Costs and consequences of the Portuguese needle-exchange program in community pharmacies

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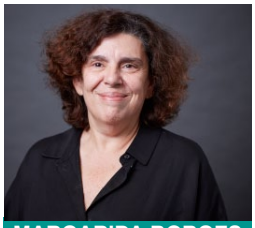

MARGARIDA BORGES

One of our research goals was to generate evidence to substantiate the decision to implement public health interventions.

L'un de nos objectifs de recherche était de produire des preuves pour justifier la décision de mettre en œuvre des interventions de santé publique.

ABSTRACT

Background: Needle-exchange programs (NEPs) reduce infections in people who inject drugs. This study assesses the impact community pharmacies have had in the Needle-Exchange Program in Portugal since 2015.

Methods: Health gains were measured by the number of human immunodeficiency virus (HIV) and hepatitis C virus (HCV) infections averted, which were estimated, in each scenario, based on a standard model in the literature, calibrated to national data. The costs per infection were taken from national literature; costs of manufacturing, logistics and incineration of injection materials were also considered. The results were presented as net costs (i.e., incremental costs of the program with community pharmacies less the costs of additional infections avoided).

Results: Considering a 5-year horizon, the Needle Exchange Program with community pharmacies would account for a 6.8% ($n = 25$) and a 6.5% reduction ($n = 22$) of HCV and HIV infections, respectively. The present value of net savings generated by the participation of community pharmacies in the program was estimated at €2,073,347. The average discounted net benefit per syringe exchanged is €3.01, already taking into account a payment to community pharmacies per needle exchanged.

Interpretation: We estimate that the participation of community pharmacies in the Needle Exchange Program will lead to a reduction of HIV and HCV infections and will generate over €2 million in savings for the health system.

Conclusions: The intervention is estimated to generate better health outcomes at lower costs, contributing to improving the efficiency of the public health system in Portugal. *Can Pharm J (Ott)* 2020;153:170-178.

Introduction

The prevalence of human immunodeficiency virus (HIV), hepatitis C virus (HCV) and hepatitis B virus (HBV) is high among people who inject drugs (PWID),[1] resulting in serious public health concerns. In PWID, infectious diseases are transmitted through 2 main channels: the sharing of drug injection equipment and unprotected sexual activity. In Portugal, the last published estimates of the number of PWID ranged

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KNOWLEDGE INTO PRACTICE

- Needle-exchange programs are available in 90 countries around the world, and use different forms of distribution, ranging from mobile vans to home visits, with community pharmacies usually playing an important role in the program due to their accessibility in terms of opening hours and broad geographical distribution.
- This study shows that, in Portugal, the participation of community pharmacies in a needle-exchange program has the potential to reduce HIV and HCV infections while saving above €2M for the health system.
- Community pharmacies may increase their impact on society by joining the needle-exchange programs, which may be a cost-effective strategy even in a setting where consumption of injectable drugs is decreasing.

MISE EN PRATIQUE DES CONNAISSANCES

- Les programmes d'échange de seringues sont disponibles dans 90 pays du monde entier et utilisent différentes formes de distribution, allant des camionnettes mobiles aux visites à domicile. Les pharmacies communautaires jouent généralement un rôle important dans le programme en raison de leur accessibilité en termes d'heures d'ouverture et de leur vaste répartition géographique.
- Cette étude montre qu'au Portugal, la participation des pharmacies communautaires à un programme d'échange de seringues a le potentiel de réduire les infections par le VIH et le VHC tout en permettant au système de santé d'économiser plus de 2 millions d'euros.
- Les pharmacies communautaires peuvent accroître leur impact sur la société en participant aux programmes d'échange de seringues, ce qui peut constituer une stratégie rentable même dans un contexte où la consommation de drogues injectables diminue.

between 12,732 and 16,285, corresponding to a prevalence rate of 194.4 to 248.6 per 100,000 inhabitants aged 15 to 65.[2] In 2016, the prevalence of HIV and HCV for PWID in treatment for addiction in Portugal varied between 7%-27% and 67%-88%, respectively, while 2.5% of screened PWID were HBV surface antigen positive.[3]

Needle-exchange programs (NEPs) improve access to kits with sterile drug-injecting equipment and condoms, reducing drug-related harms by decreasing transmission of infections among PWID.[4-7]

NEPs are available in 90 countries around the world,[8] using different forms of distribution, ranging from mobile vans to home visits. Community pharmacies play an important role in these programs, mainly due to their accessibility in terms of opening hours and broad geographical distribution. In many countries, such as Australia,[9] Belgium, France, Ireland, Netherlands, Slovenia, Spain and the United Kingdom,[10] community pharmacies are an important distribution channel for the kits.

