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ORIGINAL ARTICLE

Hepatitis C prevalence and elimination planning in Pakistan, a bottom-up approach accounting for provincial variation

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Abstract

In Pakistan, substantial changes to hepatitis C virus (HCV) programming and treatment have occurred since the 2008 nationwide serosurvey estimated a 4.8% anti-HCV prevalence. In the absence of an updated national study, this analysis uses provincial data to estimate a national prevalence and the interventions needed to achieve elimination. Using a Delphi process, epidemiologic HCV data for the four provinces of Pakistan (accounting for 97% of the population) were reviewed with 21 subject-matter experts in Pakistan. Province-level estimates were inputted into a mathematical model to estimate the national HCV disease burden in the absence of intervention (Base), and if the World Health Organization (WHO) elimination targets are achieved by 2030 (80% reduction in new infections, 90% diagnosis coverage, 80% treatment coverage, and 65% reduction in mortality: WHO Elimination). An estimated 9,746,000 (7,573,000–10,006,000) Pakistanis were living with viraemic HCV as of January 1, 2021; a viraemic prevalence of 4.3% (3.3–4.4). WHO Elimination would require an annual average of 18.8 million screens, 1.1 million treatments, and 46,700 new infections prevented anually between 2022 and 2030. Elimination would reduce total infections by 7,045,000, save 152,000 lives and prevent 104,000 incident cases of hepatocellular carcinoma from 2015 to 2030. Blood surveys, programmatic data, and expert panel input uncovered more HCV infections and lower treatment numbers in the provinces than estimated using national extrapolations, demonstrating the benefits of a bottom-up approach. Screening and treatment must increase 20 times and 5 times, respectively, to curb the HCV epidemic in Pakistan and achieve elimination by 2030.

KEYWORDS
cascade of care, elimination, hepatitis C, Pakistan, prevalence

Abbreviations: CDAF, Center for Disease Analysis Foundation; DAAs, direct-acting antivirals; HCC, hepatocellular carcinoma; HCPs, provincial Hepatitis Control Programs; HCV, hepatitis C virus; MoNHSRC, Ministry of National Health Services, Regulations and Coordination; RNA, ribonucleic acid; UI, uncertainty intervals; WHO, World Health Organization.

1 | BACKGROUND AND AIMS

Persons with chronic hepatitis C virus (HCV) are at high risk of developing advanced-stage liver disease and cancer, however, high treatment success rates and increased access to direct-acting antivirals (DAAs) in recent years have inspired a global movement towards HCV elimination by 2030.[1,2] Pakistan has a substantial HCV disease burden, demonstrated in a 2008 national serosurvey (4.8% anti-HCV prevalence), and access to care for viral hepatitis has since been evolving.[3] The Prime Minister's Programme for Prevention and Control of Hepatitis was launched in 2005, contributing 13.9 million PKR (79,089 USD) to support patients unable to afford treatment.[4] In 2009, the first sentinel surveillance system for viral hepatitis in Pakistan was established, and in 2010, provincial Hepatitis Prevention and Control Programmes (HCPs) in Punjab, Sindh, Balochistan and Khyber Pakhtunkhwa (KP) became responsible for program implementation and tracking. By 2011, the Government of Pakistan began providing free screening, diagnosis and treatment through the provincial HCPs and introduced a nationwide plan to reduce the HCV disease burden.[4,5] Cure rates in Pakistan have doubled from the early 2000s to 2013, and Pakistan reports one of the lowest treatment prices globally; generic DAAs are available for $15 USD per month.[5]

In 2020, the Ministry of National Health Services, Regulations and Coordination (MoNHSRC) developed the *Prime Minister's Programme for Elimination of Hepatitis C: Annexures to Programme PC-I (PC-I)*, with a national goal to screen 50% of the Pakistani population from 2020 to 2025 and treat all eligible patients.[4] The PC-I provides screening targets for the initial years of the national program, outlines the resources needed and demonstrates the political will to improve care for HCV-infected persons. Recent publications[6,7] forecast the interventions needed to achieve the 2030 elimination targets, defined by the World Health Organization's (WHO) Global Health Sector Strategy on viral hepatitis.[2] These publications use the seroprevalence survey conducted over a decade ago,[3] despite substantial changes in access to viral hepatitis care and programming over the past 15 years, and before the global COVID-19 pandemic that altered the landscape of HCV prevention, care and treatment.

