Research Article

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Cost-Effectiveness of Improving Hepatitis C Diagnosis and Treatment among People Who Inject Drugs in Türkiye

Türkiye'de Damar İçi Madde Kullanımı Olan Kişilerde Hepatit C Tanı ve Tedavisinin İyileştirilmesinin Maliyet-Etkililiği

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ABSTRACT

Objectives: This study aimed to develop a mathematical model of hepatitis C virus (HCV) transmission and disease progression among people who inject drugs (PWID) in Türkiye and to evaluate the cost-effectiveness of improving diagnosis and treatment over a 10-year time horizon.

Materials and Methods: A dynamic compartmental model was developed to estimate annual HCV prevalence and HCV-related mortality under four diagnosis-and-treatment coverage scenarios ranging from no diagnosis-and-treatment to high diagnosis-and-treatment coverage. A Bernoulli transmission model was used to estimate the force of infection and incorporated into the compartmental framework. Economic outcomes, including testing and treatment costs, and health outcomes, including infections prevented and quality-adjusted life years (QALYs), were projected for each scenario between 2020 and 2029. Incremental cost-effectiveness ratios (ICERs) were estimated for increasing diagnosis-and-treatment rates.

Results: Increasing diagnosis-and-treatment rates to 25%, 50%, and 75% compared with the no diagnosis-and-treatment scenario reduced cumulative HCV cases by 61%, 91%, and 98% over 10 years, respectively. HCV-related mortality decreased by 58%, 78%, and 86%, respectively. Increasing diagnosis-and-treatment coverage from 0% to 25% resulted in ICERs of $5,092 per infection prevented and $25,653 per QALY gained. Pairwise comparison of the 25% and 50% scenarios yielded ICERs of $880 per infection prevented and $4,715 per QALY gained. However, frontier analysis identified the medium strategy as dominated, as the high diagnosis-and-treatment strategy achieved greater health gains at a lower total cost and was therefore cost-saving.

Conclusion: PWID represent a key population in HCV transmission dynamics. Improving diagnosis and treatment among PWID in

ÖZ

Amaç: Bu çalışmanın amacı, Türkiye'de damar içi madde kullanan (DİMK) kişilerde hepatit C virüsü (HCV) bulaşı ve hastalık ilerlemesini modelleyen matematiksel bir model geliştirmek ve tanı ile tedavinin iyileştirilmesinin 10 yıllık bir zaman ufkunda maliyet-etkililiğini değerlendirmektir.

Gereç ve Yöntemler: Yıllık HCV prevalansı ve HCV'ye bağlı mortaliteyi, tanı ve tedavi yapılmayan senaryodan yüksek tanı ve tedavi kapsamına kadar uzanan dört farklı tanı ve tedavi kapsamı senaryosu altında tahmin etmek amacıyla dinamik bir kompartıman modeli geliştirilmiştir. Enfeksiyon kuvveti Bernoulli bulaş modeli kullanılarak tahmin edilmiş ve kompartıman modeline entegre edilmiştir. Test ve tedavi maliyetlerini içeren ekonomik sonuçlar ile önlenen enfeksiyon sayısı ve kaliteye uyarlanmış yaşam yıllarını (QALY) içeren sağlık sonuçları, 2020-2029 dönemi için her bir senaryo kapsamında projekte edilmiştir. Artan tanı ve tedavi oranları için artımlı maliyet-etkililik oranları (ICER) hesaplanmıştır.

Bulgular: Tanı ve tedavi oranının tanı ve tedavi yapılmayan senaryoya kıyasla %25, %50 ve %75'e yükseltilmesi, 10 yıllık dönemde kümülatif HCV olgu sayısını sırasıyla %61, %91 ve %98 azaltmıştır. HCV'ye bağlı mortalite ise sırasıyla %58, %78 ve %86 oranında azalmıştır. Tanı ve tedavi kapsamının %0'dan %25'e çıkarılması, önlenen enfeksiyon başına 5.092 ABD doları ve kazanılan QALY başına 25.653 ABD doları ICER ile sonuçlanmıştır. Tanı ve tedavi kapsamının %25'ten %50'ye çıkarılması, önlenen enfeksiyon başına 880 ABD doları ve kazanılan QALY başına 4.715 ABD doları ICER sağlamıştır. Bununla birlikte, maliyet-etkililik sınırı analizinde orta senaryonun, daha düşük maliyetle daha fazla sağlık kazanımı sağlayan yüksek senaryo tarafından domine edildiği gösterilmiş; yüksek tanı ve tedavi kapsamı maliyet tasarrufu sağlayan strateji olarak belirlenmiştir.

