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# Patient outcomes in public sector hepatitis C treatment programmes: a retrospective cohort analysis across five low- and middle-income countries

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## ABSTRACT

**Objectives** Given limited data on factors associated with hepatitis C virus (HCV) treatment discontinuation and failure in low- and middle-income countries, we aimed to describe patient populations treated for HCV in five countries and identify patient groups that may need additional support.

**Design** Retrospective cohort analysis using routinely collected data.

**Setting** Public sector HCV treatment programmes in India (Punjab), Indonesia, Myanmar, Nigeria (Nasarawa) and Vietnam.

**Participants** 104 957 patients who initiated treatment in 2016–2022 (89% from Punjab).

**Primary outcomes** Treatment completion and cure.

**Results** Patient characteristics and factors associated with outcomes varied across countries and facilities. Across all patients, median age was 40 years (IQR: 29–52), 30.6% were female, 7.0% reported a history of injecting drugs, 18.2% were cirrhotic and 4.9% were coinfected with HIV. 79.8% were prescribed sofosbuvir+daclastasvir. Of patients with adequate follow-up, 90.6% (89,551) completed treatment. 77.5% (69,426) of those who completed treatment also completed sustained virological testing at 12 weeks (SVR12), and of those, 92.6% (64 305) were cured. In multivariable-adjusted models, in most countries, significantly lower treatment completion was observed among patients on 24-week regimens (vs 12-week regimens) and those initiated in later years of the programme. In several countries, males, younger patients <20 years and certain groups of cirrhotic patients were less likely to complete treatment or be cured. In Punjab, treatment completion was also lower in those with a family history of HCV and people who inject drugs (PWID); in other countries, outcomes were comparable for PWID.

**Conclusion** High proportions of patients completed treatment and were cured across patient groups and countries. SVR12 follow-up could be strengthened. Males, younger people and those with decompensated cirrhosis on longer regimens may require additional support to complete treatment and achieve cure. Adequate programme financing, minimal user fees and implementation of evidence-based policies will be critical to close gaps.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is a large, multicountry analysis of data from over 100 000 patients on real-world implementation of public sector hepatitis C programmes in low-income and middle-income countries.
⇒ Multivariable-adjusted estimates were calculated to identify patient groups at risk for treatment discontinuation and failure.
⇒ Routine data from health facilities were used for this analysis; therefore, some data points may be inaccurate.
⇒ The majority of the data (89%) came from the programme in Punjab, India, and statistical power was limited for some of the analyses in the other countries.
⇒ This analysis was observational in nature, so associations identified cannot be interpreted causally and may be subject to residual confounding.

## BACKGROUND

Hepatitis C virus (HCV) is curable with generic, well-tolerated direct acting antivirals (DAA) that are now available at low cost in many low- and middle-income countries (LMIC)—as low as US$60 for World Health Organization (WHO) prequalified products.[1] Initial public sector HCV testing and treatment programmes have demonstrated remarkable success in LMIC, even with limited funding.[2] However, gaps remain, including initiating people living with HCV (PLHCV)

on treatment and ensuring that PLHCV complete prescribed regimens and are confirmed cured. Better understanding is needed of the patient population on treatment in public sector programmes. Providing additional support to patients who may be at greater risk of treatment discontinuation or failure will be critical for programme success.

While there is some evidence on patient-level characteristics that predict treatment discontinuation and failure in high-income countries, there are very limited data from LMIC. The WHO estimates that only 13% of PLHCV globally have been treated.[3] A review of the evidence published in 2020 summarised that across published studies globally, only a median of 29% (range: 12%–77%) of patients diagnosed with chronic HCV initiate treatment.[4] Of those who initiated treatment, a median of 3% (range: 0%–11%) of patients discontinued treatment and a median of 5% (range: 0%–25%) of patients completed treatment but did not complete sustained virological response testing at 12 weeks (SVR12).[4] However, gaps are likely to be greater in large public sector programmes in LMIC; indeed, in a separate 2020 analysis of data across 7 LMIC using routinely collected aggregate programme data, while data on treatment completion was not available, the number of patients with an SVR12 test conducted was 45% lower than the number of patients who initiated treatment, indicating substantial gaps in patient follow-up.[2]

Previous studies have identified predictors of treatment discontinuation and/or loss to follow-up in the HCV care cascade, including younger age,[4–7] male gender,[5 6] history of injecting drugs[4 8] and a history of psychiatric illness.[4 6] Patient-level predictors of DAA treatment failure (outside of treatment regimen and duration) reported previously include cirrhosis, genotype 1a or 3 infection, resistance-associated variants, elevated viral load (VL), (possibly) HIV coinfection, and previous treatment failure for HCV.[9–14] However, the bulk of previous evidence on this topic is from high-income countries.