This analysis builds on the PC-I and models the interventions needed to achieve the 2030 elimination targets. Center for Disease Analysis Foundation (CDAF) has been conducting analytics on hepatitis for over a decade; prevalence estimates are used as the baseline for the 2017 WHO's Global Hepatitis Report and serve as the basis for many countries' hepatitis elimination efforts.[8] As a crucial starting point, we obtained estimates of HCV prevalence and cascade of care from recent serosurveys and programmatic data from an expert panel of provincial leaders. Like many nations, access to viral hepatitis care in Pakistan in 2020 and 2021 was impacted by the COVID-19 pandemic; the effects of which were also considered in this analysis. The primary aims of this study were to estimate the prevalence of HCV in Pakistan using a bottoms-up approach (based on data from the four major provinces) and to evaluate scenarios for HCV elimination at the national level by 2030.

2 | METHODS

2.1 | The analytic approach and model features

2.1.1 | Study design

This analysis combines a literature review, Delphi process, and mathematical modelling to estimate the current and future burden of HCV in Pakistan. We estimated the cascade of care for HCV (viremic infections, diagnosed, treated) in 2021 and forecasted the HCV disease burden (new infections, hepatocellular carcinoma [HCC], decompensated cirrhosis, and liver-related deaths [LRDs]) and interventions (screens, treatments) by 2030, under both the current care paradigm and WHO elimination protocol. CDAF has leveraged this combination of consensus-finding and modelling to develop HCV disease burden predictions with leaders in 83 countries, publishing results in over 100 manuscripts.[9,10]

2.1.2 | Literature review and Delphi process

To begin, a review of published data on the epidemiology of HCV was completed for the four provinces of Pakistan (Punjab, Sindh, KP, and Balochistan). A literature search conducted in PubMed with the terms ('hepatitis C' AND 'prevalence' AND 'province') identified articles and grey literature published between 1 January 2000, and 31 September 2021 (all languages). A modified Delphi process was then utilized to access unpublished data from 21 subject-matter experts (expert panel) recruited from provinces. The expert panel included representatives from the provincial HCPs, district health departments, universities, hospitals, the Pakistan Technical Advisory Group on hepatitis (TAG), the MoNHSRC, and private industry (Section 1 in Appendix S1). Ten virtual meetings (between two and four meetings per province) were held from January–September 2021 to review epidemiologic data inputs and outputs for the model, identify data gaps, and gain consensus on results.

2.2 | The HCV disease burden model

The Markov disease progression model used in this analysis was constructed in Microsoft Excel® (Microsoft Corp.) to quantify the size of the HCV-infected population using country-specific epidemiologic data inputs. It underwent an independent review, with methodological updates published in 2022.[10,11] In brief, the model tracked HCV progression from acute infection to chronic infection (accounting for spontaneous clearance) and through end-stage liver disease and liver-related mortality or cure. Age and sex-specific progression rates are reported in Section 2 in Appendix S1. The annual number of new (incident) infections at each stage of the disease was calculated by multiplying annual progression rates times the prevalent population (stratified by 1-year age cohort and sex) in the previous disease stage. The model also accounted for all-cause mortality and

was inputted with Pakistan-specific population data and mortality data from 1950 to 2050, and Pakistan-specific HCV epidemiologic data by year of data availability. The model also calculated the annual number of screens associated with diagnosing a given number of HCV infections. Starting with the undiagnosed, antibody-positive population, the model used Pakistan-specific epidemiologic data, number of screens per person and screening eligibility criteria from Pakistan (i.e. risk category, age, fibrosis stage, and history of screening, diagnosis, sustained virologic response [SVR]) to calculate the size of the population in Pakistan eligible for screening, and the number needed to screen to diagnose one antibody positive infection. Available data on viraemic proportion were used to adjust anti-HCV diagnosed cases and estimate HCV RNA-positive diagnosed cases for Pakistan. The primary epidemiologic inputs used to customize the mathematical model for Pakistan are described below in detail.

2.3 | Epidemiologic data inputs

Epidemiologic data for the HCV-infected population in Pakistan were gathered and inputted into the model, including; background population, total viremic prevalence, incidence, newly diagnosed, treated, total diagnosed, and prevalence among high-risk populations. Data were first collected for each of the four provinces, Punjab (53%), Sindh (23%), KP (15%), and Balochistan (6%), representing 97% of the country, and then combined. The remaining 3% of Pakistan's population resides in the autonomous territories Gilgit-Baltistan (GB) and Azad Jammu and Kashmir (AJK) and the federally administered Islamabad Capital Territory (ICT). Due to insufficient epidemiological data to conduct independent analyses for these locales, population-weighted estimates were first calculated. Data were then combined with estimates from the four provinces to create a national model. In the absence of available data, group consensus from the expert panel was required to include estimates in the model.