In Portugal, the NEP was launched in 1993 in community pharmacies. After being launched, other entities joined the program, in particular, mobile vans (1994) and both governmental and nongovernmental organizations (1999). Until 2005, community pharmacies had a dominant role in the needle distribution network.[11-17]

Following a request by the National Committee Against AIDS (a governmental committee), a private consulting company performed an economic evaluation of the program in 2002.[18] The results showed that the NEP in community pharmacies in Portugal was cost-effective, as it generated better health outcomes while lowering costs, with cost savings due to averted HIV and HCV infections adding up to €405 million (between 1993 and 2001).

From 1993 to 2012, community pharmacies participating in the NEP did not receive any public funding and provided these services pro bono. Due to the economic crisis, the community pharmacies (which are privately owned) suspended their participation in the program in 2013, rejoining it 2 years later after signing an agreement with the government that enhanced the expansion of the role of community pharmacies, particularly in relation to the provision of health services. Currently, the following entities are actively participating in the program: primary health care centres, governmental and nongovernmental organizations, mobile vans and community pharmacies. The program allows PWID to drop off used injecting drug equipment and collect a kit containing 2 sterile needles and syringes, 2 alcohol swabs, 2 ampoules of double-distilled water, 2 citric acid sachets, 2 filters, 2 containers for drug preparation (clean cups) and 1 condom. This kit is financed by the government.

Since the first economic study in 2002,[18] significant changes have occurred in areas such as the frequencies of the types of drugs consumed, consumption habits and accessibility to the NEP, as well as in the epidemiology of HIV and HCV among PWID in Portugal. Therefore, the objective of this study was to conduct a prospective cost-effectiveness analysis comparing the current (since 2015) scenario of the NEP with participation of community pharmacies (intervention scenario) versus a scenario without participation of community pharmacies (status quo scenario). The results of this analysis are relevant to all stakeholders and to inform health care policy decision-making.

Methods

The clinical benefits of the NEP were estimated as the number of HIV and HCV infections averted due to the participation of community pharmacies in the program. Therefore, health gains associated with the intervention scenario were computed as the difference between the HIV and HCV new infections in the scenarios with and without the participation of community pharmacies.

The incremental costs of including community pharmacies in the Portuguese NEP were computed as the difference between the additional costs of the NEP with community pharmacies and the savings associated with the number of additionally averted HIV and HCV infections.

A time horizon of 5 years was considered in the analysis of the number of infections. Lifetime costs associated with treatments of these infections were discounted at a 5% rate, as recommended by the National Authority of Medicines and Health Products (INFARMED) guidelines.[19] The results are presented in terms of the value of the difference in costs between the scenario of the NEP with community pharmacies and the scenario without community pharmacies. There were 2 possible results: 1) the difference in costs is positive, meaning that the intervention increases costs, and 2) the difference is negative, meaning that there are (positive) "net savings" associated with the intervention.

In the base-case scenario, the participation of community pharmacists in the NEP was assumed to be complementary to the other exchange locations available in the status quo scenario. In a sensitivity analysis, a scenario where community pharmacies partially substitute for other NEP distribution sites was considered.

As this study is based on secondary and aggregate data, it was not necessary to get Institutional Ethics Review Board approval.

Health benefits

The number of new infections occurring in each scenario was separately estimated for HIV and HCV using the model presented by Jacobs et al.,[20] based on the original equation by Kaplan and O'Keefe.[21]

The model's structural equation is

$$\text{No. of new infections} = (1-q)*(1-\theta)*N*s*[1-(1-q*t)^{m}],$$

where q is the disease prevalence in the PWID population, θ is the probability of effectively cleaning the drug-injecting equipment, N is the number of circulating needles, s is the needle-sharing rate, t is the probability of infection per single injection with an infected needle and m is the number of individuals sharing the same needle.