Given the evidence gap in this area, we retrospectively analysed routinely collected public sector monitoring and evaluation (M&E) data from initial programmes in Punjab, India; Indonesia; Myanmar; Nasarawa, Nigeria; and Vietnam, with the aim to describe the characteristics of patients treated for HCV across country programmes, calculate the proportion of patients who completed treatment (defined differently across country contexts as not collecting all medication refills or being lost to follow-up), completed SVR12 testing, and were cured, and identify demographic or clinical factors that may be linked to treatment completion and/or cure. Given that most countries only collected individual-level data for patients treated for HCV (with only aggregate-level data available on screening and diagnosis), this analysis focused on patients who initiated treatment.

## METHODS

### Country selection and description

We previously published a description of implementation of initial HCV testing and treatment programmes in the public sector in Punjab, India, Indonesia, Myanmar, Nasarawa, Nigeria and Vietnam as well as Cambodia, Indonesia and Rwanda (aggregate cascade of care data only).[2] Programme strategy and rollout have been supported by the Clinton Health Access Initiative (CHAI), a technical assistance partner that operates hand-in-hand with governments to provide guidance on programme implementation. Leveraging context-specific strategies, all countries have rapidly expanded access to HCV cure by combining market-shaping to reduce prices with simplification of patient pathways. Programmes were provided with CHAI-supported Bristol Myers Squibb donations of daclatasvir (DCV). As part of this support, five countries had individual-level M&E data that could be used for this analysis and obtained relevant institutional review board (IRB) approval. More information on each country is provided in table 1.

In brief, these programmes ranged from a pilot at a small number of facilities (Vietnam) to programmes limited to a particular state (Nasarawa, Nigeria and Punjab, India) to a national programme (Indonesia, Myanmar). Programmes have moved towards operating under a simplified algorithm as outlined in the 2018 WHO guidelines[15] involving a rapid diagnostic test to screen for anti-HCV antibodies, a VL test to assess viraemia, the 12–24 weeks DAA regimen for viraemic patients involving monthly prescription refills and an SVR test 12 weeks after treatment completion. During this period, Vietnam's programme also included, where accessible, genotyping prior to treatment initiation and VL monitoring of those on treatment, in addition to the WHO recommended diagnostic algorithm; the updated guidelines no longer include these additional components.[16]

### Data collection

Routinely collected M&E data were used for analysis of patients who initiated HCV DAAs for treatment. Deidentified data were collected retrospectively from patient testing and treatment registers, laboratory logbooks, pharmacy records and/or patient charts (dependent on the data systems in each country). In Nasarawa, Nigeria and Vietnam, data were collected manually from paper documents at the facility. In Punjab, India, Indonesia and Myanmar, data were received from government electronic databases. Due to logistical constraints, data time periods and coverage differed by country based on what was available and time period/coverage of IRB approval for analysis; details can be found in table 1. In addition, data points available and definitions of variables varied by country. For instance, designation of cirrhosis status differed based on criteria within the country guidelines at the time and also may have included less objective clinical designation in some cases; the determination of treatment completion also varied. Details can be found in

**Table 1** Characteristics of country programmes contributing data

| | Punjab, India | Indonesia | Myanmar | Nasarawa, Nigeria | Vietnam |
|---|---|---|---|---|---|
| Year of programme initiation | 2016* | 2017 | 2017 | 2015 | 2017 |
| Time period of data included | February 2016–June 2021 | January 2017–February 2022 | June 2017–March 2018 | July 2017–December 2020 | June 2017–December 2018 |
| Data retrieval date | June 2021 | March 2022 | March 2020 | January 2021 | January 2019 |
| Scope of data collected | Initial patients treated and longer term scale-up | Initial patients treated and longer-term scale-up | Initial patients treated only | Initial patients treated only | Initial patients treated only |
| Data source | Custom web-based system | Excel and custom web-based system | Electronic case-based medical record system (OpenMRS) | Paper records at facilities | Paper records at facilities |
| Geographic coverage of data collected | 1 state | 17 provinces | 3 states and regions | 1 state | 7 provinces |
| N and type of health facilities/ sites included | 59—hospitals, HIV treatment centres, opioid substitution therapy centres and prisons | 38—national referral hospitals, provincial hospitals and district hospitals, prison hospitals, military hospitals, police hospitals and one private hospital | 8—general hospitals, specialist hospitals | 2—outpatient and internal medicine departments from a general hospital and a specialist hospital | 8—two national hospitals, five provincial hospitals and one district health centre |
| N patients included | 93 460 | 7424 | 2065 | 139 | 1869 |
| % of all data covered during time period on public sector DAA initiations | 100 | 100 | 100 | 8.1 | 100 |
| Programme approach to case-finding | General adult population, PLHIV, PWID, prisoners, patients from private sector tested positive | Patients at internal medicine/liver wards, PLHIV at treatment centres, PWIDs, prisoners, haemodialysis patients | Patients at medical wards, PLHIV, PWIDs, men who have sex with men, female sex workers, multi-transfused recipients, HCW, haemodialysis patients, patients from private sector or blood donors tested positive and eligible for public sector care | General adult population (provider-initiated testing and counselling), PLHIV, PWID | PLHIV, PWID, HCW, patients at liver wards; 2019 campaign targeting general population in one province |
| Patient screening, diagnosis and treatment fee structure | Free of charge | Free of charge if patients have national insurance. Non-insured patients pay for consumables and services | Free of charge (PPP patients pay for VL and treatment at subsidised prices) | Out of pocket | Out of pocket or insurance co-pay (DCV free of charge) |
| Definition of cirrhosis during time period of data included | APRI >2 and FIB-4 >3.25 in adults. Decompensated cirrhosis defined using clinical criteria (or clinician's judgement) and the Child-Pugh staging system. | APRI>1. Patients at the national hospital were staged using Fibroscan >11.7. Data on decompensated cirrhosis not available. | Initially APRI of >2; changed to >1.5 in the National Simplified Treatment Guidelines for HCV published in 2019. Decompensated cirrhosis defined using clinical criteria (or clinician's judgement) and the Child-Pugh staging system. | APRI >2. Data on decompensated cirrhosis not available. | APRI >2 or a Fibroscan >12.5 kPa; patients at provincial and district level facilities were staged using APRI while patients at the national hospital were staged using Fibroscan. Decompensated cirrhosis defined using clinical criteria (or clinician's judgement) and the Child-Pugh staging system. |

