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MAJOR ARTICLE

Modelling the Impact and Cost-effectiveness of Extended Hepatitis C Virus Screening and Treatment with Direct-acting Antivirals in a Swiss Custodial Setting

François Girardin,[1] Natalie Hearmon,[2] Erika Castro,[3] Francesco Negro,[4] Lucy Eddowes,[2] Laurent Gétaz,[5,6] and Hans Wolff[5]

[1]Medical Direction and Division of Clinical Pharmacology and Toxicology, Geneva University Hospitals, University of Geneva, Switzerland; [2]Costello Medical, Cambridge, United Kingdom; [3]Center for Addiction Medicine, Service of Community Psychiatry, Department of Psychiatry, University Hospital of Lausanne, [4]Divisions of Gastroenterology, Hepatology, and Clinical Pathology, [5]Division of Prison Health, and [6]Division of Tropical and Humanitarian Medicine, Geneva University Hospitals, University of Geneva, Switzerland

Background. Hepatitis C virus (HCV) among people living in detention (PLD) is typically high in many countries including Switzerland, where it is estimated that the HCV prevalence rate is between 5.7% and 6.2%. In Switzerland, the existing screening strategy involves routine screening of PLD who indicate they are from HCV high-risk populations based on questionnaire responses upon entry to the detention center, rather than an offer to screen all PLD.

Methods. A cost-effectiveness analysis from a Swiss healthcare provider perspective was conducted by combining a 5-year decision tree screening model with results from a Markov model of HCV treatment outcomes. This model explored the cost-effectiveness of increased HCV screening to cover all PLD compared to the current approach, using a standard test package and subsequent treatment with a single-tablet regimen in Swiss custodial settings. Sensitivity and scenario analyses examined the uncertainty of results.

Results. At the willingness-to-pay threshold of 100 000 Swiss Francs (CHF) per quality-adjusted life-year (QALY), comprehensive general screening was cost-effective compared to current risk-based screening, with a base case incremental cost-effectiveness ratio of CHF 14 312 per QALY. The net monetary benefit of screening the whole PLD population was CHF 23 298 046 and CHF 4298 per person. The proportion of PLD tested was predicted to increase from 13.6% to 67.0% under comprehensive screening.

Conclusion. The results showed that comprehensive screening strategies in detention centers in Switzerland can be cost-effective, with the probabilistic sensitivity analysis estimating an 82.3% probability of cost-effectiveness.

Keywords. cost-benefit analysis; hepatitis C; mass screening; prisons; antiviral agents.

Hepatitis C virus (HCV) affects approximately 71 million people globally and is responsible for 399 000 deaths each year, primarily due to cirrhosis and hepatocellular carcinoma [1]. HCV infection is common among people living in detention (PLD) in many countries, with an estimated global prevalence of 15.1% [2]. Each year, approximately 30 million people spend time in some form of detention [3].

In Switzerland, the HCV antibody prevalence is 0.71% among the general population [4], and the prevalence of HCV among PLD ranges between 5.7% and 6.2% [5, 6]. This is due to the large proportion of high-risk groups such as people who inject drugs (PWID) and those from countries where HCV is endemic [7, 8]. In the canton of Geneva, which has an estimated adult population of 395 000, 1789 adults are incarcerated each year [9, 10], and it is estimated that 4.1% of these are infected with HCV [6]. If infected PLD are identified, they can be treated, which could reduce the disease burden of HCV.

In detention centers across Switzerland, the existing screening strategy involves routine screening of PLD identified as from high-risk populations for HCV (such as PWID and people with tattoos), based on their responses to a questionnaire upon entry to detention [5, 11, 12]. However, different regional health resources mean screening is available more widely in some detention centers across Switzerland, such as Geneva. A comprehensive screening strategy, offering HCV screening to all PLD, would aim to increase the number of HCV RNA-positive patients identified and linked to treatment with direct-acting antivirals (DAA).

The proposed comprehensive screening strategy would require additional funding. Therefore, to assess whether this comprehensive strategy offers sufficient health gains, and potential long-term savings to payers that justify additional screening costs, it is necessary to evaluate the cost-effectiveness of increased screening.

HCV prevalence varies in detention centers across Switzerland, one reason being the different countries of origin of PLD. For example, HCV prevalence among PLD from European countries is

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Correspondence: F. Girardin, Medical Direction and Division of Clinical Pharmacology and Toxicology Geneva University Hospitals, University of Geneva, Geneva, Switzerland (francois.girardin@hcuge.ch).