The infection incidence depends on the susceptible population of PWID $[(1-q)]$, the number of unclean and shared needles in circulation $[(1-\theta)*N*s]$, and the probability of infection per sharing event $[1-(1-q*t)^{m}]$, which increases nonlinearly with the number of individuals sharing the same needle (m).

The model assumes that the number of needles in circulation (N) in a given moment is stable, as in Kaplan and O'Keefe's circulation theory.[21] According to this theory, the infection incidence decreases because the intervention reduces needles' average circulation time and therefore the exposure time, decreasing the probability of infection per sharing episode. In other words, the intervention has an impact only on the sharing rate of the needle(s) and not on the number of needles in circulation (N).

The calibration of the equations is identical for both HIV and HCV infections, except for the parameters of disease prevalence (q) and the probability of infection per shared injection (t). The equation is calibrated according to 2 principles: 1) in the status quo scenario, estimates of the number of new cases should be consistent with the historical incidence rates among PWID and their trends, and 2) calibration should use the best-available information for the equation's epidemiological parameters.

Regarding HIV incidence, national public authorities publish annually the number of notifications of HIV infections by transmission mode, including injecting drug use.[22] The HIV incidence rate between 2015 and 2019 was extrapolated using a regression model where the number of new cases of HIV among PWID between 2004 and 2014 is explained by time. Figure 1 shows the model and its good fit (R^2 = 92%). The registry of HIV notifications is considered the best source of information on incidence because HIV has been listed among compulsory notifiable diseases since 2005.

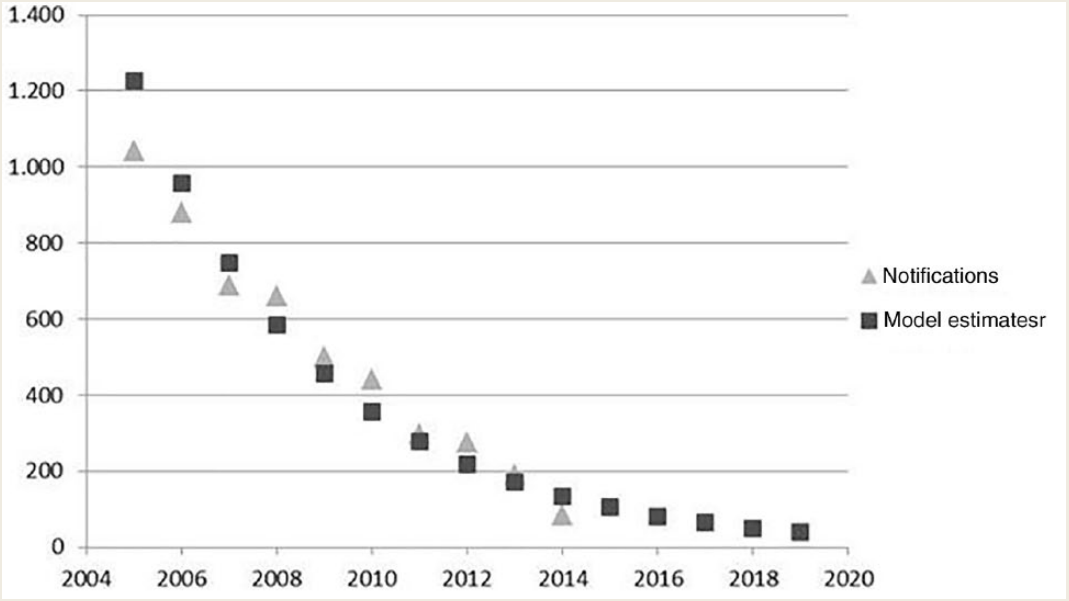
From 2014 onwards, the number of infections was predicted to decrease. Between 2015 and 2019, the number of new cases in the status quo scenario was estimated at 81, 63, 63, 50 and 39, respectively.

The number of HIV notifications among PWID in Portugal since 2004, as well as the number predicted for the years after, is shown in Figure 1. Information regarding HCV incidence was scarcer and less systematically collected. The most recently published data by the Directorate General of Health report 45 cases of acute infections in 2008 in the general population. Other published results regarding overall HCV incidence rates in Portugal are heterogeneous, ranging between 0.37/100,000 and 8/100,000 inhabitants,[22-25] corresponding to a range from a low of 37 up to a high of 810 new cases per year.

