Assessing the potential cost-effectiveness of centralised versus point-of-care testing for hepatitis C virus in Pakistan: a model-based comparison

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ABSTRACT

Objectives Pakistan has a hepatitis C virus (HCV) infection prevalence of 6%–9% and aims to achieve World Health Organisation (WHO) targets for elimination of HCV by the year 2030. We aim to evaluate the potential cost-effectiveness of a reference laboratory-based (centralised laboratory testing; CEN) confirmatory testing approach versus a molecular near-patient point-of-care (POC) confirmatory approach to screen the general population for HCV in Pakistan.

Study design We used a decision tree-analytic model from a governmental (formal healthcare sector) perspective.

Study setting Individuals were assumed to be initially screened with an anti-HCV test at home, followed by POC nucleic acid test (NAT) at nearby district hospitals or followed by NAT at centralised laboratories.

Participants We included the general testing population for chronic HCV in Pakistan.

Intervention Screening with an anti-HCV antibody test (Anti-HCV) followed by either POC NAT (Anti-HCV-POC), or reference laboratory NAT (Anti-HCV-CEN), was compared, using data from published literature and the Pakistan Ministry of Health.

Measures Outcome measures included: number of HCV infections identified per year, percentage of individuals correctly classified, total costs, average costs per individual tested, and cost-effectiveness (assessed as cost per additional HCV infection identified). Sensitivity analysis was also performed.

Results At a national level (25 million annual screening tests), the Anti-HCV-CEN strategy would identify 142 406 more HCV infections in 1 year and increase correct classification of individuals by 0.57% compared with the Anti-HCV-POC strategy. The total annual cost of HCV testing was reduced using the Anti-HCV-CEN strategy by US$7.68 million (US$0.31/person). Thus, incrementally, the Anti-HCV-CEN strategy costs less and identifies more HCV infections than Anti-HCV-POC. The incremental difference in HCV infections identified was most sensitive to the probability of loss to follow-up (for POC confirmatory NAT).

Conclusions Anti-HCV-CEN would provide the best value for money when scaling up HCV testing in Pakistan.

INTRODUCTION

Hepatitis C virus (HCV) infection constitutes a major medical and public health burden worldwide, with an estimated 1% of the world population chronically infected. Over 80% of those affected live in low-income and middle-income countries (LMICs). One-third of people with chronic, untreated HCV infection develop liver cirrhosis, and have higher morbidity and mortality rates. The prevalence of HCV infection in Pakistan is estimated to be 6%–9% of the population, in part because of the absence of a comprehensive, population-wide screening programme.
The advent of highly effective direct-acting antiviral agents (DAAs) has transformed the clinical care of HCV.8–10 Though DAAs are oral medications that can be instrumental in large-scale elimination efforts,11 the high cost of DAAs in some high-income countries led to restricted access.12 In Pakistan, the cost of generic DAAs is US$60 per treatment course, which represents one of the lowest prices worldwide.13 Nevertheless, access to treatment in Pakistan may be hindered by underdiagnosis. In 2016, the WHO developed a Global Health Sector Strategy as a roadmap to eliminate HCV as a public health threat by 2030, defined as 90% reduction in incidence and a 65% reduction in mortality, compared with the 2015 baseline.14 Other targets towards HCV elimination included the screening of 100% of donated blood in a quality-assured manner by 2030.14 Several studies have estimated targets for screening, diagnosis and treatment in Pakistan,13,15,16 such as the scale-up of HCV testing to ≥25 million individuals to diagnose and treat 900,000 and 700,000 persons per year, respectively.13 Based on model projections, Lim et al suggested a substantial scale-up to 880,000 treatments per year is required.15 The Pakistani government has also developed a policy framework based on the WHO guidelines to support rapid scale-up of HCV testing,17 and set new targets to screen 50% of the eligible population (69 million with anti-HCV screening and ~5 million with confirmatory PCR testing) between July 2020 and June 2025.18