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estimated to be 10.9% [13], but is 2% amongst PLD from Africa and Latin America [14]. The typical length of incarceration also varies between detention centers, which could affect the likelihood of PLD completing their treatment course before release. Although this model was developed using data from Champ-Dollon, a pretrial detention center in Geneva canton with typically short incarceration periods, variation in sentence durations and prevalences at other detention centers was accounted for through sensitivity and scenario analyses.

This model explored the cost-effectiveness of increased HCV screening compared to the current approach, using a standard test package and treatment with a single tablet regimen in Swiss custodial settings.

MATERIALS AND METHODS

A cost-effectiveness analysis was conducted by combining a de novo decision tree screening model with results from a published model of HCV treatment [15]. The decision tree simulated the pathway from screening to diagnosis (Figure 1) and a variety of uptake and outcome probabilities determined the proportions of the detention center population in each branch of the decision tree.

Target Population and Screening Strategies

The target population size was 5421, the number of people in Switzerland living in detention for more than one month. This was calculated from the proportion of those entering Swiss detention centers in 2015 who were incarcerated for more than 1 month and was assumed to represent the proportion of PLD who would be eligible to begin and complete treatment. The starting age was based on the mean age of the Champ-Dollon (CD) detention center population in 2007 [5].

The comparator used in the model was the current risk-based screening strategy in Swiss detention centers, whereas the intervention was the comprehensive screening strategy of screening all PLD.

Model Structure and Perspective

The cohort decision tree screening model was developed de novo to simulate HCV screening in custodial settings in Switzerland. The eligible screening population was assumed to be the whole target population, irrespective of whether or not they had been diagnosed as HCV RNA-positive or were aware of their status. In addition, a proportion of PLD were assumed to reject the screening invitation. Similarly, for PLD that did participate, it was assumed that a proportion may not collect their test results. A disutility was applied to all PLD finishing the diagnosis process with a positive test result, to represent the negative effect this would have on a person's quality of life [16, 17].

PLD diagnosed as HCV RNA-positive may choose whether to receive treatment, with those accepting treatment receiving the costs and quality-adjusted life-years (QALYs) associated with HCV treatment from the treatment model. Patients dropping out of the screening pathway before a confirmed diagnosis was made (due to lack of diagnosis, ineligibility, or contraindication) were split into HCV RNA-positive and HCV RNA-negative cohorts, according to the underlying disease prevalence at that point in the diagnostic process. Within this group, HCV RNA-positive patients received the costs and QALYs associated with natural disease progression in the treatment model, whereas HCV RNA-negative patients solely added to the diagnosis costs of the screening model, and accrued QALYs over the treatment model time horizon.

The same tests were assumed to be used for both the current and comprehensive screening arms: a 3rd-generation enzyme-linked immunosorbent assay test and quantitative polymerase chain reaction RNA test. These were offered together as a test package, and the combined sensitivity and specificity of the tests was assumed to be 1 due to their high performance [18], so that there were no false positives from this stage of the diagnostic process. However, patients in the seroconversion window when tested could receive a false-negative diagnosis.

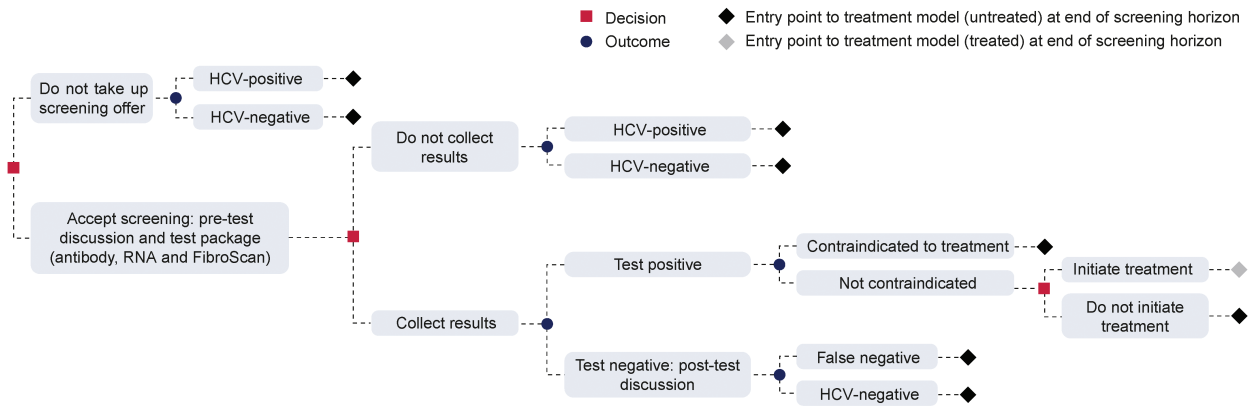

Figure 1. Screening decision tree. Abbreviations: HCV, hepatitis C virus; RNA, ribonucleic acid.