Following a personal communication with Professor Homie Razavi (from the Center for Disease Analysis [CDA]), the number of new cases of HCV among PWID in Portugal was estimated at 94 in 2014. This estimate was considered conservative given the information available and was used to calibrate the first year of the status quo scenario.

The parameters considered constant for HCV along the time horizon are the probability of infection per single injection (t), the

FIGURE 1 Data and regression estimates of human immunodeficiency virus incidence in people who inject drugs



Source: INSA (2014) and authors' estimates.[20]

TABLE 1 Parameters used to calibrate the model equations

Variable	Value	Source	Constant
Probability of HIV infection per single injection (t_{HIV})	0.7%	Based on Public Health Agency of Canada (2012)[28]	Yes
Probability of HCV infection per single injection (t_{HCV})	1.5%	Based on UK Ministry of Health (2009)[29]	Yes
Number of individuals sharing the same needle (m)	1.38	Jacobs et al. (1999)[20]	Yes
Probability of effectively cleaning the drug-injecting equipment (θ)	7.7%	Based on Mendes et al. (2003)[30]	Yes
HIV prevalence among PWID (q_{HIV})	14.5%-23.7%	SICAD (2014)[26] and authors' estimates	No
HCV prevalence among PWID (q_{HCV})	92.2%	Marinho et al. (2001)[27] and authors' estimates	Yes
Number of circulating needles (N)	770,555-1,200,277	DGS (2015)[17] and authors' estimates	No
Sharing rate (s) in status quo scenario	1%-9.8%	Mendes et al. (2003)[30] and SICAD (2012)[31]	No
Change in sharing rate (s) in intervention scenario	–7.7% to 3.7%	Assumption and authors' estimates	No

DGS, Directorate-General of Health; HCV, hepatitis C virus; HIV, human immunodeficiency virus; PWID, people who inject drugs; SICAD, General Directorate for Intervention on Addictive Behaviours and Dependencies.

number of individuals sharing the same needle (m) and the probability of effectively cleaning the drug-injecting equipment (θ).

The model was calibrated with prevalence rates of HIV declining over time and constant rates of HCV. In line with the annual report by the General Directorate for Intervention on Addictive Behaviours and Dependencies (SICAD), published in 2014,[26] and Marinho et al.,[27] prevalence estimations of HIV and HCV were 24% and 92% among PWID, respectively. Additionally, the number of circulating needles in 2014 was estimated at 1,200,277, which is the moving average of the

TABLE 2 Estimates of HIV and HCV treatment costs in Portugal

Infection	Therapy	Discounted value (€)	Source
HIV	Raltegravir	215,194	Chaudhary et al. (2010)[33]
	Efavirenz	213,251	
	Lopinavir	220,349	
	Atazanavir	220,934	Carrasco et al. (2011)[34]
	Lopinavir	235,413	
	Darunavir	236,126	
	Efavirenz	233,425	
HCV, genotype 1 naive	Sofosbuvir/peginterferon + ribavirin	65,519	Félix et al. (2014)[35]
	Telaprevir/peginterferon + ribavirin	58,059	
	Boceprevir/peginterferon + ribavirin	58,222	
	Peginterferon + ribavirin	47,422	
HCV, genotype 3	Sofosbuvir/peginterferon + ribavirin	63,383	
	Telaprevir/peginterferon + ribavirin EXP	63,736	
	Boceprevir/peginterferon + ribavirin EXP	43,454	
	Peginterferon + ribavirin	42,582	
HCV genotype 4/5/6	Sofosbuvir/peginterferon + ribavirin	59,128	
	Peginterferon + ribavirin	46,633	

EXP, people with prior exposure; HCV, hepatitis C virus; HIV: human immunodeficiency virus.

number of needles exchanged in 2013, 2014 and 2015 (an estimate was used for 2015).[17]

The parameters used to calibrate the model are summarized in Table 1. The sharing rate decrease associated with the intervention was assumed to be half of the percentage increase of exchanged needles in 2015 and 2016. In other words, if the number of needles exchanged increases, the circulation time drops, as does the probability of sharing a specific needle. The analysis assumes that if the number of needles exchanged increases by 10%, the sharing rate will be proportionately 5% lower. The number of needles exchanged by community pharmacies in 2015 was estimated at 87,761, based on the estimates available up to November 2015, an increase of roughly 7%. The number was estimated to reach 169,347 from 2016 onwards. The estimate of the future number of needles exchanged took into consideration the increasing trend in the number of community pharmacies participating in the program. According to data provided to the authors by the Portuguese National Pharmacy Association, in November 2015, there were 426 community pharmacies actively participating across the country and the average number of needles exchanged per month by each community pharmacy in November 2015 was 94. The resulting proportional reduction of the sharing rate in the intervention scenario was then estimated at 3.7% and 7.7% in 2015 and 2016, respectively, and assumed constant from 2016 onwards.

