SUPPLEMENTARY MATERIAL

S1: MODEL DETAILS AND PARAMETERS ESTIMATIONS

MODEL AND PARAMETERS

Population

The initial population of the model is a population of PWID in Paris area. As in a previous study, we supposed that the order of magnitude of this population is 10,000 (1, 2). The population is structured in 3 levels: each PWID is in a compartment in the transmission and healthcare model, a position in the network of injectors sharing drugs and a life expectancy (excluding HCV mortality).

The initial age distribution is described in Table S1.

Table S1 Age distribution according to the gender in active (i.e. injection in the last month) PWID in 2011 from ANRS-Coquelicot study.

Age	Women	Men
20	1.4	0.1
22	6.2	1.5
23	5.0	1.8
24	10.3	2.7
25	0.1	1.1
26	1.5	0.7
27	0.7	5.9
28	1.8	0.5
29	1.1	3.0
30	5.3	2.9
31	5.6	8.3
32	0.0	3.3
33	3.5	1.9
34	0.1	4.7
35	1.0	1.9
36	2.9	4.8
37	17.8	4.4
38	0.6	5.5
39	5.7	6.8
40	1.5	7.0
41	4.7	4.6
42	0.0	1.5
43	0.0	2.7
44	6.4	5.5
45	0.2	2.3

46	4.9	1.6
47	3.4	0.8
48	3.4	0.3
49	1.4	5.0
50	0.0	2.1
51	3.6	1.2
53	0.0	0.2
54	0.0	0.0
55	0.0	1.3
56	0.0	0.5
59	0.0	1.6

Each compartment in the model corresponds to:

- A state concerning the harm reduction intervention in which he/she participates
- A state related to HCV infection and care
- For chronically HCV-infected PWID, a state in the natural history model

The possible states for each of these characteristics are described below.

Social network

Model

HCV is mainly transmitted by needles/syringes sharing in the PWID population; however paraphernalia sharing (e.g. filter, spoon) seems also to play an important role (3). To take into account the global risk of infection for a PWID given that we consider only transmissions occurring during shared drug injections, we chose, as previously described by Rolls *et al.*, to model the network of the sharing partners: two PWID are linked together if they inject together even without sharing needles/syringes (4). In this network, two PWID are linked if they reported "intraveneous drug use at the same place and time" in the previous 3 months.

Compared with mixed models, taking into account the social network allows to take the neighborhood size of individuals into consideration and to propose more realistic estimations of infections parameters, for instance. Spread of the disease is also more constrained by the network on which it propagates.

One of our objectives was to simulate possible paths of HCV transmission in PWID and we need to model a random network to allow repeated generation of structures with similar topologies.

We chose a *household graph model* (5-7). These models generate networks where individuals are clustered in subgroups ("households") in which pairs have a high probability to be linked. Individuals belonging to different subgroups have a low probability to be linked.

Our model is constructed as follows

1) In a population of *n* individual, we randomly assign each member to an household of size 1 (the individual is alone in his/her household), 2 or 5, with probabilities π_1, $\pi_2$or π_5.
2) Each couple of individuals belonging to the same household is considered linked with an edge with a probability depending on the type of household they belong to $p_{ij}, (i,j) \in \{1,2,5\}^2$. Probabilities p_{22} and p_{55} are considered higher than p_{12}, p_{15}, and p_{25}.

The sizes 1,2 or 5 of the household is chosen by analysis of the Australian data (8)

Parameters

For simplicity, we assumed that $p_{11} = 0$, because structure that would be formed if $p_{11} > 0$ would be similar to household of size 2. Thus, we needed to estimate the following parameters: π_1, π_2, π_5 and p_{12}, p_{15}, p_{22}, p_{25} and p_{55}.

For this purpose, we used Approximate Bayesian Computation (ABC). ABC is a bayesian method used to infer some parameters of a model without likelihood estimation (9). Briefly, the main idea of ABC is to fit the (possibly set of) parameter(s) θ of a model thanks to simulations and computation of a (possibly set of) summary statistic(s) $s_i, i = 1, \dots, N$ that are compared to the observed values on the data s_{obs}. More precisely, we draw a sample $\theta_i, i = 1, \dots, N$ in a prior probability distribution. For each θ_i, the model is simulated with this parameter set and simulations are used to obtain the corresponding simulated statistics $s_i, i = 1, \dots, N$. Each parameter value is then weighted by $W_i = K_\delta(s_i - s_{obs})$, where K_δ is a smoothing kernel with tolerance threshold δ. The weighted sample $(\theta_i, W_i / \sum_{i=1}^{N} W_i), i = 1, \dots, N$ gives the posterior probability distribution. We used a variant of the ABC algorithm with linear adjustement to correct θ_i given the other simulations: supposing a linear relation between θ and S, each θ_i is replaced by $\theta_i^* = \theta_i - \mathrm{b}(s_i - s_{obs})$, with b estimated by linear

regression. This variant allows to obtain a tighter posterior distribution. For more details about ABC, the reader can refer to (10).

Due to the lack of data about PWID social networks in France, we used the data collected in a survey in Melbourne (Australia) (8). The data available was a network of 305 PWID in Melbourne (Australia). These data were obtained using snowball sampling (RDS): starting from an initial set of 151 PWID, each of them were asked to report a maximum of five injecting partner in the population. The investigators then tried to find these partners to make them participate in the survey, and ask them to report in turn their injecting partners, etc. The final obtained network was constituted of 305 PWID, of which 47 without identified partners. The total population size was estimated at 524 from this sample. This network is partial, due to the limitation in the number of reported injected partners.

To calibrate our household model from Melbourne data, we used ABC with the following process:

Step 1: A sample of N=90,000 parameters values for the household graph model was drawn. The parameters $\theta = (p_{12}, p_{15}, p_{22}, p_{25}, p_{55})$ were drawn in uniform prior distributions in [0, 0.2/250], [0, 0.05/250], [0, 0.2/250], [0, 0.05/250] and [0, 3/250]. The prior law distributions of π_1, $\pi_2$or π_5 were uniform distributions on [0, 0.25], [0, 0.25] and [0, 0.5] respectively, and renormalized thereafter so that they sum to 1. The parameters for the prior distributions were chosen according to an exploratory descriptive analysis of the sample.

Step 2: For each set of parameters in the sample, we simulated a corresponding household graph of size 524. This value was the estimated size of the initial PWID community in which the snowball sample was drawn according to Rolls *et al.* (8).