2.3.1 | Background population

The annual population of Pakistan was available from the United Nations Database by sex and 5-year age cohort for 1950 to 2030.[12] Population estimates by province were available from the Pakistan census database for 1951, 1961, 1972, 1981, 1998, and 2017, and data were trended linearly between gap years (i.e. 1952–1960, etc.).[13] Provincial population estimates for the remaining years (2017–2030) and the population distribution by 5-year age cohort and sex were extrapolated from national data.[12]

2.3.2 | Viraemic prevalence

Anti-HCV prevalence estimates in Punjab (8.9%), Sindh (6.2%), Balochistan (5.2%), and KP (6.5%) were adjusted for province-specific viremia (Table 1), weighted by the population, and combined to calculate a prevalence estimate and case count for 97% of the Pakistan population.[4,14–16] This prevalence estimate was then applied to the remaining 3% of the country's population to calculate the remaining cases. Finally, both case counts were summed to compute a national prevalence (Section 3 in Appendix S1). Ranges were applied to capture the uncertainty in this estimate.

Viremic prevalence by age and sex was calculated in 2020 using a population-weighted distribution of HCV-RNA (ribonucleic acid) cases reported from two studies in Sindh and one study in Punjab,[14,15,17] detailed in Section 4 in Appendix S1. When all three studies' results were combined, the viraemic prevalence was marginally higher in females, resulting in a national male-to-female prevalence ratio of 0.94, with a peak HCV prevalence in ages 35–39 years. No HCV serosurveys have been conducted for Balochistan and KP provinces or other municipalities.

2.3.3 | Incidence

For Balochistan and KP provinces, historical incidence (anti-HCV positive or HCV-RNA positive infections before spontaneous cure) were back-calculated using known prevalence and historical risk factors. The nationwide survey in 2008[3] and the two prevalence studies available for Punjab[14] and Sindh[15] (2018 and 2020, respectively) were used to calculate the average number of incident cases between these two time points by province (historical incidence). The four province-level incidence estimates and population-weighted estimates for the remaining 3% of the population were combined to estimate national historical incidence, detailed in Section 5 in Appendix S1. Future incident cases were assumed to increase/decrease at the same annual rate as prevalent HCV cases, relative to the last year of incidence data.

2.3.4 | Newly diagnosed and treated

For the public sector, the number of patients diagnosed with viraemic HCV (adjusted for province-specific viremia) and treated for HCV was available from the provincial HCPs. Private sector data (N) were estimated using a proportion diagnosed in the private sector ($y\%$), given the known number diagnosed in the public sector (x) (treatment data were assumed to follow the same trends) (Equation 1). The estimated proportion diagnosed (and treated) in the private sector was supplied by private facilities or clinics involved in HCV management and from unpublished literature. Punjab was the only province to report private-sector treatment data (Table 1).

Equation 1: Number of people newly diagnosed (or initiated on treatment) with viraemic HCV

$$N = x/(1 - y\%). \quad (1)$$

Based on similarities in access to care, treatment and diagnosis trends from Punjab were used to calculate population-weighted

estimates for ICT, and treatment and diagnosis from KP were used to compute population-weighted estimates for AJK and GB. When combined, national newly diagnosed and treated estimates were 164,000 and 215,000, in 2020, respectively.

2.3.5 | Total diagnosed

An estimated 20% of the infected population in Pakistan was diagnosed with HCV-RNA by the end of 2019 (n = 1,962,000), calculated using province-level total diagnosis rates (Table 1), weighted by prevalence in each province.

2.3.6 | High-risk populations

At the end of 2019, 11% of infections in Pakistan were estimated due to blood transfusion, and 1.2% were estimated to be among people who injected drugs. This estimate was derived using province-level estimates (experts reported similar risk factors for HCV among all provinces).

2.4 | Disease burden scenarios

Two scenarios were developed to forecast the course of the HCV epidemic and quantify the hepatitis disease burden in Pakistan. The burden of HCV was described using end-stage outcomes including HCV-liver related deaths, incident cases of hepatocellular carcinoma, and incident cases of decompensated cirrhosis. Both scenarios assumed no treatment restrictions by fibrosis stage and a 96% SVR (proportion of patients treated who achieve sustained SVR, or no detectable HCV-RNA, 12 weeks post-treatment) (Section 6 in Appendix S1).