Cost difference

Costs incurred by community pharmacies and other entities participating in the production—distribution, collection and incineration of the kits distributed in community pharmacies—were considered incremental costs associated with the intervention scenario. A panel of pharmacies that had previously participated in the NEP was convened and consulted to identify and estimate the costs incurred by community pharmacies, including costs related to storage, logistics and labour costs of providing the service. Costs incurred by other entities, outside the community pharmacies, were retrieved from public contracts available online[32] and included production, storage, distribution and incineration of the drug-injecting equipment. Cost estimates included a predicted (but nonexistent at the time, in 2015) remuneration for community pharmacies per needle exchanged of €2.5.

TABLE 3 Yearly results for a 5-year time horizon (not discounted)

Year	Needles exchanged in pharmacies	Total costs of the NEP in pharmacies	Infections avoided		Saving associated with infections avoided (€)		Net savings (€)
			HCV	HIV	HCV	HIV	
2015	87,761	271,269	5	4	105,359	700,400	534,489
2016	169,347	523,452	6	6	147,976	1,150,455	774,979
2017	169,347	523,452	5	5	124,300	894,796	495,644
2018	169,347	523,452	5	4	105,937	710,154	292,639
2019	169,347	523,452	4	3	89,170	553,918	119,636

HCV, hepatitis C virus; HIV, human immunodeficiency virus; NEP, needle exchange program.

Direct lifetime health care costs associated with the infections were retrieved from publications by other authors. The values retrieved are presented in Table 2. Given the estimates available,[33-35] the authors considered the most conservative cost estimate for HIV (€213,251). Regarding HCV, the cost used was the most conservative cost estimate for genotype 1 (€47,422), since this is the most prevalent genotype in Portugal.[23,36-39]

The HIV and HCV cost estimates in the literature assume that the evaluation time frame starts when the treatment starts. Thus, the lifetime cost estimates were additionally discounted in order to consider a lag of 3 and 15 years between the timing of the infection and the initiation of treatment of HIV and HCV, respectively.

Univariate sensitivity analyses were performed to assess the robustness of the base case. In the sensitivity analyses, the base-case calibration was varied in terms of discount rate (3% instead of 5%), lifetime infections' costs (–30%) and sharing rate decrease associated with intervention (–30% compared to base-case scenario). A scenario excluding the impact of the intervention on HCV incidence was analyzed. Since the substitutability between distribution channels is unknown, the possibility of some substitution between distribution sites was also explored. In particular, we considered a scenario where for each 3 needles exchanged in the community pharmacies, there is 1 less needle exchanged in the other distribution channels (1/3 substitution). This scenario translates to a reduction in the benefits associated with the intervention, since it is assumed that 1/3 of the needle exchanges in community pharmacies would have occurred anyway, with no reduction in the overall costs of running the program in the community pharmacies. Also, it was conservatively assumed that there would be no reductions in the costs associated with running the NEP in other networks.

Results

The model estimated that, in a 5-year time horizon, the participation of community pharmacies in the NEP would reduce by 25 the number of new HCV cases and by 22 the number of new HIV cases. In other words, over 5 years, community pharmacies might contribute to a reduction of 6.8% and 6.5% in HCV and HIV infections, respectively, among PWID in Portugal.

The overall costs per needle exchanged, including costs incurred outside the community pharmacies and their fees (which includes costs inside the community pharmacies), were estimated at €3.09. The number of needles exchanged was forecasted at 87,761 in the first intervention year and 169,347 in the following years. The incremental annual cost of the intervention was estimated at €271,269 in 2015 and at €523,452 from 2016 onwards.

The present value of lifetime costs associated with infections was estimated at €184,214 and €22,811 for HIV and HCV, respectively. The results in terms of net costs (i.e., the cost of the infections avoided less the incremental costs of the NEP with community pharmacy participation) are summarized in Table 3.