Repeat screening was not considered in the base case despite the high ongoing likelihood of infection, due to the transient nature of detention center populations. The screening model took the healthcare provider's perspective, the Department of Employment, Social Affairs, and Health, at the canton level in Switzerland.

Model Inputs

Model inputs were derived from discussions with clinical and custodial services experts, published and unpublished data and literature reviews (targeted and systematic). Results from Scott et al (converted from AUD to Swiss Francs [CHF] at a rate of 1 AUD = 0.76 CHF), a model of HCV treatment of PWID [15], were included to predict treatment effects and natural disease progression. Scott et al also reported the lifetime costs (including treatment acquisition, resource use and monitoring costs) associated with HCV treatment and no treatment [15]. The aforementioned inputs are shown in Table 1 with other key model inputs.

Population inputs are listed in Supplementary Tables 1 and 2 and were sourced from targeted literature searches. The screening test inputs and assumptions are described in Supplementary Table 3, and the uptake probability inputs for both screening programs are shown in Supplementary Table 4; these were informed by clinical expert opinion. Age-dependent utility and mortality rate inputs (Supplementary Table 5) were sourced from targeted literature searches and the Swiss Federal Statistical office, respectively. This treatment model was chosen because PWID more closely align with PLD than alternative models available. "Early-treatment", defined as treatment following initial infection, and "no treatment" cost and outcome scenarios were used in the base case.

Table 1. Key Inputs Used in the Model

Input	Value	Source
Eligible population size	5421	Assumed–expert opinion
Pre-seroconversion window (years)	0.140	Page-Shafer et al 2008 [28]
Male proportion	95.0%	Wolff et al 2011 [5]
HCV antibody prevalence	5.70%	Wolff et al 2011 [5]
HCV incidence (infections per 100 person years of exposure)	1.70	Dolan K et al 2016 [2]
Spontaneous clearance rate	19.7%	Grebely et al 2014, weighted by genotype prevalence [29]
Probability of cure for treated individuals	96.5%	Gilead model (unpublished data)
Proportion who present for testing (current screening)	13.6%	CD detention center data (unpublished data)
Proportion who present for testing (comprehensive screening)	67.0%	Expert opinion, based on CD detention center data (unpublished data)
Initial HCV RNA prevalence ratio (current compared to comprehensive screening populations)	2.74	CD detention center data (unpublished data)
Test offer and voluntary counselling cost (regardless of uptake)	CHF 49.55	TARMED TM000010 + 3X TM000030 [30]
Pre-test discussion cost	CHF 8.26	TARMED TM000030 [30]
Cost of 3rd-generation ELISA test	CHF 17.40	OFAS Code 3068.00 [31]
Cost of communicating results, HCV RNA-negative (including appointment and post-test discussion if relevant)	CHF 0.00	Assumed
Cost of communicating results, HCV viremia-positive (including appointment and post-test discussion if relevant)	CHF 90.84	TARMED TM000010 + TM000020 + TM000030 [30]
Cost of RNA test	CHF 180.00	OFAS Code 3072.00 [31]
Cost of FibroScan (including consultation)	CHF 83.62	TARMED TM393270 + TARMED TM000010 + 3× TM000030 [30]
Cost of genotyping if HCV RNA-positive	CHF 180.00	OFAS Code 3073.00 [31]
Cost of GP visits to carry out tests	CHF 115.62	TARMED TM000010 + TM000020 + TM000030 [30]
Cost of counselling and harm reduction advice	CHF 115.62	TARMED TM000010 + TM000020 + TM000030 [30]
Disutility of HCV RNA-positive result (true or false)	0.02	Based on estimate by Singer and Younossi. 2001 [16] (from Rodger 1999) [17]
Target population utility (HCV RNA-positive)	0.709	Chong et al 2009 [32]
Target population utility (HCV RNA-negative)	0.729	Chong et al 2009 [32]
Lifetime treatment cost per person of no treatment	CHF 16 627	Scott et al 2016 [15]
Lifetime treatment cost per person of early treatment	CHF 57 610	Scott et al 2016 [15]
Lifetime treatment cost per person of late treatment	CHF 28 127	Scott et al 2016 [15]
QALYs per person of no treatment	16.45	Scott et al 2016 [15]
QALYs per person of early treatment	21.70	Scott et al 2016 [15]
QALYs per person of late treatment	19.43	Scott et al 2016 [15]