Step 3: A snowball sampling process was simulated on each of these networks in the following manner (implemented in C++):

A. An initial set of 151 nodes was randomly chosen in the graph
B. For each of these nodes
    1. If the node's degree (i.e. the number of edges linked to the node) is inferior or equal to 5, all the neighbors of the index node are included in the snowball sample
    2. If the node's degree is superior to 5, 5 nodes are randomly and uniformly drawn among the neighbors to be included in the snowball sample

C. The same process is applied from B to the nodes newly included in the sample, until the sample size reached 305

Step 4: A set of summary statistics are computed for each snowball sample. These statistics are: the number of isolated nodes, the number of edges, the number of triangles in the network, the number of isolated couples and the diameter of the network (i.e. the maximum number of edges between two nodes of the network). This generates a set of inputs for the ABC constituted of N=90,000 summary statistics.

Step 5: We applied ABC using the package "abc" (11) of the statistical software R (12). The observed statistics in the Melbourne's snowball sample were: 47 isolated nodes, 263 edges, 61 triangles, 23 isolated couples, and a diameter of 17. We used an Epanechnikov kernel with a tolerance threshold corresponding to 10% of the simulations. $\pi_2$or π_5 values were logit-transformed to ensure final estimates between 0 and 1, and π_1 estimates was derived from $\pi_2$or π_5 to sum to 1. p_{12}, p_{15}, p_{22}, $p_{25}$and p_{55} were log-transformed to ensure their positivity. We applied a correction on the parameters values using linear regression, as explained above.

Step 6: The mean value of each posterior distribution was used as the final estimate for the corresponding parameter.

The results obtained were $\widehat{\pi_1}$=0.26 [95% confidence interval=0.13-0.38]; $\widehat{\pi_2}$=0.24 [0.10-0.37]; $\widehat{\pi_5}$ =0.50 [0.37-0.66]; $\widehat{p_{12}}$= 3.42e^{-4} [3.28e^{-5}-8.11e^{-4}]; $\widehat{p_{15}}$=7.52e^{-5} [6.25e^{-6}-1.88e^{-4}]; $\widehat{p_{25}}$=3.20e^{-4} [2.60e^{-5}-7.88e^{-4}]; $\widehat{p_{22}}$=1.56e^{-4} [1.07e^{-5}-4.06e^{-4}]; $\widehat{p_{55}}$=2.48e^{-3} [1.37e^{-3}-4.35e^{-3}]. We can see that according to these results, around 50% of the PWID belong to a household of size 5. $\widehat{p_{12}}$ and $\widehat{p_{22}}$ are the highest values, implying the emergence of arborescent structures in the simulated graphs. The probabilities for individuals belonging to households of 5 people to connect with people of other households $\widehat{p_{15}}$, $\widehat{p_{25}}$ and $\widehat{p_{55}}$ are lower, suggesting that such households are more isolated. However with 5 people in each household, there are 5 times more chances to connect with other households.

Example

An example of simulated household graph is given Figure S1.

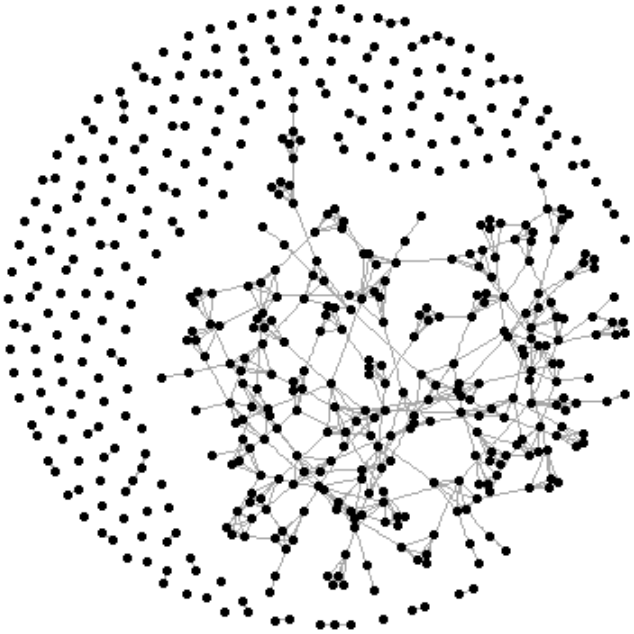

Figure S1 example of simulated household graph with N=524

Harm reduction interventions

We included the two main harm reduction interventions currently available in France at a national level: access to sterile injection equipment through harm reduction facilities, harm reduction kits in pharmacy or via automatic dispensers; and opioid substitution treatments (buprenorphine or methadone). The model is represented Figure S2, and the parameters values are given Table S2.
We assumed a mean time before access to NSP of 2 years, based on the high number of PWID reporting difficulties to access syringes (30%, see (13)). The high proportion of active PWID currently under OST, and experts' opinions suggesting that NSP and OST are initiated almost simultaneously lead us to consider a relatively short duration before entering in the NSP+OST compartment (1 year).

About 37% of PWID under OST remain under treatment 10 months of the year (14) , given 2.3 years in average before cessation of OST according to the survival function of the exponential distribution (and assuming such distribution). In addition, this data and the high proportion of PWID under OST suggest that the cessation of OST is short: we assumed a come-back under OST after 3 months. Relative risk of HCV infection in each compartment was estimated in a meta-analysis (15). In this study NSP parameters were estimated considering a high-coverage needle program (i.e. where a sterile syringe is available for 100% of the injections of the user).

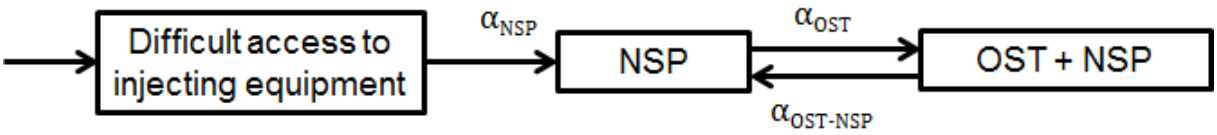

Figure S2 harm reduction interventions. NSP=Needle and syringe program, OST=Opioid substitution therapy. Each transition occurs according to exponential law. $\alpha_{OST-NSP}$ depends on the existence of a previous OST among the PWID: the return under OST is faster than the first OST initiation.

Natural history

The previously used model for chronic hepatitis C natural history included the fibrosis progression, the two cirrhosis complications (decompensated cirrhosis and HCC). We changed it to include hepatic transplant in cirrhosis complications, due to the high costs incurred. A representation of the model is given Figure S3. The corresponding parameters are described in Table S2.