Continued

Table 1 Continued

| | Punjab, India | Indonesia | Myanmar | Nasarawa, Nigeria | Vietnam |
|---|---|---|---|---|---|
| Definition of treatment completion | Picking up the prescription for the final month of treatment | Picking up the prescription for the final month of treatment | Coming for a visit post-treatment completion | Picking up the prescription for the final month of treatment | Patients who did not return for SVR12 testing were called by health facility staff to confirm whether treatment was completed |

*The programme was officially launched in June 2016, but a small number of patients initiated in the months prior.
.APRI, AST to platelet ratio index; DCV, daclatasvir; HCV, hepatitis C virus; HCW, healthcare worker; PLHIV, people living with HIV; PPP, public private partnership; PWID, people who inject drugs; SVR12, sustained virologic response at 12 weeks; VL, viral load.

table 1. In Myanmar, a small number (N=34) of patients had a treatment status listed as 'unknown'—these were counted as not completing treatment, to be conservative.

### Data analysis

StataSE V.17 was used for data analysis. Patient demographic and clinical characteristics were described by calculating the percentage of patients who were in each category, by country and overall as a summary measure. Only patients with adequate follow-up time were included in analyses of patient treatment completion (at least 12 or 24 weeks to complete regimens as appropriate) and cure (at least 12 or 24 weeks to complete regimens as appropriate, plus an additional 12 weeks to complete SVR12 testing; of note, three patients completed treatment and had an early SVR12 test, these outcomes were included). Analyses of predictors were kept separate by country, as there was substantial variability by country and the dataset from India was substantially larger than from other countries. Given that this was an analysis of real-world public sector data, patients were not excluded based on whether current clinical guidelines were followed; for instance, in Punjab, India there were 216 patients initiated on treatment between ages 12–17 that were included in this analysis.

The primary outcomes of the analysis were the proportion of patients who completed treatment (definitions of treatment completion for each country can be found in table 1) and the proportion who were cured among those who completed SVR12. Analyses were conducted separately by country. Patients who died during follow-up were excluded from these analyses, as information on cause and timing of death was not consistently available. We cross-tabulated patient demographic and clinical characteristics by these outcomes to assess the percentage of patients within each category that completed treatment/achieved cure. To identify variables that were statistically significant predictors of outcomes, multivariable-adjusted generalised linear models accounting for clustering by health facility were used (using the glm command with the *cluster* option in Stata). Variables that were individually associated with the primary outcome in one or more countries were considered for inclusion into the multivariable-adjusted model; in the model building process, variables that were not significant in any country-specific models were removed from the final multivariable-adjusted model. After building models separately for each outcome, the same final list of variables was used for multivariable-adjusted models in each country. The final model with treatment completion as the outcome adjusted for sex, age category, family history of HCV, history of injecting drugs, cirrhosis status, treatment regimen, treatment duration and year of treatment initiation. The final model with cure/treatment failure as the outcome adjusted for sex, age category, family history of HCV, cirrhosis status and treatment regimen. We dropped out variables that were too sparse to be included in the model; that meant that in some countries with smaller datasets (Myanmar and Nasarawa, Nigeria), some variables were omitted from multivariable-adjusted models. In country datasets without a particular variable, this variable was not adjusted for in the analysis. A missing indicator category was included for each variable in the model to account for missing data and minimise loss of statistical power due to missingness. Results were similar when those when missing data were removed from analyses. Statistical significance was defined as $p<0.05$.

