acceptance of treatment (with high statistical significance). Drug treatment cost was found to be the greatest cost incurred within both arms and is responsible for most of the increase in cost associated with the pharmacist-led arm, due to getting more people onto treatment. The difference in costs are reduced substantially and the probability of the new pathway being cost-effective increases considerably after taking into account moderate reductions in drug price.

Fig. 2. Varying DAA prices. Probabilistic sensitivity analyses showing the effects on (A) the cost-effectiveness plane, and (B) the cost-effectiveness acceptability curve (CEAC) of varying the price of DAAs. Plots show: (i) base case, (ii) 30% reduction in price, (iii) 60% reduction in price, and (iv) 90% reduction in price. Costs and QALYs are discounted at a rate of 3.5% per annum. Time horizon is 50 years. Results are for 1000 model simulations.

Fig. 3. Relationship between DAA prices per 12-week course and cost-effectiveness of the pharmacist-led pathway. Sensitivity analysis showing the effect of different DAA medication costs (for 12 weeks) on the modelled incremental cost-effectiveness ratio (ICER) of the pharmacist-led pathway compared to the conventional pathway. Results are for 1000 model simulations for each sensitivity analysis.

Fig. 4. Sensitivity analyses on the incremental cost-effectiveness ratio (ICER). Probabilistic sensitivity analyses showing how different assumptions change the incremental cost-effectiveness ratio (ICER) of the pharmacist-led pathway compared to the conventional pathway. Results are for 1000 model simulations for each sensitivity analysis.
Comparison with the literature

The cost-effectiveness of routine HCV screening and treatment has been shown in a range of settings, including emergency departments,18 antenatal care,19, and primary care.20 Additionally, the findings of this study are consistent with those of other interventions aimed specifically at increasing testing and treatment uptake. In an RCT in a primary care setting a complex intervention that aimed to increase patient awareness and identify high-risk patients was found to be cost-effective at increasing testing and treatment uptake.21 Drug treatment costs were notably lower, with our analysis also showing cost-effectiveness at similar drug prices. A systematic review of economic evaluations of HCV screening found that case-finding of PWID had a range of cost-effectiveness, from £2,333 to £28,120 per quality-adjusted life years (QALY) gained, when compared with no screening22 and a Belgian study has shown the cost-effectiveness of case-finding for HCV in PWID.23 Other cost-utility analyses of case-finding for HCV in PWID in the UK, which unlike our analysis used dynamic models capturing the impact of reduced onward transmission, found case-finding and the use of DBSTs to be cost-effective in specialist addiction services.24,25

A study assessing the cost-effectiveness of new community-based HCV strategies in PWID (within substance misuse services, needle exchanges, and community pharmacies) also highlighted the impact alternative strategies can have on cost-effectiveness and supports the cost-effectiveness of community pharmacy-based testing, similarly finding drug price to be the main driver of cost-effectiveness.26 The impact on uptake and cost-effectiveness that alternative HCV treatment strategies can have in PWID has also been shown using data from a RCT comparing primary and secondary care treatment with DAAs.20 One study assessing the cost-effectiveness of testing high-risk groups for HCV in community pharmacies using DBSTs found the strategy to be cost-effective, however, although still cost effective, the intervention was less efficient in PWID.27 One reason given is the lower rate of engagement in PWID, highlighting the importance of increasing testing uptake in this population. As was found in our analysis, at higher drug price discounts testing was found to be likely cost-saving.

Strengths and weaknesses of the study

The cRCT had a large sample size, recruiting 55 pharmacies with 2718 OAT patients, initiating 172 patients onto treatment. However, as this was a retrospective cost-effectiveness analysis not all necessary data were collected, so an individual level analysis was not possible. Specifically, the number of treatment assessment PCR tests per pharmacy was not available, with many patients having already had existing PCR results within 6 months, so a pathway average cost had to be applied. This requires the assumption that the PCR positive rate and drop-out rate was the same across pharmacies within each pathway. The cost of nurse travel to the pharmacies in the pharmacist-led pathway was included in the analysis, however as we conducted the analysis from the healthcare provider perspective, patient travel costs in the conventional pathway travelling to the treatment centre were not included. If patient travel costs had been included, the pharmacist-led pathway would have been more cost-effective given the typically closer proximity of the community pharmacy. The higher uptake of testing and treatment in the pharmacist led pathway may be, in part, due to the lower cost and greater convenience of receiving all care at the community pharmacy.28

Alternative drugs used in the treatment of HCV have similar prices to sofosbuvir/ledipasvir used in this study. Additionally, the effect that varying drug discount rates have on cost-effectiveness has been presented, so the results are applicable across differing drug choices and discount rates that healthcare providers may negotiate. Our cost-effectiveness model of long-term impact did not take account of changes in treatment uptake over time or secondary prevention (averting onward transmission in people successfully treated) – so our estimates of cost per QALY are likely to be conservative as a proportion of the study population are likely to be current injectors and at risk of transmitting infection to others. Reimbursement fees paid to pharmacies, which vary locally, were also not included. However, given the dominance of the much larger drug price, fees are likely to have a minimal impact on the ICER and probability of the pharmacist-led pathway being cost-effective. Accounting for the reduction in onward transmission due to HCV treatment can sometimes improve cost-effectiveness.29,30

Implications for policy and research

The identification and treatment of high-risk and hard to reach groups like PWID is essential if WHO elimination targets are to be reached. This study has demonstrated that streamlining diagnostic and treatment pathways can encourage the uptake of testing and treatment in PWID, leading to improvements in the rate of SVR12. The cost per QALY gained has been presented for a range of drug price discounts, allowing healthcare providers to apply these results locally to aid in policy decision making. This study has provided evidence that a pharmacist-led diagnostic and treatment strategy is, at realistic drug price discounts, highly likely to be cost-effective at increasing the uptake of testing and treatment of HCV in PWID. As such, pharmacist-led testing and treatment should be scaled up to reach patients in these settings.

Conclusion

While the increased diagnostic costs are low, the cost-effectiveness of the new pathway is highly dependent on drug prices and on re-infection rates. At drug list price the new pharmacist-led pathway may not be cost-effective, however at realistic drug discount rates the new pathway has been shown to be cost-effective.

Data sharing

Applications from researchers for access to the anonymised dataset for their research will be considered, requiring approval from the chief investigator and funders.

Declaration of Competing Interest

AR received grants from Gilead and Bristol-Myers Squibb during the study and received grants from Roche and AbbVie outside the study. JFD received grants from the Scottish Government Department of Health, Gilead, and Bristol-Myers Squibb during the study; and AbbVie, MSD, Janssen, Roche, and Genedrive outside the study. All other authors declare no competing interests.

CRediT authorship contribution statement

G. Myring: Formal analysis, Writing – original draft, Writing – review & editing. A.G. Lim: Formal analysis, Writing – original draft, Writing – review & editing. W. Hollingworth: Formal analysis, Writing – review & editing. H. McLeod: Writing – review & editing. L. Beer: Writing – review & editing. P. Vickereman: Formal analysis, Writing – review & editing. M. Hickman: Writing – review & editing. A. Radley: Writing – review & editing. J.F. Dillon: Writing – review & editing.
Acknowledgments

GM and HM are funded, and WH partly funded, by the National Institute for Health and Care Research Applied Research Collaboration West (NIHR ARC West). AGL and PV acknowledge support from the NIHR Health Protection Research Unit in Behavioural Science and Evaluation at the University of Bristol.

Supplementary materials


References