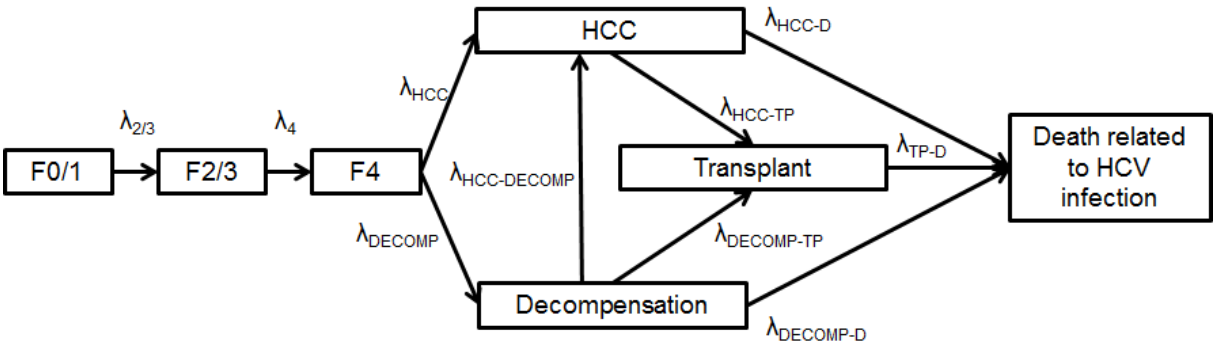

Figure S3 natural history of chronic hepatitis C in the model. F0/F1 refers to a F0 or F1 Metavir score; and F2/F3 to a F2 or F3 Metavir score. Each transition occurs according to exponential law. λ_{TP-D} depends on the time since transplant: the mortality rate is higher during the first year.

Infection and care

The model is represented in Figure S4. Briefly, starting from the susceptible state, an active (i.e. before cessation of injection) PWID can be infected with an infection rate depending on the number of his/her infectious injecting partners on the network and his/her status related to harm reduction interventions. After the acute phase of hepatitis C he/she can spontaneously recover with probability and become susceptible again or progress to chronic hepatitis C. Then, he/she can be diagnosed at a rate that depends on his/her status related to injection: active or inactive injector. Once diagnosed, he/she can be linked to healthcare, and he/she can be lost to follow-up, or be treated if his/her Metavir score is between F2 and F4 (in the current practice). Then he/she can have SVR and become susceptible again or otherwise progress to "Non SVR", in which he/she can not be treated again. When a complication of cirrhosis occurs, a PWID is automatically linked to care. The parameters values were found in the literature or using data from the ANRS-Coquelicot study. The initial incidence was fitted by ABC to obtain an initial incidence of 12/100 p-y (16, 17) (the prior and posterior distribution are presented Figure S4). The linkage to care rate was estimated using ABC from Coquelicot data in a previous modelling study (1).

Parameters values are given Table S2.

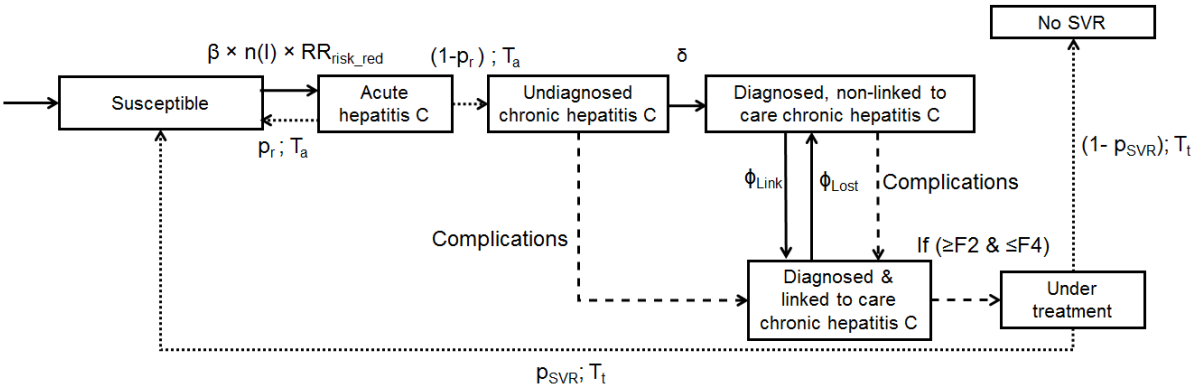

Figure S4 model for HCV infection and care. A new PWID enters the model as susceptible. Plain arrows correspond to transitions occurring according to exponential probability distributions. Dashed lines correspond to transition occurring after a fixed time with a given probability. Dotted lines correspond to transitions related to a transition in the natural history model. n(i) refers to the number of infectious injecting partners of the PWID. RR_{risk_red} refers to the relative risk of infection related to the PWID status regarding harm reduction interventions.

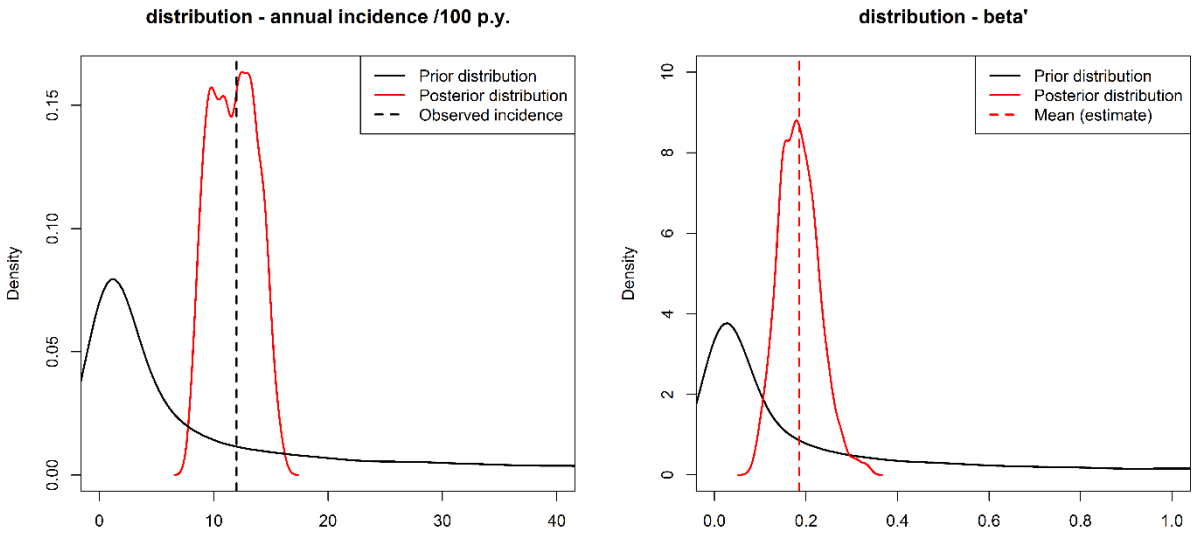

Figure S5 Prior and posterior distributions obtained by Approximate Bayesian Computation for the initial incidence (left) and the infection rate (right).