### Patient and public involvement

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

## RESULTS

### Demographic characteristics of patients initiated on treatment

Data from 104 957 patients who initiated HCV treatment in 2016–2022 were included in this analysis. The majority of patients were in the programme from Punjab, India (93,460); in addition, 7424 patients were from Indonesia, 2065 from Myanmar, 139 from Nasarawa, Nigeria and 1869 from Vietnam. Patient demographic and clinical characteristics as well as treatment outcomes are shown by country in table 2.

In terms of gender: 30.6% of patients were female. In Punjab, India, Indonesia and Vietnam, the majority of those being treated were male (69.4% in Punjab, India, 71.2% in Indonesia, 82.3% in Vietnam). This was reflective of a larger proportion of males both getting tested for HCV and testing positive for chronic HCV and a

**Table 2** Demographic and clinical characteristics of patients who initiated hepatitis C treatment, %

| | All | India (Punjab State only) | Indonesia | Myanmar | Nigeria (Nasarawa State only) | Vietnam |
|---|---|---|---|---|---|---|
| N | 104 957 | 93 460 | 7424 | 2065 | 139 | 1869 |
| Sex | | | | | | |
| Female | 30.6% | 30.6% | 28.5% | 47.8% | 54.7% | 17.7% |
| Male | 69.4% | 69.4% | 71.2% | 52.3% | 45.3% | 82.3% |
| Transgender | 0.02% | 0.02% | 0.0% | 0.0% | 0.0% | 0.0% |
| Missing | 0.02% | 0.0% | 0.3% | 0.0% | 0.0% | 0.0% |
| Age | | | | | | |
| 12–19 | 1.3% | 1.4% | 0.4% | 0.1% | 0.0% | 0.2% |
| 20–29 | 24.0% | 26.4% | 4.7% | 3.9% | 5.8% | 3.9% |
| 30–39 | 23.0% | 22.9% | 24.8% | 12.8% | 13.0% | 33.2% |
| 40–49 | 20.9% | 19.5% | 32.5% | 28.4% | 21.6% | 36.3% |
| 50–59 | 15.7% | 15.4% | 16.0% | 31.0% | 36.7% | 14.2% |
| 60–69 | 10.8% | 10.7% | 11.8% | 17.0% | 14.4% | 8.4% |
| 70+ | 4.0% | 3.7% | 7.7% | 6.7% | 8.6% | 4.0% |
| Missing | 0.3% | 0.2% | 2.2% | 0.1% | 0.0% | 0.0% |
| Family history of HCV | | | | | | |
| Yes | 0.3% | 0.1% | 0.0% | 9.5% | 0.7% | 0.0% |
| None reported | 90.9% | 99.9% | 0.0% | 90.5% | 99.3% | 0.0% |
| Not available | 8.9% | 0.0% | 100.0%* | 0.0% | 0.0% | 100.0%* |
| History of injecting drugs | | | | | | |
| Yes, reported by patient | 7.0% | 5.2% | 21.1% | 11.2% | 0.0% | 34.5% |
| None reported | 93.0% | 94.8% | 78.9% | 88.8% | 100.0% | 65.5% |
| Known HIV coinfection | | | | | | |
| Yes | 4.9% | 2.2% | 22.6% | 40.2% | 2.2% | 33.9% |
| None reported | 95.1% | 97.8% | 77.4% | 59.8% | 97.8% | 66.1% |
| Known HBV coinfection | | | | | | |
| Yes | 0.2% | 0.0% | 0.0% | 3.4% | 7.2% | 5.5% |
| None reported | 92.8% | 100.0% | 0.0% | 96.6% | 92.8% | 94.5% |
| Not available | 7.1% | 0.0% | 100.0%* | 0.0% | 0.0% | 0.0% |
| HCV genotype | | | | | | |
| 1 | 0.7% | 0.0% | 0.0% | 0.0% | 1.4% | 40.0% |
| 2 | 0.02% | 0.0% | 0.0% | 0.0% | 0.0% | 1.0% |
| 3 | 0.1% | 0.0% | 0.0% | 0.0% | 0.0% | 3.0% |
| 6 | 0.7% | 0.0% | 0.0% | 0.0% | 0.0% | 37.0% |
| Not available/missing | 98.6% | 100.0%* | 100.0%* | 100.0%* | 98.6% | 19.0% |
| Cirrhosis | | | | | | |
| Compensated | 8.3% | 8.1% | 0.0% | 17.1% | 0.0% | 38.8% |
| Decompensated | 1.0% | 0.9% | 0.0% | 8.7% | 0.0% | 2.4% |
| Cirrhotic (no additional information) | 8.9% | 7.0% | 38.1% | 0.0% | 5.0% | 0.0% |
| Non-cirrhotic | 81.8% | 84.0% | 61.8% | 74.3% | 95.0% | 58.8% |
| Missing | 0.01% | 0.0% | 0.1% | 0.0% | 0.0% | 0.0% |
| Treatment regimen | | | | | | |
| SOF/DCV | 79.0% | 78.9% | 78.3% | 100.0% | 100.0% | 62.7% |
| SOF/DCV+RBV | 0.8% | 0.1% | 1.3% | 0.0% | 0.0% | 37.3% |
| SOF/VEL | 7.6% | 8.5% | 0.0% | 0.0% | 0.0% | 0.0% |
| SOF/VEL+RBV | 11.1% | 12.5% | 0.0% | 0.0% | 0.0% | 0.0% |
| Other | 1.5% | 0.0% | 20.4% | 0.0% | 0.0% | 0.0% |
| Treatment duration | | | | | | |
| 12 weeks | 88.0% | 90.4% | 62.4% | 67.3% | 95.0% | 90.5% |