The current testing approach for HCV in Pakistan is achieved via a rapid anti-HCV antibody test (Anti-HCV) for screening, followed by a reflex nucleic acid test (NAT).19–21 In Pakistan, healthcare services, including the performance of rapid antibody tests are typically conducted in government-run basic health units (BHUs). In 2018, there were approximately 5500 BHUs, serving a population of 205 million.22 Decentralised molecular point-of-care (POC) testing (eg, via the GeneXpert® System in district hospitals) moves the site of testing closer to patients and is an alternative to reference laboratory-based NAT testing, offering reduced sample transportation time and faster results.19,20 However, POC NAT testing may be expensive to implement and poses logistical challenges, including a need for continuous electrical supply and adequate storage space for cartridges.23,24 Dried blood spot (DBS) testing from finger-prick samples (or heel-prick in infants) solves many of these problems and facilitates access to testing, particularly in remote and under-resourced regions, as it is a low-resource option that requires minimal training for sample collection.25 Despite conditional recommendations from the WHO to use DBS specimens as an alternative to HCV NAT in settings where resources or expertise are limited,3 DBS testing has some drawbacks. Some studies have indicated that DBS tests have a higher limit of detection than serum and that variable DBS sample stability can impact quantification accuracy.26–28

The cobas® Plasma Separation Card (PSC) offers another option; while currently approved only for the purpose of HIV viral load monitoring,29 the utility of the PSC for HCV testing has been recently demonstrated.30,31 While both DBS and the PSC can facilitate decentralisation of sample collection, the PSC retains the sample collection and transport advantages of DBS while maintaining sample stability and viability.24,32

A previous study has suggested that POC may be a cost-effective option in Pakistan,13 but there is still a lack of comparative health economic evidence on the optimal and cost-effective approach to scale-up HCV testing to support elimination efforts. It is recognised that effective diagnosis and treatment are both important in order to reduce burden of HCV at the population level. However, there are many published studies about the cost-effectiveness of treatment and it is assumed here that treatment drives longer-term HCV outcomes. Therefore, the primary purpose of this study was to evaluate the potential cost-effectiveness of high-throughput, reference laboratory-based confirmatory testing compared with a near-patient molecular POC approach to inform HCV testing scale-up plans in Pakistan, in order to identify those eligible for treatment.

METHODS

Analytic overview

A decision-analytic model (decision tree) was developed to compare chronic HCV testing under two scenarios: (1) screening with anti-HCV followed by POC NAT (Anti-HCV-POC) and (2) screening with anti-HCV followed by high-throughput, centralised reference laboratory-based NAT (Anti-HCV-CEN) (figure 1). We used a governmental (formal healthcare sector) perspective, excluding third-party payer and patient out-of-pocket costs. We assessed costs and outcomes over a short-term time period, assumed to be 1 month (30 days), defined as the time from anti-HCV screening to HCV infection confirmation for anti-HCV-positive individuals.

Study population

The study population was the general testing population for chronic HCV in Pakistan. The size of this population has been projected to be 25 million people annually, starting in 2018, to achieve chronic HCV elimination in Pakistan by 2030.13 A household screening programme of people aged 12 years and older, conducted in Karachi, Pakistan revealed that the mean age of the screened population was 30.5 years, with the prevalence of HCV antibody as low as 0.2% in the 12–17 years age group and highest (26.2%) in the 65–69 years group.33 As part of HCV elimination scale-up campaign, individuals were assumed to be initially screened at home (in lieu of existing practice of screening in nearby government-run basic health facilities, that have been shown to be suboptimal/underutilised).34,35 This at home screening approach is currently being used by a number of private grant-funded programmes that do house-to-house screening campaigns in Pakistan. The kits are
provided by government hepatitis programmes and the tests performed by healthcare workers deployed by the government (those already stationed in government-run basic health facilities). Anti-HCV tests are followed by POC NAT at district hospitals or by NAT at centralised reference laboratories. Screening coverage was assumed to be equal for each testing scenario.