Sonuç: DİMK, HCV bulaş dinamiklerinde kilit bir risk grubunu oluşturmaktadır. Bu grupta tanı stratejilerinin geliştirilmesi ve tedaviye erişimin artırılması, Türkiye açısından maliyet-etkili, hatta maliyet tasarrufu

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Türkiye could be cost-effective, and potentially cost-saving, while also contributing substantially toward achieving World Health Organization HCV elimination targets.
Keywords: Mathematical modelling, hepatitis C, cost-effectiveness analysis, testing and diagnosis

sağlayan bir yaklaşım olabilir ve aynı zamanda Dünya Sağlık Örgütü'nün HCV eliminasyon hedeflerine ulaşılmasına önemli katkı sağlayabilir.
Anahtar Kelimeler: Matematiksel modelleme, hepatit C, maliyet-etkililik analizi, test ve teşhis

Introduction

There are around 11 million people who inject drugs (PWID) globally and 39.4% have hepatitis C infection (1). The global rise in drug use, particularly injection drug use (IDU), has been pronounced in recent years, with notable increases reported across Europe and the Middle East (2,3). PWID are at heightened risk for blood-borne infections due to high-risk behaviors such as needle and equipment sharing. Hepatitis C virus (HCV) is especially prevalent in this population, with global estimates indicating a seroprevalence of approximately 67% among PWID (4). It is estimated that nearly 10 million PWID have been infected with HCV, with annual incidence rates ranging from 5% to 45% (5). A key challenge in controlling HCV transmission among PWID is the asymptomatic nature of the disease, which contributes to a substantial proportion of undiagnosed cases and the continuation of risky behaviors.

Türkiye's geopolitical position as a transit corridor between Europe and Asia further elevates its vulnerability to drug trafficking and associated public health risks. Despite this, there is currently no comprehensive national screening or surveillance program for HCV, impeding efforts to quantify and control the epidemic. Estimates place the national HCV prevalence around 1% (6,7); however, reliable data specific to the PWID population remain scarce. One of the few studies available reported an HCV seroprevalence of 47.1% among 4,694 inpatients at substance use treatment centers across Türkiye between 2012 and 2013 (8). Given the increasing trends in IDU and the absence of systematic monitoring, there is a pressing need to estimate the burden of HCV among PWID in Türkiye and to evaluate cost-effective prevention and treatment strategies tailored to this high-risk group.

Türkiye-specific HCV modelling and economic evaluation studies demonstrate that improving treatment rates are cost-effective in national scale and targeted screening and treatment for high-risk populations such as PWID, prisoners and refugees may yield substantial mortality reductions (9). Models by Örmeci et al. (10) and Idilman et al. (11) utilized Markov-based frameworks to evaluate the impact of improving treatment and reaching World Health Organization (WHO) targets, reporting up to 80% decrease in the number of infections and liver-related deaths. Although Idilman et al. (11) emphasize priority subpopulations, including PWID, these groups are not explicitly represented within the model structure.

Similarly, Çekin et al. (9) incorporated high-risk populations such as PWID, men who have sex with men, prisoners and refugees into their analysis; however, the underlying transmission dynamics within these populations were not explicitly defined. Despite these important contributions, a gap remains in integrating transmission dynamics, behavioral determinants of infection risk, and economic evaluation within a unified framework tailored specifically to PWID in Türkiye. This study addresses this gap by explicitly modeling PWID transmission dynamics—linking needle-sharing behavior to force of infection through a Bernoulli-based model and dynamic compartmental model—and embedding this within a cost-effectiveness framework to evaluate both epidemiologic and economic outcomes of diagnosis and treatment scale-up.

Materials and Methods

We developed a mathematical model of HCV transmission and progression for the 15-65 years old PWID population to understand HCV dynamics and to evaluate the cost-effectiveness of improved diagnosis and treatment in Türkiye for a 10-years interval. We utilized two models: Bernoulli process model and a dynamic compartmental model. Both models are populated with epidemiological, clinical, demographic and economic data from various sources and literature. Details of the model and data are explained in this section. This study was performed according to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (12) and the CHEERS checklist of the study is in the Supplemental Appendix. Since this study is based on mathematical modeling and simulation, no statistical analyses were performed.

Population and Data

The target population includes PWID aged 15-64 years in Türkiye. The population size of PWID is estimated from the United Nations global PWID study (13) with an HCV prevalence of 47% (8).

We used a cohort of 2,719 HCV patients collected across 32 centers in Türkiye. The cohort retrospectively collected in 2019 and includes a wide range of information such as demographic data, laboratory results, and treatment regimens. In our study, we utilized the fibrosis score distribution of the patients and the percentage of the patients with decompensated cirrhosis from this dataset to inform the initial conditions of our model. We only included the treatment-naïve Hepatitis C population.

The data extracted from the patient cohort were anonymized. The principal investigator of the cohort, who is also co-author of the submitted study permitted the use of cohort data for the study. Data extracted from cohort database were anonymized before access and analysis. Ethical committee approval was received from the Ethics Committee of İstanbul University-Cerrahpaşa (approval no: 59491012-604.01.02, date: March 07, 2017). Verbal consent was obtained from all participants. The study was recorded on clinical trials.gov (https://clinicaltrials.gov/study/NCT03145844). The trial registry name was "Direct Acting Agents in Hepatitis C Patients (HEPCTURKEY)" and the registration number was NCT03145844.