Standard of Care; the absence of targeted interventions for HCV care and treatment.

Starting with 2018 baseline treatment levels, treatment was projected to decline 50% between 2019 and 2023 and remain level thereafter. This scenario assumed adult patients (aged 18 and older) were eligible for treatment (Section 6 in Appendix S1).

WHO Elimination; achieve the screening goals of the PC-I and the WHO Elimination Targets for HCV.

Under the assumptions of the PC-I, 50% of the eligible population aged 12 years and older were screened for anti-HCV, all anti-positive cases were tested for RNA, and all HCV-RNA positive cases were treated (patients aged 12 and older were treatment-eligible) between 2022 and 2025 (Section 7 in Appendix S1). From 2026 to 2030, the remaining eligible population aged 12 years and older were screened, tested and treated.[4] Interventions were augmented to also achieve the WHO elimination targets by 2030,

TABLE 1 Hepatitis C epidemiological data inputs by province, Pakistan.

	Punjab		Sindh		Balochistan		Khyber Pakhtunkhwa	
	Value (year of estimate)	Source (s)	Value (year of estimate)	Source (s)	Value (year of estimate)	Source (s)	Value (year of estimate)	Source (s)
Anti-HCV prevalence	8.9% (2018)	[14]	6.2% (2020)	[15]	5.2% (2020)	[16]	6.5% (2018)	[4]
Prevalence by age and sex	NA	[14]	NA	[15]	NA	[14,15,17]	NA	[14,15,17]
Viraemic proportion	59% (2018)	[14]	62% (2020)	[15]	61% (2019)	[14,15]	61% (2019)	[14,15]
Initiated on treatment	118,700		72,100		660		18,000	
Public sector	57,043 (2020)	DS, SS	14,432 (2020)	SS	230 (2020)	SS	11,704 (2020)	SS
Private sector	61,658 (2020)	DS	80% (2020)	EC	65% (2020)	EC	35% (2020)	EC
Newly viraemic diagnosed[a]	97,900		44,900		1,700		14,700	
Public sector	39,200 (2020)	SS	8,980 (2020)	SS	600 (2020)	SS	9,560 (2020)	SS
Private sector	60% (2020)	EC	80% (2020)	EC	65% (2020)	EC	35% (2020)	EC
Total diagnosed	23% (2019)	[14]	14% (2019)	EC	12% (2020)	EC	20% (2019)	EC

Abbreviations: DS, drug sales data; EC, expert consensus; NA, not applicable; SS, surveillance system.

[a]The estimated proportion of diagnoses occurring in the private sector are drawn from observations in private facilities or clinics involved in HCV management and from unpublished literature.

defined as an 80% reduction in new infections, 90% diagnosis coverage, and a 65% reduction in mortality from 2015 to 2030.[2]

3 | RESULTS

3.1 | The HCV disease burden

An estimated 9,746,000 (7,573,000–10,006,000) Pakistanis were living with viraemic HCV as of January 1, 2021, corresponding to a viraemic prevalence of 4.3% (3.3–4.4) (Figure 1). An estimated 462,000 incident infections occurred in 2021, an incidence rate of 205 per 100,000. By the end of 2021, 21% (2,010,000) of the 9.7 million viraemic infections had been diagnosed (Figure 1). An estimated 2% (215,000) of the infected population received treatment in 2021, of which approximately 96% (207,000) achieved SVR (Figure 1). An estimated 2,865,000 cumulative patients had been treated in Pakistan historically (through the end of 2021). Each year, approximately 27,000 Pakistanis die due to HCV-related complications and 20,800 Pakistanis develop incident HCC. Provincial experts independently reported a decline in HCV diagnosis and treatment from 2019 to 2020, indicating the reduced capacity in hepatitis programming resulting from the COVID-19 pandemic.

3.2 | Standard of Care projections

Under the Standard of Care, prevalence was estimated to increase to 10,390,000 infections by 2030, with new incident infections increasing by about 5% (from 463,000 infections in 2015 to 490,000 infections in 2030). Between 2015 and 2030, incident HCC was projected to increase by about 1% (from 25,500 to 25,700 cases), LRDs were expected to decline nearly 15% (from 36,000 to 31,000 cases) and incident decompensated cirrhosis was projected to remain relatively stable (at 19,900 cases) (Figure 1). An average of 807,000 anti-HCV screens were expected annually from 2022 to 2030, with 180,000 patients treated and 476,000 new HCV infections occurring annually, on average (Table 2). Elimination targets[2] would not be reached under this scenario.