Cessation of drug injection and mortality non-related to HCV

The model takes also into account the cessation of injection: the duration of the injecting career is supposed to be 13.9 years (18, 19).

The mortality in the model depends on the gender, the age and the current injecting status (active injector or former injector). We assumed that the mortality for former injectors is similar to that of general French population, and we used the table of the mortality rates for the years 2012 in this case (20). For active injector, we applied a relative risk of 5.19 for men and 9.52 for women (21).

Table S2 Parameters for the model: initial population, infection, care and natural history

Parameter	Value	References
Population size	20×524*	
Initial distribution infection and care		
Susceptible	57.2%	ANRS-Coquelicot, see (1)
Acute hepatitis	0%*	
Non-diagnosed chronic hepatitis	9.2%	ANRS-Coquelicot see (1)
Diagnosed, non-linked to care chronic hepatitis C	11.3%	
Diagnosed and linked to care chronic hepatitis C	16.0%	
Under treatment	2.2%	

Non-responders after treatment	4.1%	
Initial distribution in the natural history model		
F0/F1	35.0%	(22)
F2/F3	51.0%	
F4	14.0%	
Decompensated cirrhosis	0.0%*	
HCC	0.0%*	
Initial distribution related to harm reduction interventions		
Difficult access to injecting equipment	30.0%*	Hypothesis, derived from (13, 23-25)
NSP	20.0%*	
NSP+OST	50.0%*	
Men among current PWID	75.5%	ANRS-Coquelicot
Infection rate by injecting partner	0.184 $y^{-1}partner^{-1}$	Fitted by ABC to have a 12/100 p-y baseline incidence (16, 17)
Relative risk of infection when under		
NSP	0.5	(15)
NSP+OST	0.21	For a high-coverage needle program (i.e. where a sterile syringe is available for 100% of the injections of the user)
Transition from "Difficult access to injecting equipment" to NSP	2y*	
Transition from NSP to NSP+OST		Hypothesis, derived from (13, 23-25)
First time	0.5y*	
Next times	0.25y*	
Transition from NSP+OST to NSP	2.3y*	
Duration of acute hepatitis C	0.5 y	(26)
Probability of spontaneous recovery	26%	
Average time from chronic infection to diagnosis		
Current PWID	1.25 y	Previously estimated from ANRS Coquelicot data (1)
Former PWID	1.45 y	
Average time before linkage to care	2.6 y	Previously fitted by ABC using ANRS Coquelicot data (1, 27)
Loss to follow-up rate	14%/y	(28)
Treatment: incoming DAAs regimens		
Duration	12 weeks	(29-37)
SVR rate – treatment naïve – all genotypes- clinical trials	95%	
Duration of injecting career	13.9 y	(18, 19)
Transition rate F0/F1→ F2/F3	0.052 y^{-1}	(38)

Transition rate F2/F3→ F4 (λ_4)	0.054 y^{-1}	
Transition rate F4→Decompensated cirrhosis	0.04 y^{-1}	
Transition rate F4→HCC	0.021 y^{-1}	
Transition rate Decompensated cirrhosis→Death related to HCV	0.306 y^{-1}	(39, 40)
Transition rate HCC→Death related to HCV	0.433 y^{-1}	
Transition rate Decompensated cirrhosis→HCC	0.021 y^{-1}	
Transition rate Decompensated cirrhosis→Transplantation	0.128 y^{-1}	
Transition rate HCC→Transplantation	0.186 y^{-1}	
Transition rate Transplantation→Death related to HCV		(41, 42)
First year	0.174 y^{-1}	
Following years	0.033 y^{-1}	
Relative risk in patients achieving SVR in F4		
Death related to HCV infection	0.13	
Decompensated cirrhosis	0.08	(43)
HCC	0.27	

[*] Hypothesis
ABC: Approximate Baysian Computation
SVR: Sustained virological response
PWID: People who inject drugs
$y^{-1:}$ per year
HCC: Hepatocellular carcinoma
DAA: Direct-acting antiviral
HCV: Hepatitis C virus

COSTS AND UTILITIES

Costs

In the analysis, we included all the relevant costs related to harm reduction interventions and chronic hepatitis C testing, healthcare and treatment on an annual basis.

Harm reduction interventions

NSP: Budget by PWID of the active file of French harm reduction facilities (CAARUD) are estimated at 630€ annually (44), thus we used this estimate for PWID in NSP in our model.

OST: The average annual budget of French healthcare centers in addictology (CSAPA) is 746,472€ for an average active file of 574 PWID (45), thus we used an estimate at 1,300€ per PWID. In addition, based on the distribution of PWID on buprenorphine and methadone, the distribution between the princeps and generic form for buprenorphine delivery, the distribution between capsule and syrup for methadone, and the average posology for each of this treatment (from (14)) and the cost of each of product (from (46)) we estimated the annual cost on OST at 530€. The final estimate is thus 1,830€ for PWID in OST in the model.

Chronic hepatitis C related costs

Testing: the cost of a serology for PWID susceptible was set at 19.575€ (47). The annual cost depends on the testing rate delta assumed in the scenario.

Ressources consumption for HCV care: These costs were only taken into account for PWID linked to the healthcare system. We used estimates from French general population (48). These costs are summarized in Table S3.

Table S3 Annual mean costs (SD) attributable to chronic hepatitis C: ambulatory costs (never treated and after HCV treatment failure) and hospitalization costs (no death and in-hospital death) (48)

Liver disease stage	**Ambulatory costs (€)**		**Hospitalization costs (€)**	
	Never treated	**After treatment failure**	**No death**	**In-hospital death**
F0/F1	70 (10)	53 (12)	278 (1,087)	337 (1,377)
F2/F3	128 (22)	86 (15)		

F4	228 (20)	71 (18)	1,295 (3,732)	6,450 (11,422)
Decompensation		96 (21)	9,874 (12,246)	16,119 (17,778)
HCC		96 (21)	11,745 (11,634)	16,643 (14,137)
Liver transplant				
First year		96 (21)	56,021 (40,329)	90,712 (55,462)
Following years		96 (21)	5,445 (11,123)	15,911 (23,307)

Treatment: the cost of new antiviral therapies was assumed to be 28,730€ for a 12-weeks treatment, which is the current cost of several DAA for a treatment course at the time of the study (49). In addition, the healthcare cost for monitoring these treatments (physician consultations and laboratory tests) were estimated used French treatment guidelines to 740€.