Model Structure

Our model structure incorporates two modeling approaches: the Bernoulli process model and a dynamic compartmental model. The Bernoulli model was used to estimate the force of infection—defined as the per capita rate at which susceptible individuals contract the infection (14)—by incorporating transmission probabilities and contact rates. The dynamic compartmental model was employed to simulate HCV transmission and disease progression among the PWID population.

Bernoulli Process Model

The Bernoulli model was used to estimate HCV transmission risk associated with IDU. Each act of IDU is considered an independent Bernoulli trial, resulting in one of two outcomes: transmission occurs or does not occur. The infectivity of HCV per injection, denoted as a_p represents the probability of transmission during a single injection event. The number of contacts per year, represented by *m*, is calculated by multiplying the needle-sharing rate *x* by the annual number of injections *y*. All parameter values used in the Bernoulli model are presented in Table 1.

Table 1. Parameters of Bernoulli model

Parameters (symbol)	Value	Source
Transmission probability of a single injection (a_p)	0.001	(15)
Needle sharing rate (*x*)	0.73	(8)
Annual number of injections (*y*)	368	(15)
Number of contacts per year (*m*)	269	Calculated
Cumulative probability of HCV transmission (*q*)	0.24	Calculated with Eq. 1

HCV: Hepatitis C virus

The cumulative probability of HCV transmission through IDU q is given in Equation 1.

$$q = 1 - (1 - a_p)^m \quad \text{(Equation 1)}$$

The cumulative annual transmission probability (*q*) was incorporated into the dynamic compartmental model as the annual transmission coefficient. Assuming homogeneous mixing among PWID, the force of infection was defined in the Equation 2.

$$\lambda(t) = q\frac{I(t)}{N(t)} \quad \text{(Equation 2)}$$

where *I(t)* denotes the number of infectious PWID and *N(t)* the total PWID population. Thus, *I(t)/N(t)* represents the proportion of infectious injecting partners, and *λ(t)* defines the annual rate at which susceptible individuals acquire HCV infection and transition to the acute infection compartment. The complete formulation of the force of infection and the system of differential equations are provided in the Supplemental Appendix.

Dynamic Compartmental Model

The transmission and progression of HCV are captured through a dynamic compartmental model over a 10-year time horizon (2019-2029). The population is stratified by infection status (HCV-negative, HCV-positive), fibrosis stage [acute, F0-F1, F2-F3, F4, decompensated cirrhosis, hepatocellular carcinoma (HCC)], treatment status (on and not on treatment at each stage), recovery, and death—resulting in a total of 14 compartments, as illustrated in Figure 1.

The model is specified as a system of ordinary differential equations and solved numerically in R. The model formulation is shown in the Supplemental Appendix. Parameter values are provided in Table 2. The transition from the HCV-negative compartment to acute infection is governed by the force of infection, which is

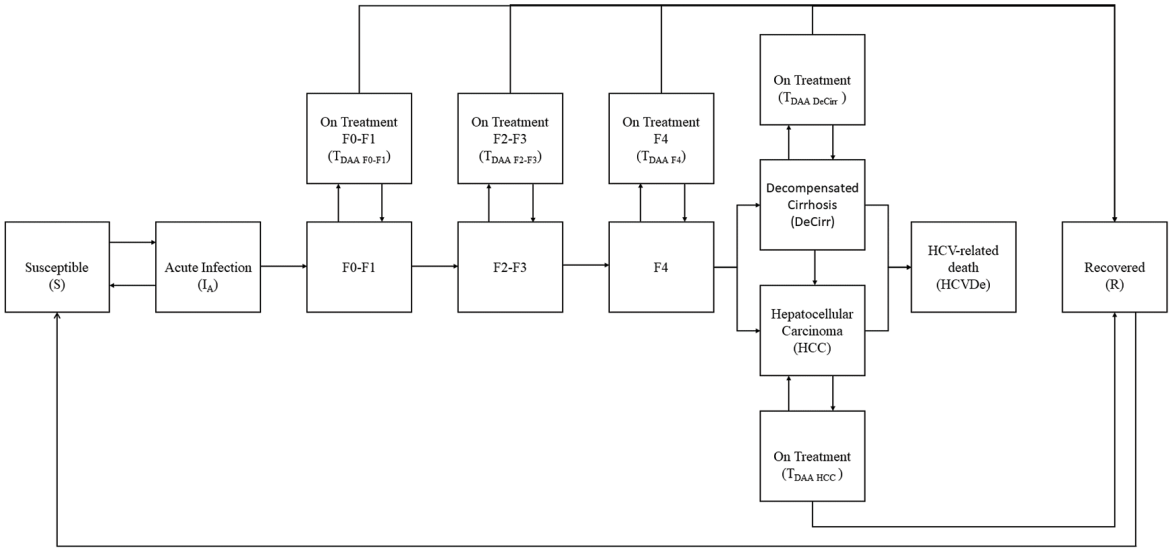

Figure 1. HCV model flow chart
HCV: Hepatitis C virus

informed by the cumulative transmission probability estimated from the Bernoulli model (see Equation 1). This integration allows the compartmental model to reflect injection-related transmission dynamics specific to the PWID population.