3.3 | WHO Elimination projections

WHO Elimination could be achieved by screening an average of 18,755,000 people annually, treating 1,064,000 annually, and reducing new infections by 10% annually (a mean annual reduction of 46,700 incident infections) (Table 2). Compared to the Standard of Care, achieving these interventions would result in the following outcomes from 2015 to 2030; total infections would decline 70% (reduced by 7,045,000), with 152,000 lives saved and 104,000 incident cases of HCC prevented (Figure 2). Between 2022 and 2030, an additional 9,576,000 patients would need to be treated to achieve elimination, a mean average of 1,064,000 treated annually (Figure 3).

4 | DISCUSSION

Our analysis found a viraemic prevalence of 4.3% (3.3–4.4) in Pakistan in 2021. Converting this statistic for comparison, we estimate 7.2% (5.5–7.3) anti-HCV prevalence in 2021, which captures the 6.5% prevalence estimated by the MoNHSRC[4] within its uncertainty interval.[3] The difference between estimates is likely due to increased data availability at the province level for this analysis. Recent blood surveys conducted in Punjab and Sindh[14,15,17] and programmatic data from Balochistan[16] found that more people are infected with HCV than previously estimated.[4] The expert panel in KP also reported a higher prevalence.[4] As well, 124,545 samples were collected in the three seroprevalence studies in this analysis[14–16]; over 2.5 times larger than the original seroprevalence survey in which 47,043 samples were collected.[3] Unlike the 2008 serosurvey, however, no prevalence data were available from KP for this study.

An estimated 9.7 million Pakistanis are living with HCV and nearly 27,000 die annually from HCV-related causes. Eliminating HCV in Pakistan by 2030 could save 152,000 lives and prevent 104,000

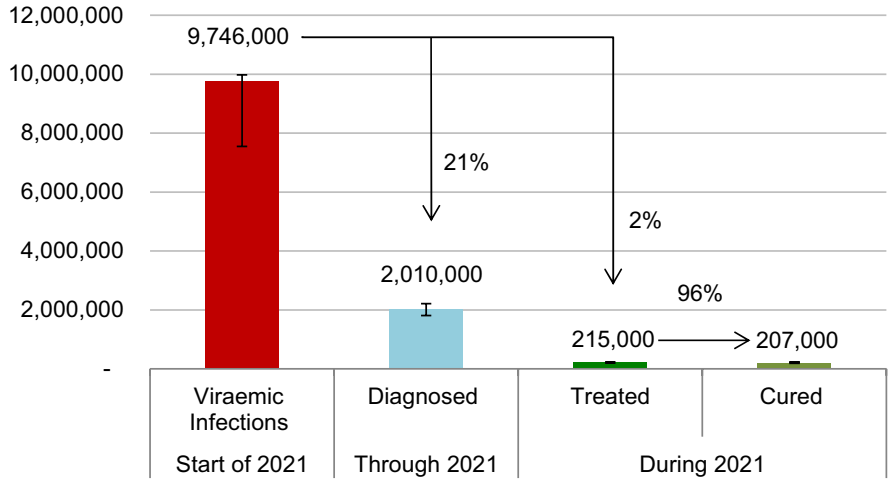

FIGURE 1 HCV cascade of care for 2021 in Pakistan. Includes the total number of viraemic infections, the number of viraemic diagnosed patients, and the number of patients treated and cured for HCV.

new cases of liver cancer through a scale-up in screening, treatment, and infection prevention. To begin, Pakistan must screen nearly 18.8 million patients for HCV annually, on average, which is 20 times the current estimate of 807,000 annual screens. Ensuring provincial HCPs are coordinated and unified would enable leaders to track and monitor cases and reduce duplicative screening.[18] Integrated testing across multiple disease domains (tuberculosis, HIV, STIs, etc.) has proven successful to increase outreach, optimize resources and improve case-finding.[19] Routine healthcare evaluations could also include hepatitis screening. As well, patients previously diagnosed through hospitals and blood banks could be identified and evaluated retrospectively, and a review of protocols could ensure proper patient referral.

