

# Assessing the impact and cost-effectiveness of needle and syringe provision and opioid substitution therapy on hepatitis C transmission among people who inject drugs in the UK: an analysis of pooled data sets and economic modelling

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## Scientific summary

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# Scientific summary

## Background

Although there is good evidence that needle and syringe programmes (NSPs) and opioid substitution therapy (OST) in combination reduce injecting risk behaviours and some evidence to show the impact on the incidence of human immunodeficiency virus (HIV), there is little evidence of their impact on hepatitis C virus (HCV) incidence among people who inject drugs (PWID). There had been no economic evaluations of NSPs undertaken in Western Europe, and few studies have considered the costs saved as a result of care and treatment being averted. In addition, previous existing studies relied on weak measures of NSP effectiveness. The aim of this project was to provide evidence on the probable impact of existing coverage levels of NSPs and changes in the extent of provision in preventing HCV infection incidence, and to assess the costs and cost-effectiveness of current NSPs provision and increasing coverage on HCV infection transmission among PWID.

## Objectives

The project answered the following research questions (RQs):

1. What is the impact of different coverage levels of NSP provision on the incidence of HCV infection among PWID?
2. What is the contribution of other risk factors to HCV infection incidence and the overall transmission of HCV infection among PWID?
3. What is the international evidence on the impact of NSPs with and without OST on the incidence of HCV infection among PWID?
4. What are the costs associated with existing NSP provision in three UK settings?
5. What is the impact and cost-effectiveness of existing provision of NSPs, compared with no provision, on HCV infection and HIV transmission and disease burden among PWID in three UK settings?
6. What are the possible strategies by which to increase the coverage of NSP provision in three UK settings, and the probable impact and cost-effectiveness of these strategies?

## Methods

Three linked data collection activities and the following analyses were undertaken:

1. Systematic review (RQ3).  
We conducted a Cochrane-registered systematic review of published studies and unpublished analyses that report on the effect of NSP exposure and/or OST on HCV infection incidence (Platt L, Reed J, Minozzi S, Vickerman P, Hagan H, French C, *et al.* Effectiveness of needle/syringe programmes and opioid substitution therapy in preventing HCV infection transmission among people who inject drugs. *Cochrane Database Syst Rev* 2016;**1**:CD012021). Risk of bias for published non-randomised studies was assessed using the ACROBAT-NRSI tool (A Cochrane Risk Of Bias Assessment Tool: for Non-Randomized Studies of Interventions), developed by the Methods Groups of Cochrane. Risk of bias was not assessed for the unpublished studies included in the review. We conducted a meta-analysis to estimate the unadjusted effects of NSP exposure and/or OST on HCV infection incidence. Meta-analysis was conducted using random-effects models, pooling univariable and multivariable models separately. We examined heterogeneity with the  $I^2$ -statistic and explored reasons for heterogeneity using univariable random-effects metaregression.

## 2. Analysis of pooled data (RQ1 and RQ2).

We collated six data sets previously used in a pooled analysis, for which the methods have been published previously. We added an additional three data sets, namely a community survey of PWID in Bristol ( $n = 336$ ), Public Health England's Unlinked Anonymous Monitoring Programme (UAMP) survey from England and Wales ( $n = 3408$ ) and the Australian Needle Syringe Programme Survey ( $n = 2391$ ), and we replaced one of the studies with updated data from Public Health Scotland's Needle Exchange Surveillance Initiative ( $n = 6988$ ), adding in an additional 6041 individuals. All sources contained comparable indicators on intervention use and new cases of HCV infection, except for UAMP, from which 1567 antibody-negative dried-blood spots were tested. A total of 14,734 observations were included, of which 7173 were anti-HCV negative and 185 were recent infections. The pooled data sets were analysed using logistic regression to model the odds of recent infection by NSP and OST exposure, adjusting for key confounders (injecting duration, sex, crack cocaine use and experience of prison) and assessing the joint effects of NSPs and OST. We combined the findings of the pooled analysis with the results of the systematic review in a meta-analysis.