Costs of implementation of the scenarios

Improvements in harm reduction interventions: as the annual cost we used for NSP and OST include the operating budget of the corresponding structures (CAARUD and CSAPA), we added no supplementary cost for the improvements of these interventions (corresponding to the opening of additional structures).

Treatment from F0: as we assumed in our analyses interferon free regimens with short treatment duration, we assumed that the treatment cost and healthcare monitoring costs would mainly be the cost of implementing this strategy.

Improvements in testing and, linkage to care to treatment: based on a previous cost-effectiveness analysis about HIV screening in France (50), we estimated that the start-up cost of improving testing would mainly be the cost of training physicians working in CSAPA. Among the 70 CSAPA in Paris metropolitan area, considering an average of 9.6 employees/CSAPA including 16% of physicians, we estimated their number to be 40 (45). Considering a two-days training with 20 participants per training receiving 330€/day and instructors 1,500€/course, and 80% of acceptance, the cost is 29,400€ for this strategy.

In a similar way, the cost related to improvements in linkage to care would concern more healthcare workers: general practitionners (20,235) and gastroenterologists-hepatologists (840) (51); and CSAPA physicians were estimated at 12M€. This estimation represents probably an overestimation of the cost of this strategy, because the amount of physician that would be trained would probably be lower. However, in a conservative way we included this cost in the corresponding scenarios.
We made the hypothesis that with interferon free regimens and such shorter durations, an improvement in the adherence to treatment could occur relatively easily and we neglected the costs related.

Utilities

The measure of the quality of life was adjusted to take into account the impact of drug injection, chronic HCV infection and treatment with new DAAs.

Drug injection

For PWID before injection cessation, we adjusted the number of life years gained by a factor 0.9 (52).

Chronic hepatitis C related utilities

Due to the lack of data about French PWID with new DAAs regimens in F0 to F4 fibrosis scores, we used utilities estimated from a cross sectional study in France in HCV infected patients under dual therapy peg-interferon/ribavirin (53). Utilities in cirrhosis complications where derived from (53).

Table S4 Utilities estimated in an HCV-infected French population according to disease stage (53) and assumptions used in the model.

	HCV-RNA-positive	**HCV-RNA-negative***
F0/F1	0.82	0.95
F2/F3†	0.76	0.85
F4	0.60	0.85
Decompensated cirrhosis/HCC	0.60	0.60
Liver transplantation (first year)	0.55	0.55
Liver transplantation (following years)	0.82	0.82
Multiplied under IFN-free regimens	0.950	

*In case of SVR. †We conservatively assumed that the utilities in F2/F3 compartment correspond to that of F3 in Schwarzinger *et al.* study.

Treatment

We assumed that the future HCV treatment will be injection-free DAAs regimens with few adverse events. Thus, by hypothesis we adjusted the number of life years gained by a factor 0.95 (54).

S2 : EVOLUTION OF THE NUMBER OF NEWLY INFECTED PEOPLE IN THE POPULATION

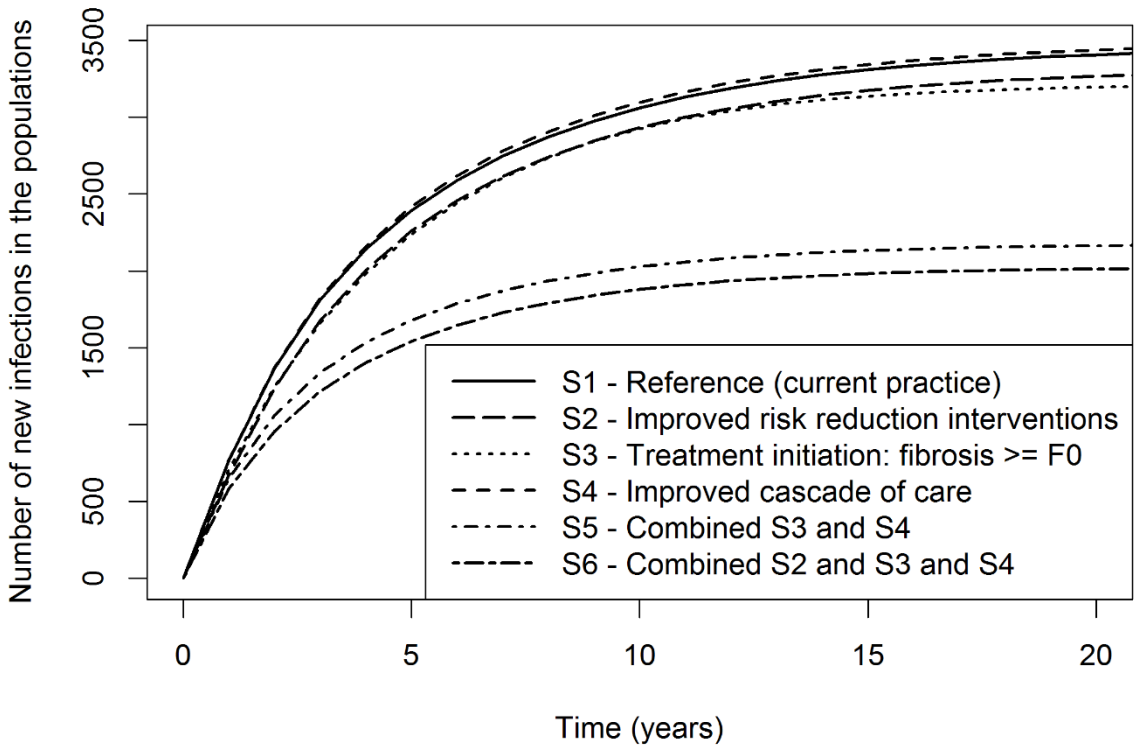

Figure S6 Evolution of the number of new infections in the population over the first 20 years.

S3: SENSITIVITY ANALYSIS

In this section, we present the results obtained by changing the key parameters in the simulations.

Treatment cost

Table S5 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. Compared with the main analysis, a 25% decrease was applied to the treatment cost.