We modeled acute HCV infection with a fixed average duration of 6 months. At the end of the acute phase, 25% of incident infections are assumed to spontaneously clear and return to the susceptible state, while the remainder progress to chronic infection. Individuals who clear infection naturally or achieve sustained virologic response (SVR) after direct-acting antiviral (DAA) therapy are assumed to become susceptible again, allowing reinfections. Reinfection following successful DAA treatment has been documented, with elevated risk among PWID due to ongoing exposure through injecting networks (16,17,18).

Because of the lack of surveillance data, the true diagnosis rate of HCV in Türkiye is unknown. In our model, we implemented a scenario-based approach with four levels of diagnosis-and-treatment coverage: no coverage (0%), low (25%), medium (50%), and high (75%) of infected individuals. We assumed a 90% SVR following DAA therapy, reflecting a conservative estimate. Real-life studies from Türkiye, including recent long-term outcome analyses, have reported SVR12/24 rates between 85% and 100% across various regimens in chronic HCV (19,20,21,22,23,24,25), and systematic reviews and meta-analyses indicate that SVR rates may be lower in patients with decompensated cirrhosis or HCC (26,27,28,29).

Table 2. Key model parameters

Parameters (symbol)	**Values (ranges)**	**Source**
Percentage of HCV-positive initial population by disease stage, %		Dataset
F0-F1	42.7	
F2-F3	37.5	
F4	17.5	
Decompensated cirrhosis	2.3	
HCC	0	
HCV progression (rates across disease stages)		
Spontaneous clearance proportion (θ)	0.25 (0.21-0.29)	(20)
Duration of acute phase (ρ)	6 (1.6-2.5) months	(30)
Transition rate from F0/F1to F2/F3 (α_1)	0.195 (0.191-0.197)	(31)
Transition rate from F2/F3 to F4 (α_2)	0.2718 (0.2613-0.2824)	(31)
Transition rate from F4 to decompensated cirrhosis (v)	0.04 (0.032-0.052)	(32)
Transition rate from F4 to HCC (o)	0.021 (0.017-0.028)	(32)
Transition rate from decompensated cirrhosis to HCC (π)	0.021 (0.017-0.028)	(33)
HCV-related mortality rate		
Transition rate from HCC to HCV-related death (μ)	0.43 (0.32-0.5)	(33)
Transition rate from decompensated cirrhosis to HCV-related death (σ)	0.31 (0.13-0.40)	(32)
Treatment related parameters		
Treatment duration (χ)	12 (9.6-14.4) weeks	(20)
Proportion of achieving SVR among on DAA (γ)	0.9 (0.75-0.95)	(34)
Transition rate from recovered to susceptible (ψ)	1 (0.8-1.2) year	Expert opinion
Population parameters		
Initial population size (PWID)	396,772	(13)
Entry rate (c), %	0.7 (0.5-0.8)	(35)
The non-HCV related mortality rate (ω), %	0.5 (0.4-0.6)	(35)

HCV: Hepatitis C virus, HCC: Hepatocellular carcinoma, PWID: People who inject drugs, SVR: Sustained virologic response, DAA: Direct acting agents

Costs and QALYs

We incorporated HCV testing and treatment costs into the model based on published sources (Table 3). Testing costs included the anti-HCV antibody test for diagnosis, HCV-RNA testing for viral load confirmation, and FibroScan® assessment for fibrosis staging. DAA acquisition costs were included separately, based on average regimen prices reported in the literature. In Türkiye, DAAs have been reimbursed by the Social Security Institution (SGK) since 2016, making them accessible to all patients covered under the national health insurance scheme. In addition, treatment-related costs were stratified by disease stage, reflecting substantially higher expenditures for patients with advanced fibrosis, cirrhosis, HCC, or decompensated cirrhosis. All costs were estimated from the payer perspective and standardized to 2020 values using the health component of the Turkish consumer price index.

Health outcomes in the model is measured with quality-adjusted life years (QALYs). QALY values of each disaese stage and treatment status have been collected from the literature and presented in Table 4. In line with standard economic evaluation guidelines, both costs and health outcomes were discounted at an annual rate of 3% (36).

Scenario Analysis and Model Outcomes

Due to the absence of a national surveillance system for HCV, data on diagnosis rates are substantially limited in Türkiye. To assess the potential impact of diagnosis-and-treatment coverage on disease dynamics, we simulated four alternative scenarios within the compartmental model framework: (i) no diagnosis-and-treatment (0%), (ii) low diagnosis-and-treatment (25%), (iii) medium diagnosis-and-treatment (50%), and (iv) high diagnosis-and-treatment (75%). These values represent annual diagnosis-and-treatment coverage levels applied throughout the simulation period.