An internationally standardised measure of an individual's NSP coverage was used, which was defined as the percentage of injections for which a new needle had been obtained (calculated as the average number of new needles obtained divided by the average number of injections). Binary measures of NSPs and OST were combined to form a measure of harm reduction coverage with four categories: (1) full harm reduction (on OST and  $\geq 100\%$  NSP coverage), (2) partial harm reduction (on OST and  $\leq 100\%$  NSP coverage), (3) partial harm reduction (no OST,  $\geq 100\%$  NSP coverage) and (4) minimal harm reduction (no OST,  $< 100\%$  NSP coverage).

## 3. Economic evaluation (costing analysis and cost-effectiveness analysis; RQ4 and RQ5).

We collected cost data from three cities in the UK for the financial year 2013–14. Sites were selected through a combination of convenience sampling based on the availability of impact data for the cost-effectiveness analysis, existing relationships with service managers and the feasibility of conducting a costing study. We collected cost data for three fixed sites, six pharmacies and three 'other' modalities (a mobile outreach service, a drop-in centre and an out-of-hours pharmacy). For pharmacies, only a subsample was costed in detail owing to the existence of multiple pharmacy NSPs in each setting. Data were collected through staff interviews, the review of service statistics and financial reports. We estimated the total and unit economic costs for distributing clean needles to PWID. Our approach to costing was incremental to existing services and was particularly focused on needle and syringe exchange. We followed standard methods for costing in an economic evaluation of a health intervention; we include all costs regardless of the payer and estimated a 'shadow cost', whereby the price does not accurately represent the value of resources. We estimated the cost-effectiveness of current NSP provision compared with no provision. Findings were fed back to collaborators and NSP staff to discuss plausibility as well as strategies to increase intervention coverage. For all analyses, health benefits [quality-adjusted life-years (QALYs)] and costs (health-care provider perspective) were attached to each HCV disease stage and we used recently published utility weights for injectors. Economic model results are presented as incremental cost-effectiveness ratios (ICERs) and probabilistic uncertainty analyses were used to estimate the uncertainty around the ICER, as well as the probability that the intervention is cost-effective at different willingness-to-pay (WTP) thresholds.

## 4. Modelling impact (RQ4–6).

An existing dynamic deterministic model of HCV infection transmission and OST/NSP intervention coverage among PWID was adapted. Intervention efficacy estimates were taken from the pooled analysis. The model fits were used to estimate the impact of historical and current NSP coverage levels for reducing HCV infection prevalence and disease burden in that setting, as well as the future impact of increasing or decreasing NSP coverage levels. The model estimated the contribution of different behavioural risk factors (e.g. homelessness and crack cocaine use) for increasing HCV infection transmission in these settings. All analyses focused on three settings (Bristol, Dundee and Walsall), which were selected based on varying levels of HCV infection prevalence and the availability of detailed behavioural data.

Patient and public involvement included an advisory group consisting of members of the National Needle Exchange Forum (a virtual network), Addaction (London, UK) and the Hepatitis C Trust (London, UK), who were consulted on all aspects of the study design and emerging findings. Preliminary findings of the pooled analysis and the costing analysis were also presented at the annual meeting of the National Needle Exchange Forum (a virtual network), attended by NSP employees and service users.