Abbreviations: CD, Champ-Dollon; CHF, Swiss Franc; ELISA, enzyme-linked immunosorbent assay; GP, general practitioner; HCV, hepatitis C virus; OFAS, Office Fédéral des Assurances Sociales; QALY, quality-adjusted life-year; RNA, ribonucleic acid; TARMED, Tarif Médical.

Model Outputs

The primary outputs from the screening model were combined with the outputs from the treatment model to give an incremental cost-effectiveness ratio (ICER) and net monetary benefit (NMB) (comprehensive vs current screening program). The NMB is defined as the incremental effects (QALYs) multiplied by the chosen willingness-to-pay (WTP) threshold, minus the incremental costs. Thus, a positive NMB indicates that the intervention (comprehensive screening) is cost-effective.

Secondary outputs calculated were the cost of diagnosis per HCV patient identified (both initiating treatment and completing the diagnostic process) and total cost of diagnosis for the entire detention center population. The number needed to screen to detect one HCV RNA-positive person was calculated separately, with scenarios where false-negative diagnoses (representing 0.01% of patients) were included and excluded.

Analyses

A deterministic sensitivity analysis (DSA) was conducted to identify the key drivers of the model. The variation for several parameters was informed by expert opinion (shown in Supplementary Table 6); the default variation for other parameters was 20%. Parameters were ranked by their impact on the cost-effectiveness results, from greatest to smallest.

A probabilistic sensitivity analysis (PSA) was conducted from 1000 Monte Carlo simulations to test the robustness of model results. Where standard deviation values were not available in the literature for parameters, a default standard deviation (20% of the mean) was used for the PSA. Two parameters with values close to 100% (the probability of cure for treated individuals and male proportion) had alternative standard deviations applied to achieve a valid beta distribution. The distributions selected for each variable type are detailed in Supplementary Table 7. The PSA results were presented in a scatter plot and cost-effectiveness acceptability curve (CEAC). The impact of varying the target population prevalence on the NMB and ICER was also investigated.

RESULTS

Base Case

Comprehensive screening was shown to be cost-effective compared to current screening, with a base case ICER of CHF 14 312 per QALY, much lower than the assumed WTP threshold of CHF 100 000 per QALY. The WTP threshold of CHF 100 000 was chosen as this falls within the range of recommended WTP thresholds for cost-effectiveness analyses [19], and alternative WTP thresholds were tested as part of sensitivity analyses. The associated NMB was CHF 23 298 046 for the whole target population, and CHF 4298 per person. The total incremental cost of the comprehensive screening program, including diagnosis and treatment, was CHF 3 891 445. The number needed to screen to detect one positive person was 23.04 in the comprehensive screening group and 8.40 in the current screening group.

The proportion of PLD tested increased from 13.6% to 67.0% and the proportion of the HCV-positive population diagnosed increased from 35.4% to 63.7% under the comprehensive screening program. Additionally, the cost of screening per person completing the diagnosis pathway was similar: CHF 636.95 and CHF 627.69 for the comprehensive and current screening programs, respectively. The number of HCV RNA-positive PLD initiating treatment increased from 65 to 117 under the comprehensive screening program. Furthermore, the cost of screening per HCV RNA-positive person linked to treatment was CHF 13 942 and CHF 5011 in the comprehensive and current screening programs, respectively.

Sensitivity Analyses

The DSA identified the inputs with the greatest influence on the ICER to be: QALYs gained from the treatment model (both treatment and no treatment arms), respective HCV prevalence in the current and comprehensive screening populations, and the probability that PLD accepted their screening invitation. These are displayed in the tornado diagram in Figure 2, along with the remaining top 10 drivers of the model results. Results from the DSA also showed that the NMB and other incremental screening statistics (the number of patients initiating treatment, proportion tested, cost per person linked to treatment, and cost per person completing the diagnosis pathway) were most sensitive to the same parameters as the ICER (results not shown).