The intervention scenarios represent different levels of diagnosis and subsequent treatment coverage rather than diagnosis alone. In the model, individuals who are diagnosed are assumed to be promptly linked to care and initiate DAA treatment. This assumption reflects the Turkish healthcare system, in which universal health insurance through the SGK provides reimbursement for DAA therapy for all eligible patients with chronic HCV infection, minimizing financial barriers to treatment. Consequently, the intermediate steps of the care cascade (linkage to care, treatment initiation, and treatment completion) were not modeled explicitly. Following treatment, individuals achieve SVR according to the model parameter

Table 3. Test and treatment costs (10)

	Costs (USD)
Anti-HCV	3.84 (10)
HCV-RNA test/PCR	53.83 (10)
FibroScan®	105.73 (10)
Treatment cost by disease stage	
F0-F4	1,622 (10)
Cirrhosis	2,916 (10)
Decompensated cirrhosis	27,216 (10)
Hepatocellular carcinoma	35,980 (10)
DAA	31,470 (10)

HCV: Hepatitis C virus, PCR: Polymerase chain reaction, DAA: Direct acting agents

Table 4. QALYs by disease stage (37,38)

Input	**QALY**
Acute HCV infection	1*
On treatment for all heath states	0.95 (37)
F0-F1	0.93 (38)
F2-F3	0.83 (38)
F4 (cirrhosis)	0.81 (38)
Decompensated cirrhosis	0.70 (38)
Hepatocellular carcinoma	0.67 (38)
Recovered	1

*: Expert opinion, HCV: Hepatitis C virus, QALYs: Quality-adjusted life years

γ; those who do not achieve SVR continue to progress through the natural history of disease.

For each scenario, the model projected the annual changes in HCV prevalence and HCV-related mortality, as well as the corresponding healthcare costs and QALYs, over a 10-year time horizon. The outputs of these scenario analyses were compared to evaluate the relative epidemiological and economic implications of expanding diagnosis-and-treatment coverage among the target population.

Cost-Effectiveness Analysis

To evaluate the impact of diagnosis-and-treatment on HCV prevention, we conducted a cost-effectiveness analysis by estimating the incremental cost per QALY gained and per infection averted compared with the no diagnosis-and-treatment scenario. The incremental cost-effectiveness ratio (ICER) was calculated by dividing the difference in total costs by the difference in health outcomes between each scenario and the next best alternative. To assess the sensitivity of the results to discounting assumptions, we repeated the analysis using discount rates of 0% and 5%, in addition to the base case of 3%.

Sensitivity Analysis

We conducted a one-way sensitivity analysis to assess the impact of parameter uncertainty on model outcomes. The parameter ranges used are presented in Table 2. Where available, ranges were derived from published literature; in the absence of empirical data, a ±20% variation from the base value was assumed. The analysis quantified the relative influence of each parameter on the projected number of HCV cases in 2029, using the medium diagnosis-and-treatment scenario as the reference case. Results were visualized using a tornado diagram to illustrate the parameters with the greatest impact on model outcomes.

Results

We present total number of HCV cases and HCV-related deaths under each scenario over 10-years period in Figure 2. Under the "no diagnosis" scenario, the number of HCV infections doubles in 10-years from around 180,000 cases in 2019 to 280,000 cases in 2029. A similar trend could be observed in the number of HCV-related deaths with an average increase of up to 26-fold in the absence of testing and treatment. While this case is unrealistic, it provides us with an upper limit on what could happen without any testing and treatment efforts. The low diagnosis-and-treatment scenario shows that total infected cases could decrease by 61% while the medium and high- diagnosis-and-treatment scenarios yield substantially larger reductions of 91% and 98%, respectively, highlighting the potential for disease elimination. For liver-related mortality, model projections represent cumulative outcomes; therefore, comparisons are made relative to the no-treatment scenario to better capture the impact on mortality. Over a 10-year horizon, low, medium, and high diagnosis-and-treatment scenarios are projected to reduce total HCV-related deaths by 58%, 78%, and 86%, respectively.

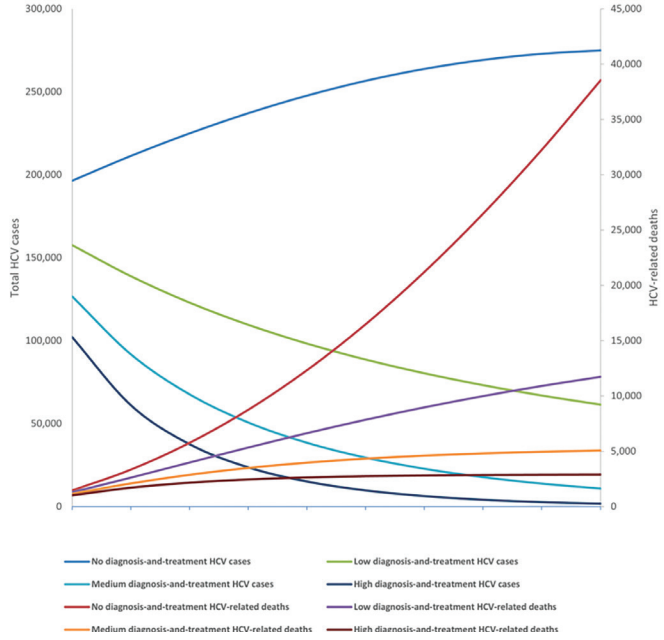

Figure 2. Estimated number of HCV cases and HCV-related deaths for no, low, medium and high diagnosis-and-treatment scenarios, 2020-2029
HCV: Hepatitis C virus

Figure 3 presents projections of acute infections and infections in F0-F4 stages across diagnosis-and-treatment scenarios. Consistent with the trends described above, the no diagnosis-and-treatment scenario shows persistently high levels of transmission and a growing chronic burden over time. In contrast, increasing diagnosis leads to a clear and progressive decline in both acute infections and total cases, with the steepest reductions observed under the high-diagnosis-and-treatment scenario.