## Results

### Systematic review

In the systematic review we identified 28 studies (21 published, 7 unpublished) from 5670 records from North America ( $n = 13$ ), the UK ( $n = 5$ ), Europe ( $n = 4$ ), Australia ( $n = 5$ ) and China ( $n = 1$ ), comprising 1736 HCV incident infections and 6513.04 person-years of follow-up. Overall HCV incidence ranged between 0.09 and 42 cases per 100 person-years across the studies. Only two studies were judged to be at moderate overall risk of bias, 12 were judged as being at serious risk of bias and seven were judged as being at critical risk of bias; seven unpublished data sets were not assessed. Findings suggest that current OST (from 12 studies across all regions) reduces the risk of HCV infection acquisition by 50% [rate ratio (RR) 0.50, 95% confidence interval (CI) 0.40 to 0.63;  $I^2 = 0\%$ ;  $p = 0.89$ ]. This effect was maintained in sensitivity analyses excluding unpublished data sets or papers judged to be at critical risk of bias. We found no evidence of differential impact by the proportion of female participants in the sample, region of study, main drug used, history of homelessness or experience of prison. Weaker evidence was found for high NSP coverage derived from seven studies from North America and Europe only (RR 0.77, 95% CI 0.38 to 1.54) with high heterogeneity ( $I^2 = 78.8\%$ ;  $p < 0.001$ ). This effect remained consistent in sensitivity analyses. After removing studies from North America, high NSP coverage in Europe was associated with a 56% reduction in HCV infection acquisition risk (RR 0.44, 95% CI 0.24 to 0.80) with less heterogeneity ( $I^2 = 12.3\%$ ;  $p = 0.337$ ). There was moderate evidence for the impact of combined high coverage of NSPs and OST from four studies, resulting in a 71% reduction in the risk of HCV infection acquisition (RR 0.29, 95% CI 0.13 to 0.65).

### Pooled analysis

Findings from the pooled analysis suggested that in unadjusted analysis, PWID currently using OST had a 65% reduced odds of HCV infection [odds ratio (OR) 0.35, 95% CI 0.26 to 0.48]. High coverage with needles/syringes ( $\geq 100\%$ ) was not significantly associated with reduced odds of HCV infection (OR 0.83, 95% CI 0.60 to 1.16). Adjusting for the confounding effects of sex, experience of prison or injecting crack cocaine did not alter the intervention effects. When examining the effects of combined harm reduction interventions, the risk of new HCV infection was more than halved (54%) among those on full harm reduction, defined as receiving OST and  $\geq 100\%$  NSP coverage [adjusted odds ratio (AOR) 0.44, 95% CI -0.27 to 0.71], compared with those on minimal harm reduction (no OST,  $\leq 100\%$  NSP coverage). There were reduced odds of HCV infection acquisition among those on partial harm reduction [i.e. those exposed to high NSP coverage but not on OST (AOR 0.59, 95% CI 0.36 to 0.96)] and a higher effect for those on OST but with low NSP coverage (AOR 0.59, 95% CI 0.36 to 0.96). Full harm reduction compared with minimal exposure reduced the risk of injecting with a used needle/syringe by 50% (AOR 0.48, 95% CI 0.38 to 0.62), reduced reuse of the same needle/syringe for injecting by 40% (AOR 0.59, 95% CI 0.40 to 0.88) and reduced the frequency of injecting (AOR -41.2, 95% CI -45.5 to -38.0). There was weaker evidence for an association with injecting site infections or shared used of filters and spoons for drug preparation. Full harm reduction was associated with twice the odds of testing for both HCV infection and HIV (AOR 1.9, 95% CI 1.56 to 2.23 and AOR 1.9, 95% CI 1.6 to 2.20, respectively). Combining estimates of NSP effectiveness from the systematic review with two data sets not already represented in the review indicated that high NSP coverage reduced the risk of HCV infection acquisition by 39% (RR 0.61, 95% CI 0.43 to 0.87) with moderate heterogeneity ( $I^2 = 30\%$ ;  $p = 0.189$ ).

### Costing analysis and cost-effectiveness

We observed a degree of variation in costs across the three different commissioning areas evaluated, and variation in costs and outputs was observed across fixed sites and pharmacies. The primary cost driver in

most settings was the cost of supplies; this accounted for an average of 60% of total costs across sites (range 23–80%). This was followed in most cases by administrative and overhead costs, which accounted for 6–45% of total costs. There was some considerable uncertainty in our estimates owing to the fact that cost and output data on NSP distribution are not routinely collected within the UK. The unit cost per opioid needle distributed varied from £0.21 to £1.65, and the unit cost per opioid client (annually) varied from £19.01 to £124.13. Some fixed sites handled a larger number of image and performance enhancing drug users, resulting in a greater cost per opioid client; however, there was no clear distinction in the unit cost per opioid needle between modes of distribution.