Access to HCV treatment in Pakistan has increased in recent years. Treatment expansion is evident in the data; an annual average of 60,700 patients were treated through the Prime Minister's Programme from 2005 to 2010, and after the launch of the provincial programmes in 2011, annual treatment increased to 230,000 in 2015 and again to 354,000 in 2018. During this time, interferon and combination therapies were replaced with DAA oral drugs which are short (12 weeks or less), have few side effects, and are effective in preventing advanced liver disease, cancer, and death. Branded DAA's were first introduced in Pakistan in 2014, followed by generic DAAs in 2015, resulting in large-scale local generic production and a substantial price drop.[5] Cure rates improved in-kind; Pakistan reported a 64% average SVR before 2014 (accounting for the variation in treatment efficacy by genotype), increasing to a 96% SVR in 2017.[5] Despite making significant strides in treatment access, additional efforts are needed to eliminate HCV. 215,000 patients were treated in 2020, suggesting annual treatment must increase five times to reach the target of >1 million patients treated annually to achieve elimination. One bottleneck to elimination programming is the availability of specialists to administer treatment. Care for patients with cirrhosis and decompensation currently must be managed by gastroenterologists or infectious disease specialists, however, general practitioners could initiate treatment for most non-cirrhotic patients since medication dosage and combinations are fixed. This approach has been successful during several national program rollouts.[20,21]

To achieve WHO targets, the elimination program must also reduce new HCV infections by an average of 46,700 cases each year (a 10% reduction annually), however, new infections are increasing (Section 8 in Appendix S1). New infections in Pakistan are mainly healthcare-associated, spread via improper screening of blood transfusions (only 50% of blood donations are screened for HCV),[22] poor infection control in healthcare settings,[23] unsafe community practices including unnecessary therapeutic injections for common ailments such as fever and fatigue,[24] and sharing shaving razors at the barber; a major risk factor for males.[3] Optimizing a safe and clean blood supply with the Pakistan Blood Transfusion Authority, ensuring healthcare providers have access to auto-disable syringes, and instituting infection control committees in hospitals to track and reduce new infections, could curb this trend.[25]

This analysis is subject to limitations, many of which are inherent to mathematical modelling and forecasting.[10,11] The greatest limitation is the availability and quality of data, which affects the accuracy of forecasts. Uncertainty intervals address some of these unknowns but may not capture all sources of bias, including selection bias due to missing data, sampling bias and measurement bias. In this analysis, the greatest uncertainty in prevalence was for KP province due to the lack of data. Applying the lowest estimated prevalence for KP (1.5% anti-HCV positivity, agreed upon by the expert panel to be the lowest probable)[4] to the model would estimate a 4.1% national viraemic prevalence, which is within the uncertainty interval. Additionally, one of the three studies used to estimate HCV prevalence by age and sex was likely sampled in a high-prevalence district. However, since the sampling technique of this study was of high quality, and since age-specific prevalence estimates were combined with two other sources and weighted for the total population of Pakistan, the national prevalence was not affected. Another study limitation is the lack of private-sector data. In combination with high-quality programmatic data for the public sector combined with expert panel discussions with practising healthcare practitioners, we believe the best possible estimates for the private sector were utilized. Expert panel discussions also strengthened the analysis results. As practising healthcare workers in their respective regions, experts helped to conserve the heterogeneity of epidemiologic data by province within the national estimate. In the absence of an updated national serosurvey and with the existence of robust, provincial programmes, conducting local-level analyses was a crucial step to assess the current state of HCV in Pakistan.

CDAF facilitators are trained to identify and challenge assumptions and cognitive biases, gather balanced feedback from multiple sources and engage local representatives through the Delphi process. This was particularly evident when discussing the distribution of HCV care by sector. In previous MoNHSRC analyses, 60% of national treatments and 60% of diagnoses in Pakistan were estimated to occur in the private sector. This analysis found varying proportions for the private sector by province, ranging from 35% to 80% (Table 1). While the average of this range remains 60%, applying 60% of treatments in the private sector to each province would increase the total number of patients treated in Pakistan in 2020 by 15% (from 215,000 to 248,000). Local input ensured that the differences in health infrastructure and access to care by province were incorporated.