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Reference scenario	19,405 (173)	18.402 (0.055)	15.846 (0.055)	3,461 (85)	992 (45)		
S2 – Improved risk reduction interventions	20,386 (175)	18.405 (0.056)	15.864 (0.055)	3,319 (83)	949 (42)	Extended dominance	Extended dominance
S4 – Improved testing/linkage to care	20,758 (145)	18.494 (0.057)	16.083 (0.057)	3,491 (87)	1,191 (49)	14,700	Extended dominance
S3 – Treatment initiation: fibrosis ≥F0	22,207 (211)	18.424 (0.054)	16.382 (0.054)	3,216 (112)	1,470 (70)	Dominated	Extended dominance
S5 – Combined S3 and S4	22,900 (194)	18.509 (0.055)	16.694 (0.054)	2,176 (100)	1,050 (65)	142,800	4,100
S6 – Combined S2 and S3 and S4	23,703 (201)	18.513 (0.055)	16.701 (0.054)	2,025 (99)	971 (62)	200,700	114,700

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Table S6 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. Compared with the main analysis, a 50% decrease was applied to the treatment cost.

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Reference scenario	18,048 (165)	18.402 (0.055)	15.846 (0.055)	3,461 (85)	992 (45)		
S2 – Improved risk reduction interventions	19,040 (168)	18.405 (0.056)	15.864 (0.055)	3,319 (83)	949 (42)	Extended dominance	Extended dominance
S4 – Improved testing/linkage to care	19,316 (138)	18.494 (0.057)	16.083 (0.057)	3,491 (87)	1,191 (49)	13,800	Extended dominance
S3 – Treatment initiation: fibrosis ≥F0	19,849 (185)	18.424 (0.054)	16.382 (0.054)	3,216 (112)	1,470 (70)	Dominated	Extended dominance
S5 – Combined S3 and S4	20,576 (165)	18.509 (0.055)	16.694 (0.054)	2,176 (100)	1,050 (65)	84,000	3,000
S6 – Combined S2 and S3 and S4	21,444 (171)	18.513 (0.055)	16.701 (0.054)	2,025 (99)	971 (62)	217,000	124,000

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Table S7 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. Compared with the main analysis, a 75% decrease was applied to the treatment cost.

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Reference scenario	16,690 (159)	18.402 (0.055)	15.846 (0.055)	3,461 (85)	992 (45)		
S3 – Treatment initiation: fibrosis ≥F0	17,490 (164)	18.424 (0.054)	16.382 (0.054)	3,216 (112)	1,470 (70)	Extended dominance	1,500
S2 – Improved risk reduction interventions	17,694 (164)	18.405 (0.056)	15.864 (0.055)	3,319 (83)	949 (42)	Dominated	Dominated
S4 – Improved testing/linkage to care	17,874 (134)	18.494 (0.057)	16.083 (0.057)	3,491 (87)	1,191 (49)	12,900	Dominated
S5 – Combined S3 and S4	18,252 (142)	18.509 (0.055)	16.694 (0.054)	2,176 (100)	1,050 (65)	25,200	2,400
S6 – Combined S2 and S3 and S4	19,186 (148)	18.513 (0.055)	16.701 (0.054)	2,025 (99)	971 (62)	233,500	133,400

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Initial incidence

Table S8 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. The initial incidence used was 22/100 p.y. (vs. 12/100 p.y. in the main analysis), corresponding to a study among PWID in Montréal, Canada (derived from local data – SurvUDI network (56, 57)).

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Reference scenario	21,408 (200)	18.377 (0.056)	15.657 (0.054)	4,983 (98)	1,648 (60)		
S2 – Improved risk reduction interventions	22,295 (170)	18.382 (0.057)	15.682 (0.056)	4,816 (94)	1,587 (57)	Extended dominance	Extended dominance
S4 – Improved testing/linkage to care	22,708 (161)	18.476 (0.054)	15.899 (0.054)	5,266 (106)	2,060 (71)	13,100	5,400
S3 – Treatment initiation: fibrosis ≥F0	28,685 (305)	18.389 (0.056)	16.196 (0.056)	6,128 (168)	3,337 (123)	Dominated	Extended dominance
S5 – Combined S3 and S4	30,180 (382)	18.494 (0.057)	16.591 (0.057)	5,182 (199)	3,053 (150)	415,100	10,800
S6 – Combined S2 and S3 and S4	30,635 (387)	18.494 (0.053)	16.601 (0.052)	4,850 (205)	2,839 (150)	Dominated	45,500

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Table S9 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. The initial incidence used was 42/100 p.y. (vs. 12/100 p.y. in the main analysis), corresponding to a study among PWID in London, United-Kingdom (58).

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Reference scenario	21,904 (195)	18.348 (0.058)	15.493 (0.056)	6,270 (103)	2,300 (68)		
S2 – Improved risk reduction interventions	22,832 (178)	18.354 (0.057)	15.514 (0.055)	6,126 (108)	2,244 (71)	Extended dominance	Extended dominance
S4 – Improved testing/linkage to care	23,193 (176)	18.460 (0.059)	15.733 (0.057)	6,863 (122)	2,956 (88)	11,500	5,400
S3 – Treatment initiation: fibrosis ≥F0	33,489 (344)	18.346 (0.055)	15.989 (0.056)	9,543 (197)	5,875 (161)	Dominated	Extended dominance
S5 – Combined S3 and S4	40,284 (526)	18.450 (0.057)	16.383 (0.057)	11,485 (306)	8,111 (266)	Dominated	Extended dominance
S6 – Combined S2 and S3 and S4	40,503 (539)	18.452 (0.056)	16.396 (0.056)	11,020 (306)	7,744 (262)	Dominated	26,100

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Mean time to diagnosis

Table S10 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. The mean time to diagnosis was set at 2.0 years (vs. 1.25/1.45 years for active/inactive PWID in the main analysis) corresponding to a study among PWID in Montréal, Canada (derived from local data – SurvUDI network (56, 57)).

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Reference scenario	20,832 (168)	18.388 (0.052)	15.813 (0.052)	3,436 (84)	958 (42)		
S2 – Improved risk reduction interventions	21,773 (170)	18.395 (0.054)	15.836 (0.054)	3,298 (78)	918 (42)	Extended dominance	Extended dominance
S4 – Improved testing/linkage to care	22,200 (155)	18.494 (0.057)	16.083 (0.057)	3,491 (87)	1,191 (49)	12,900	Extended dominance
S3 – Treatment initiation: fibrosis ≥F0	24,407 (232)	18.413 (0.057)	16.333 (0.058)	3,262 (107)	1,467 (64)	Dominated	Extended dominance
S5 – Combined S3 and S4	25,223 (227)	18.509 (0.055)	16.694 (0.054)	2,176 (100)	1,050 (65)	Extended dominance	5,000
S6 – Combined S2 and S3 and S4	25,962 (234)	18.513 (0.055)	16.701 (0.054)	2,025 (99)	971 (62)	198,000	105,600

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Table S11 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. The mean time to diagnosis was set at 7.8 years (vs. 1.25/1.45 years for active/inactive PWID in the main analysis) corresponding to a study among PWID in London, United-Kingdom (59).