This pattern is further reflected in the projected number of HCC and decompensated cirrhosis cases (Figure 4). The no diagnosis-and-treatment scenario results in the highest disease burden, whereas the low diagnosis-and-treatment scenario yields a 72% reduction in cases. Additional reductions of 17% and 5% are observed under the medium and high diagnosis-and-treatment scenarios, respectively, with HCC cases approaching near-zero levels under high diagnosis.

Cost-Effectiveness Analysis

Table 5 presents the cost-effectiveness results of improving diagnosis and treatment, with both costs and health outcomes discounted at an annual rate of 3%. In the base case, the no-treatment scenario represents an unrealistic benchmark with no treatment and, consequently, no treatment-related costs. The low diagnosis-and-treatment scenario results in $7.4 billion in testing and treatment costs, with an additional $400 million incurred when diagnosis is improved to the medium level. However, total costs decrease by approximately $300 million under the high diagnosis-and-treatment scenario, rendering it cost-saving relative to the medium scenario.

Although the pairwise comparisons presented in Table 5 evaluate the incremental effects of increasing diagnosis-and-treatment coverage between consecutive scenarios, construction of the cost-effectiveness frontier (Supplementary Table A1) indicates that the medium diagnosis-and-treatment strategy is strictly dominated by the high diagnosis-and-treatment strategy, which achieves greater health gains at a lower total cost.

Total QALYs increase from 3.2 million in the no diagnosis-and-treatment scenario to 3.7 million under high diagnosis-and-treatment. The cost per infection prevented, compared to the next best alternative, is $5,092 for the low scenario and $880 for the medium scenario, while the high scenario is cost-saving. Similarly, the ICERs per QALY gained are $25,653 and $4,715 for the low and medium scenarios, respectively, with the high scenario again being cost-saving and dominates the medium scenarios.

Using Türkiye's gross domestic product per capita (USD 8,798 in 2020) as the cost-effectiveness threshold, all scenarios except the low diagnosis-and-treatment scenario are cost-effective when evaluated in terms of QALYs, and the high diagnosis-and-treatment scenario is cost-saving compared with the medium scenario.

Cost-effectiveness results with 0% and 5% discounting is reported in the Supplemental Appendix (Tables A2 and A3).

Sensitivity Results

We conducted a one-way sensitivity analysis to assess the robustness of the model and identify key drivers of the results. The top 15 most influential parameters are presented in Figure 5. The model is most sensitive to the SVR rate and the transmission contact rate. The SVR rate directly affects treatment success and indirectly reduces transmission, as successfully treated individuals no longer contribute to onward transmission. The transmission contact rate, a key component of the force of infection, determines the rate at which susceptible individuals become infected and therefore strongly influences overall disease dynamics. The duration of the acute phase and the proportion of spontaneous clearance were identified as the next most influential parameters in the analysis.

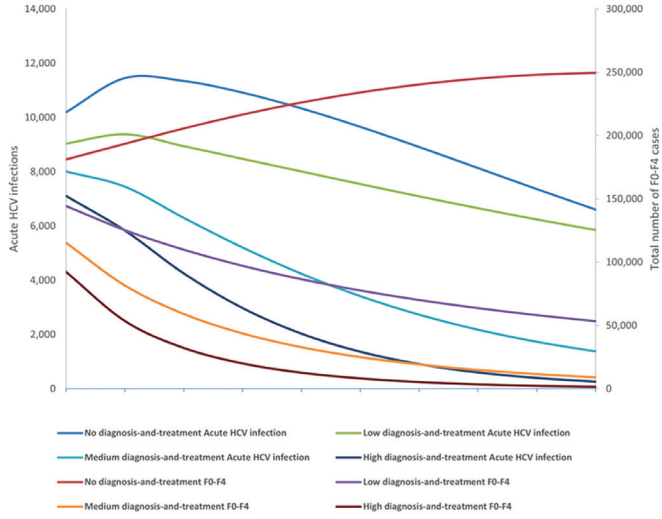

Figure 3. Estimated number of acute infections and infections in stages F0-F4 for no, low, medium and high diagnosis-and-treatment scenarios, 2020-2029
HCV: Hepatitis C virus