The results from the PSA (Supplementary Figures 1 and 2) showed that the comprehensive screening program had an 83.1% probability of being cost-effective at a WTP threshold of CHF 100 000 per QALY, implying the findings were fairly robust. As the CEAC in Supplementary Figure 2 shows, the probability of cost-effectiveness did not change considerably when the WTP threshold was varied. For example, at an alternative WTP threshold of CHF 50 000, based on the commonly used USD 50 000 threshold [19], comprehensive screening was estimated to have an 81.7% probability of cost-effectiveness.

Scenario Analyses

At a WTP threshold of CHF 100 000, the NMB was positive for target population prevalences from 1% to 50%, indicating that comprehensive screening was cost-effective compared to current screening over a broad range of HCV prevalences (Supplementary Figure 3A).

As expected, the NMB increased as the prevalence in the detention center population increased. A linear relationship between target population prevalence and NMB was seen between prevalences of 1% and 40%, and (at a higher rate of increase) above 60%. The ICER was correspondingly found to decrease over the range of prevalences tested (Supplementary Figure 3B).

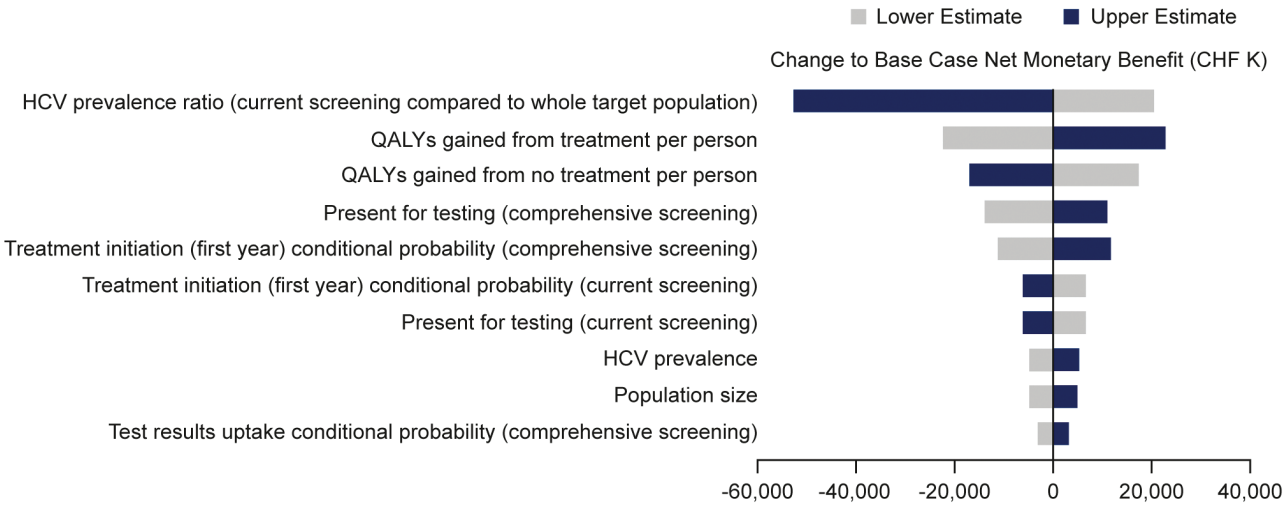

Figure 2. Tornado plot showing results of the deterministic sensitivity analysis. Abbreviations: CHF, Swiss Franc; HCV, hepatitis C virus; QALY, quality-adjusted life year.

HCV screening of PLD may prove more cost-effective in countries where HCV is more prevalent in detention centers.

In detention centers where PLD are incarcerated for longer periods, or where incidence rates are expected to be relatively high, repeated screening may be more appropriate. A scenario was considered where screening was conducted annually for 5 years, with an assumed HCV incidence rate of 1.7 infections per 100 person-years of exposure [2]. A discount rate for clinical outcomes (QALYs) and costs of 3% was used here, based on the World Health Organization recommended rate [20]. The associated ICER and NMB were CHF 30 018 per QALY and CHF 24 842 961, respectively. This showed that repeated comprehensive screening was cost-effective but slightly less so than one-time screening. Comprehensive screening also demonstrated cost-effective outcomes when the HCV incidence rate was varied. With a higher HCV incidence rate of 14.1 infections per 100 person-years of exposure (taken from a study examining HCV incidence in Australian PLD) [21], the ICER was CHF 11 810 per QALY. At the lower estimate of the HCV incidence rate, 0.4 infections per 100 person-years of exposure (taken from a study of HCV infection among males in Rhode Island prisons in the United States) [22], the ICER was CHF 56 584 per QALY.