For each period, the savings associated with the additional infections avoided were higher than the incremental costs of the intervention (i.e., the intervention scenario is a dominant strategy when compared to the status quo scenario).

The discounted savings over a 5-year horizon were estimated to be €2,073,347. Equivalently, each needle exchanged by the NEP in community pharmacies results, on average, in €3.01 of savings for taxpayers.

Sensitivity analysis proved the intervention scenario to be a robust dominant strategy. A 30% decrease in the infections' costs had the highest impact on results, with a 61% reduction in net savings; an alternative 3% discount rate, lower than the national Portuguese guidelines' base case but recommended by the Centers for Disease Control and Prevention for the cost-effectiveness analysis of community public health prevention interventions,[40] increased the savings by 22%; reducing the impact of the intervention on the needle-sharing rate (parameter *s*) by 20% reduced net savings by 41%. In the scenario where HCV prevention benefits are ignored, the NEP with community pharmacies persists as a dominant intervention with discounted net savings above €1.5 million, a 25% reduction versus the base case. Finally, in the scenario where the NEP in community pharmacies is considered to substitute

for other distribution networks by 1/3, the intervention is no longer dominant but the present value of the cost per averted infection was estimated at €4085.

Discussion

The results of this analysis comparing a scenario with the participation of community pharmacies in the NEP versus a status quo scenario showed that community pharmacy-based needle exchange is a dominant strategy, generating higher health benefits and simultaneously costs savings for society. This result proved to be robust through a variety of sensitivity analyses where the parameters in the model associated with the highest uncertainty were varied. In all sensitivity analyses, the participation of community pharmacies in the NEP was a cost-effective strategy (with a cost per averted infection lower than €4100 in the worst case studied and positive net savings [dominant strategy] in all other cases).

We used a model from the literature[20,41,42] to estimate the number of HIV and HCV infections that were averted. We were conservative in the values used for calibrating the model. For example, HIV prevalence estimates used in the model were those leading to HIV incidence rates in line with the number of new cases notified in Portugal. This approach underestimates the potential health gains, due to the well-known notification bias. The use of a higher disease prevalence when calibrating the model would have led to higher health benefits. Furthermore, we also consider the model itself to be conservative, since it includes all costs of drug-injecting equipment but not all the benefits related to the NEP. For example, the model does not take into account the potential beneficial impact of the NEP on the transmission of other illnesses, such as HBV and tuberculosis. Moreover, the kits dispensed under the NEP also include condoms, which aim to reduce sexually transmitted diseases and unwanted pregnancies. Consideration of these potential health benefits would improve the cost-effectiveness of the intervention program.

The comparability of the results across countries is difficult to determine due to differences in costs, PWID behaviour and infections' prevalence and time horizon considered in the analysis, among other aspects. Furthermore, most of the literature presents cost-effectiveness analyses of NEP (considered as a whole) versus no NEP,[20,43-46] while the current study represents a cost-effectiveness analysis comparing the effectiveness of the Portuguese distribution network without community pharmacies with a network including community pharmacies. Nevertheless, the overall findings of the present study are in line with those reported in the literature, which also conclude that the NEP is a cost-effective strategy (regardless of the distribution site) in other countries.[18,41-44]

Conclusion

The estimates presented in this work show that the participation of community pharmacies in the needle-exchange program in Portugal has the potential to reduce HIV and HCV infections while saving over €2 million for the health system. Therefore, the participation of community pharmacies in this program is a dominant strategy compared to a program without them. The intervention generates better health outcomes at lower costs than those of the NEP without the community pharmacies, contributing to improving the efficiency of the public health system in Portugal. Although not easily geographically generalizable outside Portugal, our findings suggest that the inclusion of community pharmacies in the distribution network of kits in the context of a NEP is a cost-effective strategy even in a setting where the consumption of injectable drugs is decreasing. ■

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Homie A. Razavi, PhD, is the manager-director of the Center for Disease Analysis (CDA) in Louisville CO (USA). In recent years, he has been leading a team of epidemiologists and modellers to quantify the epidemiology of hepatitis C virus (HCV) and forecast the future impact of HCV disease burden. The authors express their gratitude to Dr. Razavi for sharing his research group estimates of HCV incidence among people who inject drugs in Portugal, which allowed us to fine-tune the model for the HCV infection incidence.

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