Patient and public involvement
The clinical data in this study were derived from published literature. Thus, no patients were involved in the study development or in conduction of this analysis beyond their involvement in previous published studies. As this research did not directly involve human subjects, informed consent was not required. There are no additional plans to disseminate the results of this study beyond the publication of this article.

Decision tree
The decision tree (figure 2) modelled individuals in the testing population under the two scenarios (Anti-HCV-POC and Anti-HCV-CEN) by initially dividing them into HCV positive and HCV negative based on the population prevalence of chronic HCV in Pakistan. Depending on the test performance of the anti-HCV and NAT tests, individuals with HCV infection may test either positive (true positive (TP)) or negative (false negative (FN)), and individuals without HCV infection may test either positive (false positive (FP)) or negative (true negative (TN)). Individuals who tested TP or FP for HCV antibodies under the Anti-HCV-POC scenario were modelled to attend a nearby district hospital for phlebotomy and POC NAT or were otherwise lost to follow-up (LTFU), implying non-compliance with a recommendation to receive confirmatory NAT. The model assumed no potential for LTFU under the Anti-HCV-CEN because PSC samples would be collected immediately after individuals receive a positive anti-HCV test at home and automatically transported to a reference laboratory for confirmatory NAT. Individuals who received NAT were assumed to generate either indeterminate tests or valid test results. Individuals who tested TP or TN were considered to have been correctly classified and thus exited the model. Individuals who tested either FN or FP, were LTFU or had indeterminate test results were considered to have been incorrectly classified and thus exited the model.

Probabilities
Table 1 includes a summary of the probabilities used in the model. The population prevalence of HCV in Pakistan was obtained from the published literature. The performance of the anti-HCV screening test was estimated based on a published review of multiple screening technologies, of which we used data on the performance of the SD Biosensor Standard Q HCV test on account of its superior performance. The performance of POC NAT testing was estimated based on two studies that reported the performance of the GeneXpert POC system under field conditions (table 1). The performance of centralised NAT testing was based on a synthesis of results of evaluations of the performance of the cobas® 6800/8800 system under field conditions. The probability of being LTFU after screening positive for anti-HCV (ie, not attending POC NAT testing) was estimated based on review of the HCV testing and treatment cascade, which found a wide variation in LTFU, including data from a study from Pakistan that reported that only 18% of those individuals who
We used an estimate reported by the review that was based on multiple studies performed in the community and designed to improve the HCV care cascade, which will naturally follow efforts to increase testing for chronic HCV. The probabilities of obtaining indeterminate NAT results were obtained from field studies of the GeneXpert system and the cobas system.

Costs
Data related to costs were obtained from the literature or the Pakistan Ministry of Health (MOH) (table 1). Costs were divided into five categories: (1) sample collection (phlebotomy for POC NAT and PSC card for central NAT); (2) waste management (incineration and waste transport) for POC; (3) sample transportation for central NAT; (4) consumption of electricity for NAT; and (5) testing consumables for all tests. The cost estimation did not include the fixed capital equipment or the maintenance costs of POC NAT or central NAT technology.

Testing systems were assumed to be procured based on a reagent-rental model (ie, the instrument is ‘free’ with the purchase of reagents) instead of direct purchase. The cost of phlebotomy was obtained from the Pakistan MOH and included estimates for the cost of blood collection tubes and syringes, as well as phlebotomists’ time, which was estimated from local hourly wages and estimated number of hourly phlebotomies performed. The per-test cost of waste management was obtained from the literature. The per-test cost of electricity was obtained from estimates of electricity consumption of the respective NAT technologies, number of tests per hour and the per unit cost of electricity in Pakistan. The costs of testing consumables for all tests were based on the respective technologies and obtained from the Pakistan MOH. Costs obtained in local currency units (Pakistan Rupee) were converted into US Dollars using the official exchange rate of the State Bank of Pakistan (February 2021). Costs were not discounted given the short time period from an initial screening test.
Table 1 Parameters of the decision analytic model comparing HCV testing with Anti-HCV-CEN and Anti-HCV-POC in Pakistan