Continued

Table 2 Continued

| | All | India (Punjab State only) | Indonesia | Myanmar | Nigeria (Nasarawa State only) | Vietnam |
|---|---|---|---|---|---|---|
| 24 weeks | 11.8% | 9.3% | 37.6% | 32.7% | 5.0% | 9.2% |
| Other | 0.2% | 0.2% | 0.0% | 0.0% | 0.0% | 0.3% |
| Year of treatment initiation | | | | | | |
| 2016 | 18.6% | 20.9% | 0.0% | 0.0% | 0.7% | 0.0% |
| 2017 | 22.5% | 21.2% | 18.0% | 80.9% | 10.8% | 40.4% |
| 2018 | 19.3% | 17.9% | 25.9% | 19.1% | 43.2% | 59.6% |
| 2019 | 22.0% | 22.3% | 29.2% | 0.0% | 45.3% | 0.1% |
| 2020 | 11.4% | 12.4% | 4.3% | 0.0% | 0.0% | 0.0% |
| 2021 | 6.2% | 5.2% | 21.3% | 0.0% | 0.0% | 0.0% |
| 2022 | 0.1% | 0.0% | 1.4% | 0.0% | 0.0% | 0.0% |
| Outcome (N=100 101)† | | | | | | |
| Confirmed cured via SVR12 | 64.2% | 66.5% | 34.8% | 79.8% | 25.9% | 61.2% |
| Failed treatment | 5.1% | 5.5% | 1.2% | 8.6% | 2.2% | 0.4% |
| Did not complete treatment | 9.3% | 8.6% | 20.4% | 1.5% | 13.7% | 6.3% |
| Completed treatment but did not return for SVR12 | 20.1% | 18.2% | 42.0% | 8.6% | 58.3% | 32.0% |
| Died | 1.2% | 1.2% | 1.6% | 1.6% | 0.0% | 0.2% |

*This information was not collected/not available in the database.
†A total of 4856 patients did not have adequate follow-up time in the dataset to complete treatment based on date of treatment initiation and date of data collection, and therefore, were excluded from this and all subsequent analyses.
DCV, daclatasvir; HBV, hepatitis B virus; HCV, hepatitis C virus; RBV, ribavirin; SOF, sofosbuvir; SVR12, sustained virologic response at 12 weeks; VEL, velpatasvir.

higher proportion of people who inject drugs (PWIDs) being male in those countries (>92%). In Myanmar and Nasarawa, Nigeria, the proportion of males and females treated were closer to equal. In terms of age: the median age was 40 years (IQR: 29–52), with the youngest population in Punjab's programme (50.7% were age 39 years or younger) and older populations in Myanmar (54.7% were age 50+ years) and Nasarawa, Nigeria (59.7% were age 50+ years).

In terms of other demographic characteristics: 0.3% reported a family history of HCV. 7.0% had a reported history of injecting drugs, most common among programme participants in Vietnam (34.5%) and Indonesia (21.1%), where this population was a focus of the programme, and in Myanmar (11.2%) where PWID and cirrhotic patients were prioritised for the limited, free-of-charge public treatment courses. 4.9% of patients were reported or confirmed to be coinfected with HIV, ranging from 2.2% in Punjab, India and Nasarawa, Nigeria to much higher in Myanmar, Vietnam and Indonesia (40.2%–33.9% and 22.6%, respectively), whose programmes had a focus on coinfection or prioritisation of free treatment for coinfected patients. 0.2% had known coinfection with hepatitis B virus and 0.02% with tuberculosis (data not shown).