Overall, we found that needle and syringe exchange services are highly likely to be cost-effective at almost any WTP threshold and are, in fact, cost-saving in some settings, despite some uncertainty in total outputs. In Dundee the large majority of iterations from the model were cost-saving, and in both Bristol and Walsall, the large majority of iterations were considerably below a WTP threshold of £13,000 per QALY gained. The difference in cost-effectiveness between cities is partly driven by the population size of PWID and the HCV infection prevalence in each study setting. Walsall had the smallest city-wide population of PWID, so a reduction in infections and deaths had less of an overall impact on cost-effectiveness. These cost-effectiveness estimates do not reflect the substantial gains from averting other health problems associated with injecting drug use, including HIV and other infections. Previous research has indicated that NSPs are highly effective in averting HIV infection; incorporating these health gains would substantially improve cost-effectiveness.

### Impact modelling

Findings from the impact modelling suggest that removing OST (current coverage 81%) and NSPs (coverage 56%) in Bristol would increase HCV infection incidence by 329% [95% credible interval (CrI) 110% to 953%] by 2031 and at least double (132% increase, 95% CrI 51% to 306%) the number of new infections over the next 15 years. In Dundee, which has the second highest NSP coverage (49%) of the three settings, removing NSP would result in a 61% increase (95% CrI 12% to 219%) in new infections, whereas removing OST (coverage 70%) alone would result in a 129% (95% CrI 43% to 543%) increase. Increasing NSP coverage to 80% has the largest impact in Walsall, which has the lowest current NSP coverage (28%), resulting in a 27% decrease (95% CrI 7% to 43%) in new infections and a 41% decrease (95% CrI 11% to 72%) in incidence by 2031 compared with 2016. Increasing NSP coverage to 80% results in an approximately 4% absolute drop in prevalence over 15 years in all settings owing to the slow turnover of the population of PWID. Findings show that experience of homelessness and crack cocaine injection increase transmission risk and, if these factors are removed, this could avert approximately 60% of HCV infections over the next 15 years.

### Conclusions

There is evidence from both the systematic review and the pooled analysis that current use of OST compared with no intervention reduces the risk of HCV infection acquisition. The intervention effect from the systematic review is strong but the evidence is considered to be of low quality because it is derived from observational studies with serious risk of bias. This is in part attributable to the ACROBAT-NRSI risk-of-bias assessment tool that we used, which compares study designs to randomised controlled trials as a gold standard rather than assessing studies on their own merit. Findings from the review show weak and low-quality evidence that NSP exposure reduces the risk of HCV infection acquisition, but with regional variation and with a strong effect observed in Europe, as well as less heterogeneity across the studies. Findings from both the review and pooled analysis suggest that the impact of combined high coverage of NSPs and OST was greater. Findings show difficulties in measuring NSP coverage, most probably as a result of misclassification of intervention coverage. Policies to ensure that NSPs can be accessed widely alongside the provision of OST are needed, and obstacles preventing the concurrent use of both NSPs and OST could be removed to maximise the reduction in HCV infection transmission. NSPs are cost-saving interventions in some sites and cost-effective in others. Despite variations in coverage, NSPs and OST are probably

preventing considerable HCV infections in the UK. Increasing NSP coverage will have the most impact in settings with low coverage. Scaling up other interventions, such as HCV infection treatment, are needed to decrease epidemics to low levels in higher-prevalence settings. Further research is needed to improve our understanding of the mechanisms through which NSPs and OST achieve their effect, and of the optimum contexts to support their implementation.

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