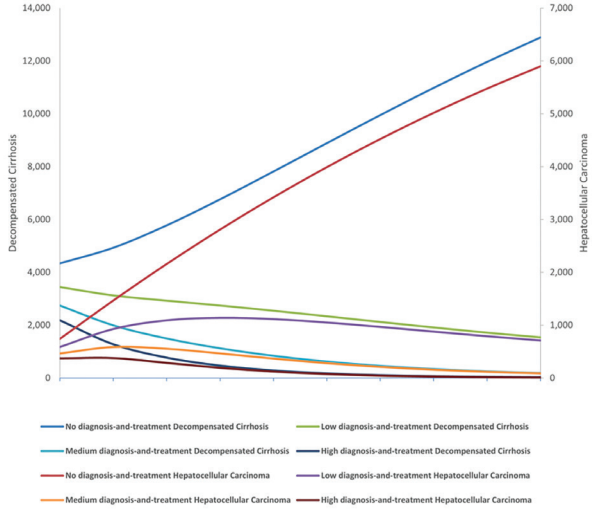

Figure 4. Estimated number of decompensated cirrhosis and hepacellullar carcinoma for no, low, medium and high diagnosis-and-treatment scenarios, 2020-2029

Table 5. Cost-effectiveness of diagnosis-and-treatment coverage strategies among people who inject drugs (PWID) in Türkiye (2020-2029)

	Total infections (2020-2029)	Total QALYs (2020-2029)	Total cost (2020-2029), $	Incremental cost prevented, $	Infections prevented	Incremental QALYs prevented	ICER infections prevented, $	ICER QALY, $
No diagnosis-and-treatment	2,454,480	2,906,867	0					
Low (25%)	997,403	3,196,115	7,420,163,380	7,420,163,380	1,457,077	289,248	5,092	25,653
Medium (50%)	469,632	3,294,669	7,884,851,199	464,687,819	527,772	98,553	880	4,715
High (75%)	264,366	3,335,426	7,578,245,318	Cost-saving	205,266	40,757	Cost-saving	Cost-saving

QALYs: Quality-adjusted life years, ICER: Incremental cost-effectiveness ratios

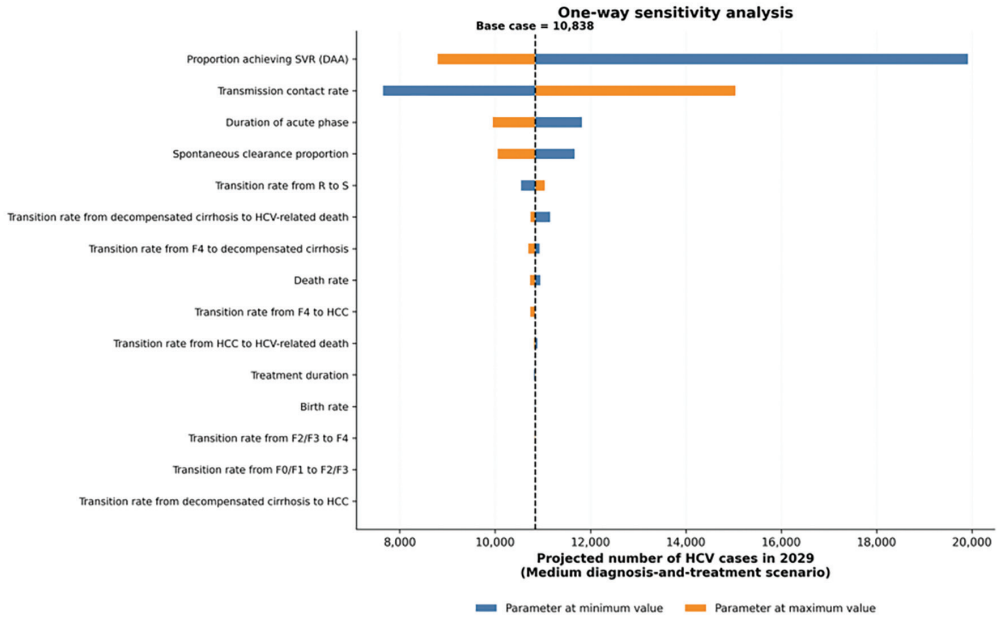

Figure 5. One-way sensitivity analysis of the projected number of HCV cases in 2029 under the medium diagnosis-and-treatment scenario. The vertical reference line represents the base-case estimate (10,838 projected HCV cases). Each parameter was varied individually between its minimum and maximum values reported in Table 2 while all remaining parameters were held at their base-case values

SVR: Sustained virologic response, DAA: Direct acting agents, HCC: Hepatocellular carcinoma, HCV: Hepatitis C virus

Discussion

In this study, we developed a mathematical model of HCV transmission and disease progression among PWID in Türkiye and analyzed the potential impact of increasing diagnosis-and-treatment rates on future disease spread. Our results show that, in the absence of diagnosis and treatment, HCV prevalence and HCV-related mortality could increase substantially. Although this no diagnosis-and-treatment scenario is unrealistic, it provides a useful benchmark for demonstrating the critical role of diagnosis and treatment as prevention strategies. Increasing diagnosis-and-treatment rates led to substantial reductions in both HCV prevalence and HCV-related deaths. In particular, the high diagnosis-and-treatment scenario resulted in a 98% reduction in HCV prevalence, suggesting that expanded diagnosis and treatment among PWID could make an important contribution to achieving WHO elimination goals.