In the absence of suitable results from treatment models in the literature that considered PLD, the Scott et al [15] study was chosen as a population likely to be more closely aligned with PLD than the general population. The published model also considered a "late-treatment" scenario, denoting treatment prior to development of compensated cirrhosis. A further scenario analysis conducted using these late-treatment cost and QALY estimates, provided a more conservative estimate of the benefits of treatment, giving an ICER of CHF 15 330 per QALY. This shows that with QALY and cost estimates that are less favorable toward the impact of treatment than the base case, the screening model ICER is still well below the WTP threshold of CHF 100 000 per QALY. PSA results from this scenario estimated that the probability of cost-effectiveness was over 80% at the WTP threshold of CHF 100 000 per QALY.

DISCUSSION

This study showed that comprehensive screening strategies in Swiss detention centers can be extremely cost-effective compared to the current setup, with a base case ICER of CHF 14 312 per QALY and 83.1% probability of being cost-effective at the CHF 100 000 per QALY WTP threshold. A key driver of this was the increased testing rates, which were conservatively estimated, and would likely increase the number of diagnoses and result in more patients being linked to care. Among the literature, there is no consensus about the cost-effectiveness of HCV screening in detention centers; previous analyses have estimated that it is cost-ineffective in England and Wales [23] and cost-effective in the United States [24].

Strengths of this model included that inputs were informed by clinical experts working closely with current Swiss HCV screening programs in detention centers or by data from a Swiss detention center (Champ-Dollon). Additionally, the model included the possibility of a detainee dropping out at any point along the pathway from diagnosis to treatment; hence the effect of dropout rates on the cost-effectiveness of comprehensive screening could be investigated. Sensitivity analyses also enabled investigation of a range of parameter values and allowed realistic interpretation of results.

Limitations of the model were that the costs and benefits associated with treatment were obtained from a published model of treatment and natural disease progression that did not exactly match with the screening model target population. However,

when varying the treatment costs and QALYs in the sensitivity and scenario analyses, all ICERs were well below the chosen WTP threshold, demonstrating that results were not sensitive to the treatment model inputs. Additionally, various assumptions had to be made during model development, but each was clearly stated and made with the model objective in mind. Equally, several input parameter values were not available in the literature or from other data sources. In these cases, values for similar parameters in the literature were used or assumptions were made. These have been clearly stated and guided by expert opinion and were not anticipated to have a significant effect on the model results. In addition, the analysis was focused on the Swiss detention system, and therefore the results will have most relevance to countries with similar existing HCV screening programs and treatment availability.

HCV is not the only blood-borne disease that is more common among PLD than the general population. Human immunodeficiency virus (HIV) prevention programs in prisons, where the prevalence of HIV is much greater than in the general population, have been shown to prevent transmission of HIV and thus provide substantial cost savings to society [2, 25]. It is therefore possible that effective screening and management of HCV infection in prisons could generate similar societal benefits to HIV [7, 8]. However, currently, the prospect of comprehensive screening and treatment of HCV in prisons remains a challenge due to custodial services' limited resources. Investment in HCV treatments may act as a strain on custodial services budgets and encourage them not to screen for HCV, against national and international recommendations. There are approximately 6863 prisoners in Switzerland. In countries where prison population numbers are greater (eg, Canada [41 145], France [70 710], and the United States [2 121 600]) [26], the upfront costs of screening and treatment but also the long-term health benefits, could be much greater than in Switzerland.

This analysis could inform policy-making decisions, and comprehensive screening programs could be considered in detention centers with large proportions of high-risk individuals and where detainees are incarcerated for enough time to complete a treatment course. Due to a Swiss policy for DAA reimbursement adopted in May 2017, with improved access for PWID and HIV coinfected patients (regardless of liver fibrosis stage), it is now feasible to provide high levels of DAA treatment coverage for these patients in a custodial setting [27]. Additionally, as of 1 October 2017, all HCV viremia-positive patients can be treated regardless of their stage of disease. Successfully treating infected PLD prior to their release would likely reduce the risk of infection to other members of the public, resulting in a benefit to society overall through reducing the clinical and economic burden of HCV.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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