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Range</th>
<th>Distribution</th>
<th>Source</th>
</tr>
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<tr>
<td><strong>Probabilities</strong></td>
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<td></td>
</tr>
<tr>
<td>HCV prevalence</td>
<td>0.068</td>
<td>0.054–0.082</td>
<td>Beta</td>
<td>Reference 7</td>
</tr>
<tr>
<td>Anti-HCV test performance*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.948</td>
<td>0.928–0.962</td>
<td>Beta</td>
<td>Reference 37</td>
</tr>
<tr>
<td>Specificity</td>
<td>1.000</td>
<td>0.996–1.000</td>
<td>Beta</td>
<td>Reference 37</td>
</tr>
<tr>
<td>LTFU if anti-HCV+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HCV-POC</td>
<td>0.29</td>
<td>0.10–0.33</td>
<td>Beta</td>
<td>Reference 39</td>
</tr>
<tr>
<td>Anti-HCV-CEN</td>
<td>0.00</td>
<td></td>
<td></td>
<td>Analytic assumption†</td>
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<tr>
<td>Indeterminate test</td>
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<tr>
<td>Anti-HCV-POC</td>
<td>0.052</td>
<td>0.040–0.060</td>
<td>Beta</td>
<td>Reference 20</td>
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<tr>
<td>Anti-HCV-CEN</td>
<td>0.038</td>
<td>0.031–0.046</td>
<td>Beta</td>
<td>Reference 41</td>
</tr>
<tr>
<td><strong>POC test performance‡</strong></td>
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<tr>
<td>Sensitivity</td>
<td>0.989</td>
<td>0.791–1.000</td>
<td>Beta</td>
<td>Reference 13.70</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.978</td>
<td>0.783–1.000</td>
<td>Beta</td>
<td>Reference 13</td>
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<tr>
<td><strong>Centralised (batch) test performance§</strong></td>
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</tr>
<tr>
<td>Sensitivity</td>
<td>0.969</td>
<td>0.775–1.000</td>
<td>Beta</td>
<td>Reference 38</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.998</td>
<td>0.798–1.000</td>
<td>Beta</td>
<td>Reference 38</td>
</tr>
<tr>
<td><strong>Costs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capillary tube (sample collection)</td>
<td>US$0.25</td>
<td>US$0.20–US$0.30</td>
<td>Lognormal</td>
<td>Pakistan MOH</td>
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<tr>
<td>Needle and syringe (phlebotomy)</td>
<td>US$0.37</td>
<td>US$0.29–US$0.44</td>
<td>Lognormal</td>
<td>Pakistan MOH</td>
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<tr>
<td>Hourly wage (phlebotomist)</td>
<td>US$0.63</td>
<td>US$0.32–US$0.95</td>
<td>Lognormal</td>
<td>Pakistan MOH</td>
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<tr>
<td>Waste management (POC)</td>
<td>US$0.40</td>
<td>US$0.20–US$0.60</td>
<td>Lognormal</td>
<td>Reference 42</td>
</tr>
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<td>PSC card</td>
<td>US$5</td>
<td>US$2.50–US$7.5</td>
<td>Lognormal</td>
<td>RDS (internal data)</td>
</tr>
<tr>
<td>Sample transportation/sample</td>
<td>US$0.07</td>
<td>US$0.06–US$0.09</td>
<td>Lognormal</td>
<td>MOH</td>
</tr>
<tr>
<td>Price per kWh (Pakistan)</td>
<td>US$0.63</td>
<td>US$0.31–US$0.95</td>
<td>Lognormal</td>
<td>Public data</td>
</tr>
<tr>
<td>Laboratory tests (consumables)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>SD Biosensor Standard Q HCV Ab</td>
<td>US$0.31</td>
<td>US$0.25–US$0.37</td>
<td>Lognormal</td>
<td>Pakistan MOH</td>
</tr>
<tr>
<td>Roche cobas 6800/8800</td>
<td>US$15.94</td>
<td>US$12.75–US$19.13</td>
<td>Lognormal</td>
<td>Pakistan MOH</td>
</tr>
<tr>
<td>Cepheid GeneXpert</td>
<td>US$20.00</td>
<td>US$16.00–US$24.00</td>
<td>Lognormal</td>
<td>Pakistan MOH</td>
</tr>
<tr>
<td><strong>Other parameters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phlebotomies per hour</td>
<td>12</td>
<td>6–18</td>
<td>Normal</td>
<td>Pakistan MOH</td>
</tr>
<tr>
<td>Power factor</td>
<td>0.68</td>
<td>0.60–0.75</td>
<td>Normal</td>
<td>Reference 71</td>
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<tr>
<td>EC Roche cobas 6800/8800 (VA)</td>
<td>2000</td>
<td>1600–2400</td>
<td>Normal</td>
<td>Reference 72</td>
</tr>
<tr>
<td>EC Cepheid GeneXpert (VA)</td>
<td>824</td>
<td>659–989</td>
<td>Normal</td>
<td>Reference 73</td>
</tr>
<tr>
<td>Tests/hour Roche cobas 6800/8800</td>
<td>32</td>
<td>26–38</td>
<td>Normal</td>
<td>Reference 74</td>
</tr>
<tr>
<td>Tests/hour Cepheid GeneXpert</td>
<td>4</td>
<td>2–6</td>
<td>Normal</td>
<td>Reference 73</td>
</tr>
</tbody>
</table>