Provincial expert panels independently reported a decline in HCV diagnosis and treatment from 2019 to 2020, demonstrating attrition of hepatitis programming due to the COVID-19 pandemic. The report was unable to address the duration of recovery from the COVID-19 pandemic (after 2020) or the effects of destabilization due to conflict in and around the region, as these are global unknowns. However, the base scenario was designed to be less optimistic, by simulating reduced interventions into the future. To account for programmatic delays, the elimination plan was also offset by 1 year. One benefit of modelling analytics is that, after a baseline is established, forecasts can be revised readily as new data become

TABLE 2 Screening, treatment and reduction in new infections by scenario, Pakistan, 2022–2030

	2022	2023	2024	2025[a]	2026	2027	2028	≥2029	Annual average
Anti-HCV screens									
Standard of Care	807,000	807,000	807,000	821,000	814,000	810,000	804,000	798,000	807,000
WHO Elimination	9,410,000	22,595,000	19,753,000	11,619,000	22,619,000	22,365,000	21,994,000	21,474,000	18,755,000
HCV RNA PCR screens									
Standard of Care	188,000	188,000	189,000	193,000	192,000	192,000	192,000	191,000	191,000
WHO Elimination	595,000	1,441,000	1,289,000	776,000	1,517,000	1,528,000	1,543,000	1,569,000	1,292,000
Initiated on HCV treatment									
Standard of Care	180,000	180,000	180,000	180,000	180,000	180,000	180,000	180,000	180,000
WHO Elimination	491,000	1,189,000	1,060,000	636,000	1,240,000	1,240,000	1,240,000	1,240,000	1,064,000
New HCV infections									
Standard of Care	463,000	467,000	470,000	472,000	475,000	479,000	483,000	487,000	476,000
WHO Elimination	463,000	431,000	353,000	288,000	245,000	209,000	157,000	123,000	262,000
WHO Elimination – New infections to prevent (from previous year)	–	32,000	78,000	65,000	43,000	36,000	52,000	34,000	46,700

Abbreviations: HCV, hepatitis C virus; PCR, polymerase chain reaction; RNA, ribonucleic acid; WHO, World Health Organization.

[a]The decline in screening and treatment projected for 2025 in the WHO Elimination scenario was extracted from the Prime Minister's Programme Annexures (PC-I), Section 7 in Appendix S1.