Our findings also suggest that HCV diagnosis and treatment among PWID are cost-effective and may even become cost-saving, given the high transmission risk in this population. Although treatment costs remain considerable, diagnosis is relatively inexpensive, and the prevention of secondary infections can reduce the overall costs of diagnosis and treatment under higher-coverage scenarios. In terms of infections prevented and QALYs gained, the ICERs for the low, medium, and high diagnosis-and-treatment scenarios indicate that expanded diagnosis and treatment are either cost-effective or cost-saving, highlighting their value as both clinical and public health interventions.

Our results are comparable with those of previously published studies. Although none of the studies conducted in Türkiye specifically focused on PWID, and direct numerical comparisons are difficult because of differences in time horizons and diagnosis/treatment coverage scenarios, the overall conclusions are consistent. For example, Örmeci et al. (10) and Idilman et al. (11) suggested that increasing diagnosis and treatment rates could markedly reduce the number of HCV cases, and that achieving WHO targets for diagnosis (90%) and mortality reduction (65%) could decrease HCV prevalence by approximately 80% by 2030. Similarly, the high diagnosis-and-treatment scenarios in both previous studies and our model suggest major reductions in HCV prevalence and mortality. However, despite these improvements, the results also indicate that increasing diagnosis and treatment alone may not be sufficient to fully eliminate the disease.

Çekin et al. (9) reported that active screening and treatment programs are cost-effective for PWID, refugees, and prisoners, and recommended prioritizing PWID and refugees for targeted screening interventions. Although our study does not explicitly model an active screening and treatment program, improving diagnosis-and-treatment rates among PWID would likely require similar public health interventions and additional resource allocation. While the current diagnosis rate among PWID in Türkiye is not well established, achieving even a 50% diagnosis-and-treatment rate among infected individuals would likely require targeted screening efforts in this high-risk and vulnerable population.

Potential strategies to improve diagnosis rates include routine HCV screening within harm reduction programs such as AMATEM, integrated human immunodeficiency virus and HCV testing in voluntary counseling and testing centers, and prison-based

screening programs, given the substantial overlap between PWID and incarcerated HCV-positive populations. Community-based outreach, peer-supported testing initiatives, and simplified linkage-to-care pathways may also help improve engagement with diagnosis and treatment services among PWID.

Study Limitatons

Our study has several limitations. One of the key model parameters, the size of the PWID population in Türkiye, is subject to considerable uncertainty because of the limited availability of real-world epidemiological data. Therefore, the parameter values used in the model were informed by expert opinion and available estimates.

Another important limitation is that we did not incorporate the additional costs associated with increasing diagnosis rates. Achieving higher diagnosis-and-treatment coverage beyond the current status quo would likely require targeted public health interventions, such as screening, counseling, outreach, and linkage-to-care programs specifically designed for PWID. These interventions would increase the overall costs of diagnosis and treatment and could consequently increase the ICERs per infection prevented and per QALY gained. However, because there is currently no large-scale real-world implementation of such programs for PWID in Türkiye, reliable cost data for these interventions are not available. As a result, these costs were not included in our analysis.

Finally, uncertainty was assessed using one-way sensitivity analysis only, and a probabilistic sensitivity analysis was not performed. Although the one-way analysis identified the SVR rate and transmission contact rate as the most influential parameters, it does not capture the joint uncertainty across all model inputs. Therefore, the economic results should be interpreted with appropriate caution. Future studies should incorporate probabilistic sensitivity analysis when sufficient data are available to specify parameter distributions and correlations reliably.

Conclusion

In conclusion, HCV has the potential to become a major public health and economic burden, and the number of cases among PWID could increase considerably in the absence of improved diagnosis and treatment in this high-risk population. Using the best available data, our findings suggest that increasing diagnosis-and-treatment rates among PWID could be cost-effective, and potentially even cost-saving, while contributing substantially toward achieving WHO elimination targets. However, improving HCV control among PWID in Türkiye will require better surveillance data, more accurate estimates of the PWID population, and improved access to high-risk and hard-to-reach populations through targeted public health interventions.

Ethics

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of İstanbul University-Cerrahpaşa (approval no: 59491012-604.01.02, date: March 07, 2017).

Informed Consent: Verbal consent was obtained from all participants.

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For transparency, the authors note that an artificial intelligence-assisted language model (ChatGPT, OpenAI) was utilized to support text editing and language correction. This assistance was limited to linguistic refinement; all scientific content, critical analysis, and final editorial decisions were made exclusively by the authors.

Footnotes

Authorship Contributions

Concept: E.Y., Ş.Ü., Ü.Ü., F.T., Design: E.Y., Ş.Ü., Ü.Ü., F.T., Data Collection or Processing: Ş.Ü., Ü.Ü., F.T., Analysis or Interpretation: E.Y., Ş.Ü., Literature Search: Ş.Ü., Writing: E.Y.

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