## Clinical characteristics

The proportion of patients with cirrhosis varied across countries: 41.2% in Vietnam (38.8% compensated and 2.4% decompensated), 38.1% in Indonesia (no information available in database on type of cirrhosis), 25.8% in Myanmar (17.1% compensated and 8.7% decompensated), 16.0% in Punjab, India (8.1% compensated, 0.9% decompensated, 7.0% with no further information on type of cirrhosis) and 5.0% in Nasarawa, Nigeria (where cirrhosis data were missing for many patients and largely presumed based on duration of prescribed treatment). In Vietnam, the most common genotypes were 1 (40.0%) and 6 (37.0%); a small proportion were genotype 3 (3.0%) and 19.0% did not have genotype data available. In terms of treatment regimen: In Myanmar, Nasarawa, Nigeria and Vietnam, all patients were prescribed sofosbuvir/DCV (SOF/DCV)-based regimens. In Indonesia, 79.6% were prescribed SOF/DCV-based regimens and the remaining patients were on other regimens including SOF+simeprevir-based regimens and elbasvir/grazoprevir. In Punjab, India, 79.0% were prescribed SOF/DCV based regimens and 21.0% were prescribed SOF and velpatasvir (SOF/VEL)-based regimens. In India and Vietnam, ribavirin (RBV) was added to treatment for some cirrhotic patients due to lower cost, whereas in Nasarawa, Nigeria and Myanmar, cirrhotic patients were typically prescribed 24 weeks of SOF/DCV. In terms of treatment duration: >90% of patients in Punjab, India, Nasarawa, Nigeria and Vietnam were prescribed 12 weeks of treatment; in Indonesia 37.6% of patients were prescribed 24 weeks of treatment and in Myanmar, 32.7% of patients were prescribed 24 weeks of treatment.

## Treatment outcomes

Of 100 101 patients who initiated treatment and had adequate follow-up time in the dataset to assess treatment completion, 1244 deaths were reported (note: deaths were not routinely assessed in all contexts and were

not necessarily related to HCV). Among the remaining patients, 90.6% (89 551) completed treatment. 77.5% of patients who completed treatment also completed SVR12 testing (69 432); completion of SVR12 testing was comparatively lower in Nasarawa, Nigeria (32.5% of patients who completed treatment), Indonesia (46.1%) and Vietnam (65.8%) Among patients with SVR12 results, cure rates were >90% across all countries; overall, 92.6% (64 305) were cured.

### Predictors of treatment completion

Table 3 reports the percentage of patients who completed treatment disaggregated by demographic and clinical characteristics; more detail on the full multivariable-adjusted regression models by country can be found in online supplemental table 1. Treatment completion was high among most groups. In multivariable-adjusted analyses, in all countries with sufficient sample size, significantly lower treatment completion was observed among patients on 24-week regimens (vs 12-week regimens) (Punjab: 86.5% vs 91.8%, Indonesia: 68.9% vs 85.5%; Myanmar 96.9% vs 99.3%, Vietnam 91.8% vs 93.9%, all p<0.05). Significantly lower treatment completion was also observed among those initiated in later years of the programme. In several countries, there was significantly lower treatment completion among younger patients <20 years compared with some or all older age categories (Punjab, India, Myanmar, Vietnam), and certain groups of cirrhotic patients (decompensated patients in Punjab, India and Vietnam, compensated patients in Myanmar and Vietnam) compared with non-cirrhotic patients. In Punjab, India, treatment completion was also lower in males (89.2% vs 96.0%, p<0.001), those with family history of HCV (84.1% vs 91.3% in the general population; p=0.001), and PWID (76.8% vs 92.0% in the general population, p=0.03). In other countries, PWID had comparable outcomes to the general population; in Indonesia, PWID were more likely to complete treatment (88.4% vs 76.8%, p<0.001).

In all countries, there were significant differences in treatment completion across health facilities. In Punjab, India and Indonesia, treatment completion varied from <50% to 100% depending on the facility (note: a much larger number of facilities contributed data compared with other countries); in Myanmar, it varied from 96% to 99%, in Nasarawa, Nigeria, it varied from 72% to 95%, and from Vietnam it varied from 85% to 100%.

### Predictors of cure

Table 4 reports the percentage of patients who were cured, among those with SVR12 data available, disaggregated by patient characteristics. The full multivariable-adjusted regression model results can be found in online supplemental table 2. In Punjab, India and Myanmar, males who completed SVR12 testing were significantly less likely to be cured compared with females; the opposite was true in Vietnam. In Punjab, India, Indonesia and Myanmar, individuals in the youngest age categories were less likely to be cured. Cirrhosis category was a significant predictor in Punjab, India, with 91.5% of cirrhotic patients cured compared with 92.4% of non-cirrhotic patients (p=0.05) and in Myanmar, with 86.4% of decompensated cirrhotic patients cured compared with 90.7% of non-cirrhotic patients (p=0.002). In Punjab, India, patients on SOF/VEL+RBV more likely to be cured compared with SOF/DCV, although the difference between groups was relatively small (94.4% vs 92.1%, p<0.001).