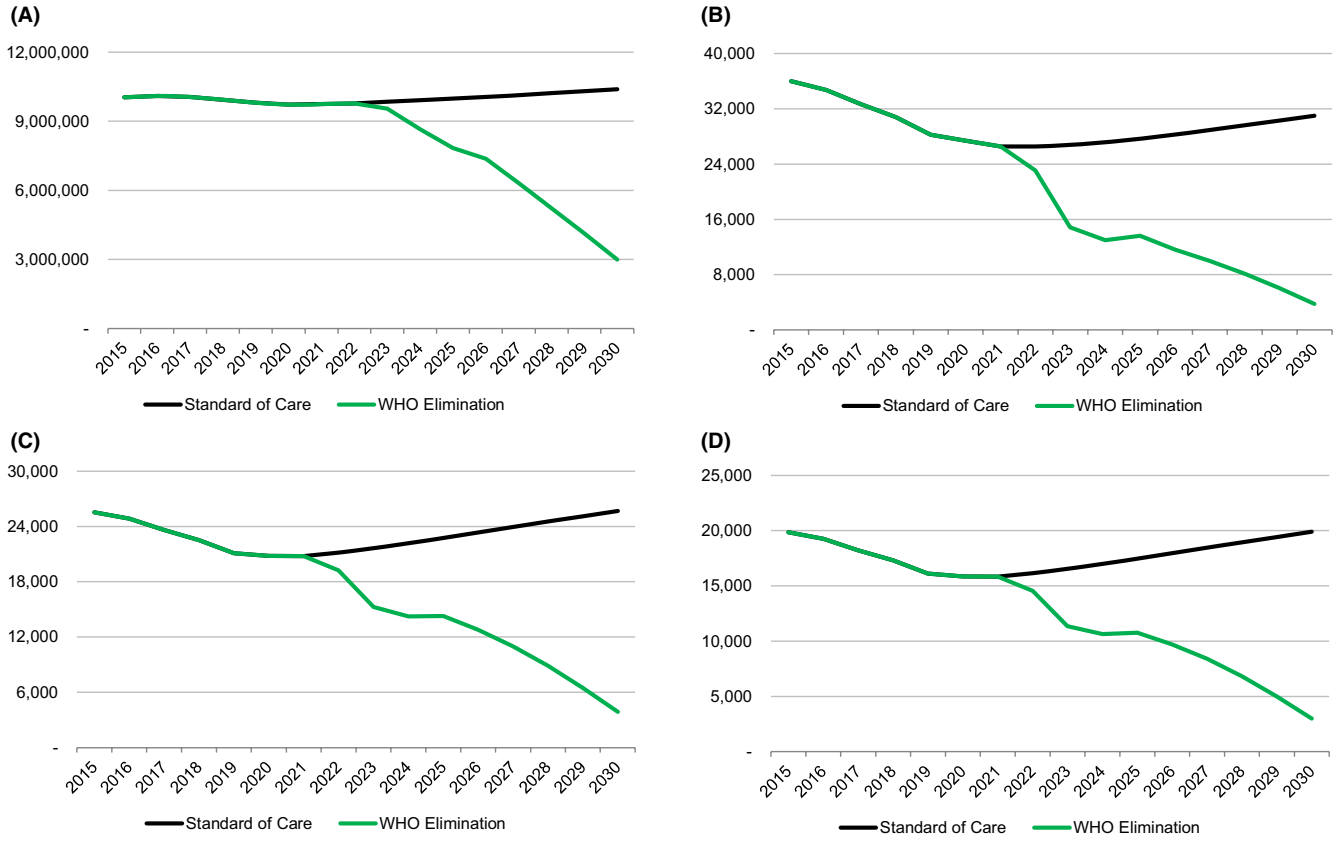

FIGURE 2 Hepatitis disease burden outcomes by scenario in Pakistan, 2015–2030. (A) Total viraemic HCV infections. (B) Incident cases of HCV-liver related deaths. (C) Incident cases of hepatocellular carcinoma. (D) Incident cases of decompensated cirrhosis

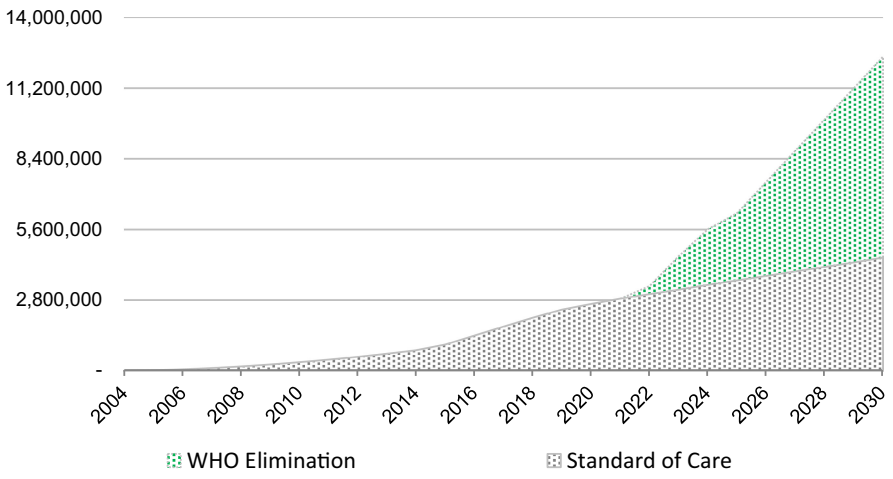

FIGURE 3 Cumulative number of patients treated for hepatitis C by scenario, 2004–2030. For 2004–2020, the annual number of patients treated for HCV was compiled from provincial Hepatitis Control Program data for the public sector and, for the private sector, estimates were gathered from expert observations in private facilities/clinics involved in HCV management and/or unpublished literature. For 2021–2030, treatment estimates were based on the current treatment trends (Standard of Care) and number of treatments needed to achieve the WHO Targets for HCV elimination (WHO Elimination).

available. The disease projection and forecasting components of the model also allowed us to leverage data from various years and locations across Pakistan to create a standardized cascade of care and elimination plan.

Implementing a national hepatitis elimination program requires engagement from governmental authorities, healthcare provider associations, patients, and patient representatives at the national and subnational levels early on in strategic planning. This analysis

allowed key hepatitis stakeholders in Pakistan to examine the needs of each region, and gain consensus on the current state of care and steps forward. Results can be leveraged to update the national elimination plan and inform public health decision-making as the country recovers from the pandemic and refocuses efforts on HCV elimination.

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CONFLICT OF INTEREST

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DATA AVAILABILITY STATEMENT

For a period of 1 year after publication, the authors will share the data used in the figures in an Excel format after a written request to the corresponding author. Data sharing will be limited to government agencies, academic institutions and non-profit organizations, and will not apply to for-profit or consulting organizations. Additionally, select data from the manuscript will be available publicly on the Polaris Observatory Website https://cdafound.org/polaris-countries-dashboard/

ETHICAL APPROVAL

Ethics approval was not required for this study as it does not involve human participation or personally identifiable data/information.

PATIENT CONSENT STATEMENT

Patient consent was not required for this study as it does not involve human participation.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

This analysis does not include any previously published material.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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