LTFU refers to proportion of patients who test anti-HCV positive but do not show up at facility for RNA testing (i.e, the proportion of patients who test anti-HCV positive but do not show up at facility for testing).

*SD Biosensor Standard Q HCV Ab.
†PSC sample collected at home is sufficient for cobas-RNA test. Therefore, there is no referral for phlebotomy.
‡Cepheid GeneXpert.
§Roche cobas 6800/8800.
Ab, antibody; Anti-HCV-CEN, screening with Anti-HCV followed by centralised/batch NAT testing; Anti-HCV-POC, screening with Anti-HCV followed by POC NAT testing; CEN, centralised laboratory testing; EC, electric consumption; HCV, hepatitis C virus; kWA, kilowatt hour; LTFU, lost to follow-up; MOH, Ministry of Health; NAT, nucleic acid testing; POC, point of care; PSC, Plasma Separation Card; RDS, Roche Diagnostic Systems; VA, volt-ampere.
to confirmatory test (assumed 30 days). Table 1 includes a summary of the parameters used for cost estimation.

Outcomes and cost-effectiveness
A baseline analysis was performed to estimate the following metrics under each testing scenario: (1) number of HCV infections identified per year; (2) percentage of individuals correctly classified (as either TP or TN); (3) total costs; (4) average costs per individual tested; and (5) cost-effectiveness in terms of cost per additional HCV infection identified.

Sensitivity analysis
A univariate sensitivity analysis was performed, re-estimating results with each parameter of the model at low and high values while holding all other parameters constant. The low and high values were 95% CIs when available and ±20% for probabilities or ±50% for costs when 95% CIs were unavailable. Monte Carlo simulation (1000 runs) was used to conduct probabilistic sensitivity analyses to assess overall parameter uncertainty in the model and further test the robustness of results. Baseline values were used as means, and standard errors were estimated assuming ranges were equivalent to 95% CIs (four times the standard error(SE)). Beta distributions were assumed for probabilities, lognormal distributions for costs and normal distributions for counts. The analysis was performed using TreeAge Pro 2021 (TreeAge Software, LLC) and this report conforms to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement.

RESULTS
Baseline analysis
The results of the baseline analysis are shown in table 2. Given an annual testing population of 25 million individuals, the Anti-HCV-CEN strategy identified 142,406 more HCV infections in 1 year compared with the Anti-HCV-POC strategy. The Anti-HCV-CEN strategy increased correct classification of individuals (TP and TN) by 0.57% compared with the Anti-HCV-POC strategy. The total annual cost of HCV testing in Pakistan was estimated to be US$41.65 million (US$1.67 per person) under Anti-HCV-CEN and US$49.31 million (US$1.97 per person) under Anti-HCV-POC. Anti-HCV-CEN reduced HCV testing costs in Pakistan by US$7.68 million (US$0.31 per person). In the incremental analysis, Anti-HCV-CEN was superior to Anti-HCV-POC (ie, is less costly and identifies more HCV infections).