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Reference scenario	20,966 (187)	18.297 (0.055)	15.598 (0.053)	3,316 (76)	803 (37)		
S2 – Improved risk reduction interventions	21,870 (172)	18.298 (0.06)	15.618 (0.058)	3,188 (75)	770 (36)	Extended dominance	Extended dominance
S4 – Improved testing/linkage to care	22,200 (155)	18.494 (0.057)	16.083 (0.057)	3,491 (87)	1,191 (49)	6,300	2,500
S3 – Treatment initiation: fibrosis ≥F0	23,225 (213)	18.311 (0.059)	16.031 (0.058)	3,279 (97)	1,346 (56)	Dominated	Dominated
S5 – Combined S3 and S4	25,223 (227)	18.509 (0.055)	16.694 (0.054)	2,176 (100)	1,050 (65)	Extended dominance	4,900
S6 – Combined S2 and S3 and S4	25,962 (234)	18.513 (0.055)	16.701 (0.054)	2,025 (99)	971 (62)	198,000	105,600

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Mean time to linkage to care

Table S12 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. The mean time to linkage to care was set at 4.0 years (vs. 2.6 years in the main analysis).

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Reference scenario	20,858 (184)	18.366 (0.058)	15.762 (0.057)	3,423 (83)	928 (43)		
S2 – Improved risk reduction interventions	21,805 (172)	18.371 (0.055)	15.783 (0.055)	3,278 (81)	885 (41)	Extended dominance	Extended dominance
S4 – Improved testing/linkage to care	22,200 (155)	18.494 (0.057)	16.083 (0.057)	3,491 (87)	1,191 (49)	10,500	4,200
S3 – Treatment initiation: fibrosis ≥F0	24,353 (214)	18.395 (0.055)	16.291 (0.057)	3,308 (99)	1,476 (61)	Dominated	Extended dominance
S5 – Combined S3 and S4	25,223 (227)	18.509 (0.055)	16.694 (0.054)	2,176 (100)	1,050 (65)	Extended dominance	4,900
S6 – Combined S2 and S3 and S4	25,962 (234)	18.513 (0.055)	16.701 (0.054)	2,025 (99)	971 (62)	198,000	105,600

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Loss to follow-up rate

Table S13 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. The annual loss to follow-up rate was set at 20%/year (vs. 14%/year in the main analysis).

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Reference scenario	20,559 (179)	18.4 (0.056)	15.835 (0.056)	3453 (82)	985 (45)		
S2 – Improved risk reduction interventions	21,508 (167)	18.406 (0.06)	15.856 (0.057)	3314 (76)	942 (41)	Extended dominance	Extended dominance
S4 – Improved testing/linkage to care	22,200 (155)	18.494 (0.057)	16.083 (0.057)	3,491 (87)	1,191 (49)	17,500	Extended dominance
S3 – Treatment initiation: fibrosis ≥F0	24,556 (217)	18.421 (0.057)	16.380 (0.056)	3,214 (102)	1,470 (63)	Dominated	Extended dominance
S5 – Combined S3 and S4	25,223 (227)	18.509 (0.055)	16.694 (0.054)	2,176 (100)	1,050 (65)	Extended dominance	5,400
S6 – Combined S2 and S3 and S4	25,962 (234)	18.513 (0.055)	16.701 (0.054)	2,025 (99)	971 (62)	198,000	105,600

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Table S14 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. The annual loss to follow-up rate was set at 30%/year (vs. 14%/year in the main analysis) by authors' choice.

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Reference scenario	20,304 (176)	18.397 (0.057)	15.820 (0.057)	3,443 (82)	972 (43)		
S2 – Improved risk reduction interventions	21,266 (179)	18.400 (0.054)	15.840 (0.053)	3,306 (81)	932 (43)	Extended dominance	Extended dominance
S4 – Improved testing/linkage to care	22,200 (155)	18.494 (0.057)	16.083 (0.057)	3,491 (87)	1,191 (49)	19,500	Extended dominance
S3 – Treatment initiation: fibrosis ≥F0	24,548 (242)	18.424 (0.055)	16.384 (0.054)	3,210 (109)	1,468 (70)	Dominated	Extended dominance
S5 – Combined S3 and S4	25,223 (227)	18.509 (0.055)	16.694 (0.054)	2,176 (100)	1,050 (65)	Extended dominance	5,600
S6 – Combined S2 and S3 and S4	25,962 (234)	18.513 (0.055)	16.701 (0.054)	2,025 (99)	971 (62)	198,000	105,600

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Risk of reinfection following a SVR

Table S15 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. The risk of reinfection per infected injecting partner β was divided by 3 after a previous infection successfully treated (60, 61).

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Reference scenario	20,694 (179)	18.413 (0.055)	15.873 (0.054)	3,260 (77)	816 (37)		
S2 – Improved risk reduction interventions	21,679 (175)	18.412 (0.055)	15.886 (0.053)	3,133 (76)	785 (38)	Extended dominance	Extended dominance
S4 – Improved testing/linkage to care	22,136 (153)	18.500 (0.056)	16.104 (0.055)	3,276 (85)	999 (46)	16,600	Extended dominance
S3 – Treatment initiation: fibrosis ≥F0	24,345 (228)	18.427 (0.054)	16.396 (0.055)	2,994 (96)	1,271 (56)	Dominated	Extended dominance
S5 – Combined S3 and S4	24,998 (234)	18.515 (0.054)	16.705 (0.054)	2,018 (92)	907 (57)	190,800	5,200
S6 – Combined S2 and S3 and S4	25,782 (222)	18.515 (0.056)	16.708 (0.055)	1,897 (90)	854 (55)	Dominated	261,300

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Harm reduction

Table S16 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. The initial distribution and transition rates in the harm reduction interventions model were changed for a worst case: initial distribution in NSP=40% and in NSP+OST=45% vs. 30% and 50% respectively in the main analysis.