In Punjab, India, Indonesia and Vietnam, there were significant differences in cure rates across health facilities. In Punjab, India, cure rates ranged across facilities from <60% (in two facilities with <10 patients treated) to 100%, in Indonesia cure rates ranged from 73% to 100%, and in Vietnam they varied from 92% to 100%. In countries with data on facility level available, strong outcomes were seen across all tiers of health facilities, even smaller health centres without specialists providing care.

## DISCUSSION

### Summary of key findings

In this analysis of data from over 100 000 patients initiated on DAAs across five different programmes in LMIC, the proportion of patients who completed treatment and were cured was quite high overall and across most patient groups examined. Approximately 90% completed treatment, 77% of those who completed treatment completed SVR12 testing, and 93% of those who completed SVR12 testing were cured. SVR12 testing coverage was limited in Indonesia, Nasarawa, Nigeria and Vietnam. In several countries, males, younger patients and cirrhotic patients were significantly less likely to complete treatment and be cured. Those on 24-week regimens were also less likely to complete treatment across most countries. In Punjab, India, treatment completion was also lower in those with a family history of HCV and in PWID; in other countries, outcomes were comparable or more favourable for PWID and PLHIV. Treatment completion was significantly lower in more recent years of the programme. Within each country, there were significant differences in patient outcomes across health facilities, indicating differences in service delivery and/or patient characteristics at different facilities that could influence outcomes. Additional support may be needed in certain facilities and certain patient groups to ensure treatment completion and confirm cure. The findings from this analysis are encouraging in that in the early phases of these public sector programmes, outcomes demonstrated high treatment completion and a high proportion of patients cured, supporting the feasibility and real-world effectiveness of public sector HCV elimination programmes.

## LIMITATIONS

This analysis has a number of limitations. Data were retrospective, routinely collected programme M&E data, so there may be issues with data accuracy and completeness

**Table 3** Treatment completion classified by patient characteristics across countries*

| | India (Punjab State only) | Indonesia | Myanmar | Nigeria (Nasarawa State only) | Vietnam |
|---|---|---|---|---|---|
| | % completed treatment | %completed treatment | % completed treatment | % completed treatment | % completed treatment |
| N | 79 894/87 522 | 5785/7297 | 2003/2033 | 120/139 | 1749/1866 |
| Total % | 91.3 | 79.3 | 98.5 | 86.3 | 93.7 |
| Sex | | | | | |
| Female | 96.0 | 78.5 | 98.7 | 85.5 | 94.6 |
| Male | 89.2 | 79.9 | 98.4 | 87.3 | 93.6 |
| Transgender | 88.2 | – | – | – | – |
| Unknown | – | 0.0 | – | – | – |
| Age | | | | | |
| 12–19 | 83.5 | 85.7 | 100.0† | – | 100.0† |
| 20–29 | 86.4 | 76.2 | 97.5 | 100.0† | 91.7 |
| 30–39 | 91.7 | 84.2 | 98.9 | 83.3 | 93.9 |
| 40–49 | 94.8 | 80.8 | 98.6 | 83.3 | 93.9 |
| 50–59 | 94.5 | 76.4 | 99.1 | 90.2 | 94.3 |
| 60–69 | 93.1 | 74.6 | 97.1 | 80.0 | 92.4 |
| 70+ | 90.0 | 72.4 | 99.3 | 83.3 | 93.2 |
| Missing | 91.1 | 76.9 | 100.0† | – | – |
| Family history of HCV | | | | | |
| Yes | 84.1 | – | 99.5 | 100.0† | – |
| None reported | 91.3 | – | 98.4 | 86.2 | – |
| History of injecting drugs | | | | | |
| Yes | 76.8 | 88.4 | 99.6 | – | 93.8 |
| None reported | 92.0 | 76.8 | 98.4 | 86.3 | 93.7 |
| Known HIV coinfection | | | | | |
| Yes | 75.3 | 84.7 | 98.8 | 100.0† | 94.8 |
| No | 91.6 | 77.7 | 98.4 | 86.0 | 93.2 |
| Known HBV coinfection | | | | | |
| Yes | 33.3† | – | 100.0 | 100.0 | 93.1 |
| No | 91.3 | – | 98.5 | 85.3 | 93.8 |
| Cirrhosis | | | | | |
| Compensated | 89.8% | – | 98.3% | – | 92.1% |
| Decompensated | 79.5% | – | 99.4% | – | 93.2% |
| Cirrhotic (no additional information) | 88.4% | 69.6% | – | 100.0%† | – |
| Non-cirrhotic | 91.7% | 85.2% | 98.5% | 85.6% | 94.8% |
| Missing | – | 50%† | | | |
| Treatment regimen | | | | | |
| SOF/DCV | 91.6% | 78.9% | 98.5% | 86.3% | 94.1% |
| SOF/DCV+RBV | 64.2% | 90.4% | – | – | 93.1% |
| SOF/VEL | 89.8% | – | – | – | – |
| SOF/VEL+RBV | 90.3% | – | – | – | – |
| Other | 85.2% | 80.0% | – | – | – |
| Treatment duration | | | | | |
| 12 weeks | 91.8 | 85.5 | 99.3 | 85.6 | 93.9% |