Sensitivity analysis
The incremental difference in HCV infections identified was most sensitive to the probability of LTFU (for POC confirmatory NAT). At 0% LTFU (ie, all individuals attending a POC visit), Anti-HCV-CEN still identifies more infections, but the incremental difference in HCV infections identified decreases to 8693 (from 142,406 assuming 29% LTFU at baseline). At 33% LTFU, the incremental difference in HCV infections identified increases to 489,934 more HCV infections identified per year. The incremental costs were also most sensitive to the probability of LTFU (for POC confirmatory NAT), changing from −US$0.49 (−US$12,988.86 per year nationally) at 0% LTFU to US$0.12 (US$294,769.5 per year nationally) with a 33% rate of LTFU (figure 3).

The impact of parameter uncertainty in the model was represented graphically using probabilistic sensitivity analysis results in an incremental cost-effectiveness scatterplot (figure 4). Anti-HCV-CEN is superior to Anti-HCV-POC (lower cost and greater number of HCV cases identified) in 71.1% of the simulations and inferior to Anti-HCV-POC (higher cost and fewer HCV cases identified) in 0.4% of the 1000 iterations of the Monte Carlo simulation.

DISCUSSION
We developed a decision-analytic model to compare chronic HCV testing under two scenarios: Anti-HCV-POC and Anti-HCV-CEN. The analysis projects that the Anti-HCV-CEN testing approach would identify more HCV infections and would increase the correct classification of individuals (TP and TN) at a lower cost compared with the Anti-HCV-POC strategy. Correctly identifying more chronically infected patients and providing the necessary treatment reduces onward disease transmission and

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Overall comparison of HCV testing with Anti-HCV-CEN and HCV testing with Anti-HCV-POC in Pakistan</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Anti-HCV-POC</td>
</tr>
<tr>
<td>HCV infections identified per year</td>
<td>1359892</td>
</tr>
<tr>
<td>Individuals correctly classified</td>
<td>98.64%</td>
</tr>
<tr>
<td>Total costs</td>
<td>US$49331577</td>
</tr>
<tr>
<td>Costs per individual screened</td>
<td>US$1.97</td>
</tr>
<tr>
<td>ICER (US$/additional HCV infection identified)</td>
<td>—</td>
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</table>

*Reduces costs and increases effectiveness, measured as HCV infections identified. Anti-HCV-CEN, screening with anti-HCV followed by central/batch NAT testing; Anti-HCV-POC, screening with anti-HCV followed by POC NAT testing; CEN, central laboratory testing; HCV, hepatitis C virus; ICER, incremental cost-effectiveness ratio; NAT, nucleic acid testing; POC, point of care.
contributes to Pakistan’s goal of eliminating HCV by the year 2030. Compared with the general population, patients with chronic HCV are at a significantly higher risk of developing costly HCV-related complications, including hepatic fibrosis, cirrhosis, and hepatocellular carcinoma.

While the Anti-HCV-POC approach shortens the time between screening and treatment initiation, LTFU is common. The cobas PSC addresses challenges of LTFU whereby patients fail to adhere to recommended confirmatory follow-up testing. LTFU due to non-compliance with testing and treatment protocols has been described as a substantial challenge in Pakistan. To our knowledge, this is the first study in Pakistan to estimate the potential cost and accuracy of using the cobas PSC to collect samples for HCV testing. Given that over 60% of the Pakistan population resides in rural areas where access to testing is constrained, the cobas PSC has the potential to reduce LTFU and increase access to advanced molecular diagnostic testing regardless of geography or proximity to central laboratories. Investment in information technology tools could also reduce LTFU through improved patient tracing, rapid sharing of test results and linkage to care. Moreover, advanced molecular laboratory infrastructure available in central reference laboratories can be utilised for blood donation screening—an

Figure 3  Tornado diagram of incremental costs comparing Anti-HCV-CEN to Anti-HCV-POC. The black bars represent minimum values while the grey bars represent high values (values are stated in parentheses). CEN, central laboratory testing; HCV, hepatitis C virus; P, probability; POC, point of care.