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Reference scenario	19,789 (181)	18.406 (0.056)	15.833 (0.055)	3,599 (82)	1,037 (43)		
S4 – Improved testing/linkage to care	21,204 (164)	18.495 (0.057)	16.069 (0.055)	3,648 (91)	1,256 (51)	15,900	Extended dominance
S2 – Improved risk reduction interventions	21,731 (184)	18.405 (0.056)	15.864 (0.055)	3,319 (83)	949 (42)	Dominated	Dominated
S3 – Treatment initiation: fibrosis ≥F0	23,810 (241)	18.423 (0.056)	16.373 (0.056)	3,407 (109)	1,573 (69)	Dominated	Extended dominance
S5 – Combined S3 and S4	24,433 (242)	18.513 (0.056)	16.693 (0.055)	2,323 (108)	1,132 (68)	179,400	5,400
S6 – Combined S2 and S3 and S4	25,962 (234)	18.513 (0.055)	16.701 (0.054)	2,025 (99)	971 (62)	Dominated	191,100

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Quality of life

Table S17 Quality of life data used for the sensitivity analysis from (62, 63)

	HCV-RNA-positive	**HCV-RNA-negative***
F0/F1	0.931	0.95
F2/F3†	0.902	0.95
F4	0.872	0.89
Decompensated cirrhosis/HCC	0.794	0.81
Liver transplantation	0.843	0.843
Multiplied under IFN-free regimens	0.950	

*In case of SVR. †We conservatively assumed that the utilities in F2/F3 compartment correspond to that of F3 in Siebert *et al.* study.

Table S18 Results of the sensitivity analysis. The costs, life expectancy and adjusted life expectancy are discounted according to French guidelines. The scenarios were sorted by increasing costs. The quality of life data we used for the impact of HCV infection were changed for those of a German study (62, 63), see Table S17.

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Base case	20,762 (184)	18.402 (0.055)	16.561 (0.057)	3,461 (85)	992 (45)		
S2 – Improved risk reduction interventions	21,731 (184)	18.405 (0.056)	16.569 (0.056)	3,319 (83)	949 (42)	Extended dominance	Extended dominance
S4 – Improved testing/linkage to care	22,200 (155)	18.494 (0.057)	16.719 (0.052)	3,491 (87)	1,191 (49)	15,600	9,100
S3 – Treatment initiation: fibrosis ≥F0	24,566 (242)	18.424 (0.054)	16.742 (0.055)	3,216 (112)	1,470 (70)	Dominated	Extended dominance
S5 – Combined S3 and S4	25,223 (227)	18.509 (0.055)	16.929 (0.052)	2,176 (100)	1,050 (65)	Extended dominance	14,400
S6 – Combined S2 and S3 and S4	25,962 (234)	18.513 (0.055)	16.932 (0.056)	2,025 (99)	971 (62)	198,000	246,300

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Injecting partners network

Table S19 Results of the sensitivity analysis. The connectivity of the social network was supposed to be lower than in the main analysis, using the lower bounds of the confidence intervals for the probabilities of linking 2 individuals (see supplementary material S1): $\widehat{p_{12}}$=3.28e^{-5}; $\widehat{p_{15}}$=6.25e^{-6}; $\widehat{p_{25}}$=2.60e^{-5}; $\widehat{p_{22}}$=1.07e^{-5}; $\widehat{p_{55}}$=1.37e^{-3} vs. $\widehat{p_{12}}$= 3.42e^{-4}; $\widehat{p_{15}}$=7.52e^{-5}; $\widehat{p_{25}}$=3.20e^{-4}; $\widehat{p_{22}}$=1.56e^{-4}; $\widehat{p_{55}}$=2.48e^{-3} in the main analysis.

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Base case	20,659 (183)	18.407 (0.057)	15.891 (0.055)	3,075 (78)	865 (42)		
S2 – Improved risk reduction interventions	21,575 (176)	18.414 (0.056)	15.914 (0.055)	2,930 (80)	821 (39)	Extended dominance	Extended dominance
S4 – Improved testing/linkage to care	22,076 (175)	18.496 (0.061)	16.126 (0.06)	3,064 (84)	1,028 (46)	15,900	Extended dominance
S3 – Treatment initiation: fibrosis ≥F0	23,841 (215)	18.432 (0.053)	16.420 (0.052)	2,703 (97)	1,213 (59)	Dominated	Extended dominance
S5 – Combined S3 and S4	24,662 (212)	18.512 (0.056)	16.709 (0.055)	1,843 (89)	877 (55)	161,600	4,900
S6 – Combined S2 and S3 and S4	25,437 (201)	18.513 (0.055)	16.712 (0.054)	1,707 (79)	808 (48)	775,000	258,300

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

Table S20 Results of the sensitivity analysis. Results of the sensitivity analysis. The connectivity of the social network was supposed to be higher than in the main analysis, using the upper bounds of the confidence intervals for the probabilities of linking 2 individuals (see supplementary material S1): $\widehat{p_{12}}$= 8.11e^{-4}; 1.88e^{-4}; $\widehat{p_{25}}$=7.88e^{-4}; $\widehat{p_{22}}$=4.06e^{-4}; $\widehat{p_{55}}$=4.35e^{-3} vs. $\widehat{p_{12}}$= 3.42e^{-4}; $\widehat{p_{15}}$=7.52e^{-5}; $\widehat{p_{25}}$=3.20e^{-4}; $\widehat{p_{22}}$=1.56e^{-4}; $\widehat{p_{55}}$=2.48e^{-3} in the main analysis.

Scenario	Average lifetime cost (sd) (€)	Average life expectancy (sd) (years)	Adjusted average life expectancy (sd) (QALYs)	Average number of new infections (sd)	Average number of reinfections after SVR (sd)	ICER (€/LY)	ICER (€/QALY)
S1 – Base case	20,976 (175)	18.394 (0.055)	15.774 (0.054)	4,046 (90)	1196 (48)		
S2 – Improved risk reduction interventions	21,960 (172)	18.394 (0.058)	15.79 (0.057)	3,910 (84)	1154 (45)	Dominated	Extended dominance
S4 – Improved testing/linkage to care	22,364 (154)	18.485 (0.054)	16.010 (0.053)	4,167 (101)	1465 (59)	15,300	5,900
S3 – Treatment initiation: fibrosis ≥F0	25,847 (280)	18.414 (0.052)	16.323 (0.053)	4,117 (134)	1950 (85)	Dominated	Extended dominance
S5 – Combined S3 and S4	26,300 (288)	18.506 (0.056)	16.671 (0.056)	2,838 (133)	1406 (85)	187,400	6,000
S6 – Combined S2 and S3 and S4	26,965 (261)	18.509 (0.053)	16.679 (0.053)	2,651 (120)	1306 (77)	221,700	83,100

sd: standard deviation; y: year ; QALY: quality-adjusted life-year, SVR: sustained virological response, ICER: incremental cost-effectiveness ratio. Cost, life expectancy and quality-adjusted life expectancy are discounted according to French guidelines (55): discount rate of 4% for individuals younger than 30, which was linearly decreased to 2% between 30 and 50 years of age, and set at 2% after 50. The scenarios were sorted by increasing costs. Dominated=more expensive and less effective. Extended dominance=at least one more expensive scenario is more cost-effective.

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