Figure 4  Incremental cost-effectiveness scatterplot comparing Anti-HCV-CEN to Anti-HCV-POC. CEN, central laboratory testing; HCV, hepatitis C virus; POC, point of care.
important component of HCV elimination efforts. High prevalence of anti-HCV antibodies among blood donors is well documented in Pakistan. Available infrastructure could also be deployed in other disease elimination programmes, including HIV, HBV, Mycobacterium tuberculosis, human papillomavirus and SARS-CoV-2.

A limited number of economic evaluations of HCV elimination diagnostic strategies have been previously conducted in Pakistan. Chhatwal et al investigated the cost of HCV elimination in Pakistan using different combinations of tests for screening and confirmation of viraemia. A testing strategy involving the use of a POC screening test followed by the GeneXpert test for detection of viraemia and assessment of treatment response yielded the lowest annual cost. This finding is different to this study and may be attributed to differences in the study design and application of different costing parameters. Other HCV-related economic evaluation studies with relevance to Pakistan did not assess the cost-effectiveness of a comprehensive array of HCV diagnostic testing approaches.

The WHO strategy for the period 2022–2030 has set an ambitious goal that would require the diagnosis of 90% of all patients with HCV and cure for 80% of people with HCV by the year 2030.

Our study has the potential health policy implications in Pakistan. Given that, in Pakistan, healthcare expenditure makes up only 0.9% of gross domestic product (GDP) and budgets are therefore severely constrained, our analysis provides decision-makers with evidence on the most cost-effective approach to scale-up HCV screening in order to achieve elimination by 2030. Pakistan has recently included HCV testing and treatment in its list of essential health services and the government has pledged to increase healthcare funding to 3% of GDP by 2025.

Though choices still have to be made on what needs to be prioritised, decision-makers can balance short-term investments in HCV against investment in other priority areas. The COVID-19 pandemic has strained budgets and impacted HCV service delivery; however, evidence is accumulating that attention should shift back to HCV elimination as soon as is appropriate.

Our analysis suggests that a centralised reference laboratory testing approach supplemented with novel sample collection methods, such as the cobas PSC, would provide the best value for money in Pakistan. In line with WHO and European Association for the Study of the Liver HCV testing and treatment guidelines, there is a possibility to innovate further and allow ‘real-reflex’ testing with the PSC. Two spots could be sampled on the PSC to enable laboratory-based anti-HCV testing and subsequent confirmatory testing (eg, on the cobas® HCV test for use with cobas 6800/8800 systems) without the need for additional sampling.

As to access for funding for hepatitis crisis remains a major barrier for most LMICs, strategies to overcome fiscal constraints must be developed and tailored according to national income. More efficient delivery of interventions with lower budget impact may also be achieved by first targeting HCV high-risk groups, or by targeting cohorts based on mean age at disease presentation, though caution is needed to avoid missing those infected. A cost-effectiveness analysis for screening of HCV in Japan also supports early diagnosis combined with non-interferon-based treatment, with improved cost effectiveness in high-prevalence groups.

In developing HCV testing and scale-up plans, a comprehensive accounting of all costs along the entire continuum of a patient testing journey is warranted to objectively inform resource allocation decisions. An analysis that focuses solely on the price of the consumables may significantly underestimate the full cost burden associated with testing. High-throughput testing that is synergised with highly accurate assays can leverage the economies of scale to support expanded access to HCV testing at lower costs. Fully automated high-throughput solutions can play a key role in rapidly scaling up testing and can accelerate streamlined linkage to care and treatment. The appropriate infrastructure must also be in place to support rapid screening scale-up. Integration of screening into existing healthcare services has been shown to reduce overall costs. Further, existing centralised, high-throughput systems may be more amenable to scale-up than POC testing which requires more operational support. Integration of services may also aid with the provision of sufficient human resources to ensure continuity and sustainability of elimination programme. Egypt is poised to become the first country to eliminate HCV. This success is partly attributed to the availability of high-throughput molecular diagnostic solutions. Testing platforms have now been repurposed for donor blood screening and COVID-19 pandemic testing.

Our study is subject to several limitations. First, there is a lack of head-to-head test performance studies that directly compare POC confirmatory testing with reference laboratory testing using the PSC. The model test performance inputs of POC NAT testing and central NAT testing were based on a synthesis of results of evaluations of the performance under different field conditions. An analysis including the DBS approach (a potential alternative to the cobas PSC) was beyond the scope of this study. However, deterioration of DBS viral recovery has been widely discussed in HIV and HCV studies, whereas PSC has been demonstrated to exhibit high stability up to 4 weeks. Second, we did not account for potential societal costs, including patient transport costs to the GeneXpert testing locations and related productivity.
losses associated with time off from work. We also did not consider the costs associated with returning results to patients following laboratory-based confirmatory testing. We assumed that these costs would be negligible. Third, we did not capture the long-term downstream impact of testing, including potential reduction in onward disease transmission, treatment outcomes or the impact of FN results. We postulate that expanded access to testing followed by appropriate treatment would curtail disease transmission among patients achieving sustained virological response. Fourth, our analysis does not consider the fiscal or feasibility of implementation. This may be an area of future research. Finally, due to the focus on testing costs and outcomes over a short time horizon we did not estimate long-term clinical impacts associated with testing strategies using measures such as the quality-adjusted life year (QALY) or the disability-adjusted life year (DALY). Future research could explore the lifetime costs and benefits using these measures (QALY/DALY) to enable comparisons with interventions for other diseases.

CONCLUSIONS

Given the high prevalence of HCV infection in Pakistan and the humanistic burden of illness associated with chronic HCV, a focus on expanding screening programmes and linkage to care is critical towards meeting WHO 2030 elimination targets. The base case results from this study suggest that a reference laboratory-based approach would provide the best value for money when scaling up HCV screening in Pakistan. High-throughput centralised testing can rapidly expand access. Additionally, this analysis underscores the value of novel sample collection technologies, such as the cobas PSC, which may help overcome challenges associated with rural population testing, LTFU and specimen transport. It also demonstrates that an HCV screening approach that assumes the use of the cobas PSC to collect blood samples for confirmatory testing is highly likely to be cost-effective compared with a near-patient molecular PCR approach. The cobas PSC has the potential to significantly increase access to HCV testing in ‘hard-to-reach’ rural areas in Pakistan and may play an essential role in helping other countries to scale-up testing to meet WHO HCV elimination goals.

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Contributors

JBB, SC and LPG led the study design. JBB, JK, MBM and MMC prepared the draft manuscript. All authors (JBB, JK, SC, MMC, LPG, MBM and SSH) reviewed the analysis, contributed to the interpretation of data, revised the manuscript for important intellectual content and provided substantial modifications to the final manuscript. JKK accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Competing interests

JBB and SC served as paid consultants to Roche Molecular Systems, Inc. JKK is an employee of Roche Diagnostics Solutions. MBM is an employee of Roche Molecular Systems, Inc. MMC was an employee of Roche Molecular Systems, Inc. at the time this study was conducted and remains a stockholder. LPG served as a paid consultant to Roche Molecular Systems, Inc. and received grants or has contracts with Gilead Sciences. SSH has no conflicts of interest to declare. COBAS is a trademark of Roche. All other product names and trademarks are the property of their respective owners.

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, or reporting, or dissemination plans of this research.

Patient consent for publication

Not applicable.

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All data relevant to the study are included in the article or uploaded as supplementary information. All data relevant to the study are included in the article.

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