Continued

Table 3 Continued

| | India (Punjab State only) | Indonesia | Myanmar | Nigeria (Nasarawa State only) | Vietnam |
|---|---|---|---|---|---|
| | % completed treatment | %completed treatment | % completed treatment | % completed treatment | % completed treatment |
| 24 weeks | 86.5 | 68.9 | 96.9 | 100.0† | 91.8% |
| Other | 97.2 | – | – | – | 100.0%† |
| Year of treatment initiation | | | | | |
| 2016 | 97.1 | – | – | 0.0† | – |
| 2017 | 94.0 | 82.8 | 98.7 | 100.0 | 95.8 |
| 2018 | 92.3 | 86.0 | 97.7 | 91.7 | 92.4 |
| 2019 | 86.9 | 84.6 | – | 79.4 | 100.0† |
| 2020 | 83.6 | 76.9 | – | – | – |
| 2021 | 80.1 | 66.2 | – | – | – |
| 2022 | – | 0.0 | – | – | – |

*Patients who died were excluded from this analysis, as the data did not consistently indicate the timing of death (pretreatment or post-treatment completion).
†Sample size was <10 people in this category.
DCV, daclatasvir; HBV, hepatitis B virus; HCV, hepatitis C virus; RBV, ribavirin; SOF, sofosbuvir; VEL, velpatasvir.

affecting analyses. For instance, 7.0% of patients in the dataset reported history of injecting drugs, lower than might be expected; this could be due to under-reporting by patients and/or inconsistent solicitation/recording of this information by healthcare workers (HCW). In Myanmar, the proportion of patients prescribed 24 weeks of treatment was higher than the proportion classified as cirrhotic, which may relate to clinical discretion/differences in reporting over time. Private sector data were not included. Programmes were implemented differently across country contexts and some country data were limited to the very initial stages of the programme, so it was difficult to make direct comparisons between countries; the older programme data may be less relevant. The majority of the data (89%) came from the programme in Punjab, India, and statistical power was limited for some of the analyses in the other countries. This analysis was observational in nature, so associations identified cannot be interpreted causally and may be subject to confounding. Given the large sample sizes and high level of statistical power, it is possible that some findings were statistically significant due to chance; we focused on risk factors identified as significant across multiple countries or outcomes and those with larger relative differences in outcomes, indicating greater public health relevance. Finally, the dataset was limited to patients who initiated treatment, so it was not possible to assess risk factors for linkage to care which in many contexts may have more patient loss to follow-up than what is observed after treatment initiation. Future studies should focus on risk factors for patient lost to follow-up between diagnosis and treatment initiation.

### Predictors of treatment completion and cure

In this analysis, certain populations appeared to be at higher risk of treatment discontinuation. Our finding in Punjab, India that males were less likely to complete treatment has previously been reported in other country contexts showing that males were more likely to be lost to follow-up from HCV services[5 6] and has also been reported in antiretroviral therapy programmes for PLHIV in LMIC.[17] While a definitive explanation for this finding cannot be provided here, this could be due to males presenting later to care, or reduced integration into the healthcare system in males participating in the programme. Males were also significantly less likely to achieve cure in Punjab, India and Myanmar, which may relate to treatment adherence issues. In certain contexts, this group may benefit from additional follow-up and support to complete their treatment. Similarly, in several countries, adolescents 12–19 years were less likely to complete treatment and, among those with SVR12 results, were less likely to be cured. Younger age has been reported previously as a risk factor for lost to follow-up in HCV programmes[4–7] and HIV treatment programmes as well,[18] possibly due to stigma, competing priorities or generally feeling healthy. Younger patients may need additional support to ensure adherence and treatment completion. In addition, in several countries, those with cirrhosis and on 24-week treatment regimens (which represented many overlapping patients) were significantly less likely to complete treatment; those with cirrhosis were also less likely to achieve cure in some countries. This could be due to a number of factors including more complications, hospitalisation or death in these patients or pill fatigue on longer regimens. This group

Table 4 Proportion of patients cured classified by patient characteristics across countries*

| | India (Punjab State only) | Indonesia | Myanmar | Nigeria (Nasarawa State only) | Vietnam |
|---|---|---|---|---|---|
| | % cured | % cured | % cured | % cured | % cured |
| N | 58 902/63 746 | 2576/2667 | 1648/1826 | 36/39 | 1143/1151 |
| Total % | 92.4 | 96.6 | 90.3 | 92.3 | 99.3 |
| Sex | | | | | |
| Female | 95.0% | 96.5% | 92.2% | 92.9% | 98.5% |
| Male | 91.0% | 96.6% | 88.4% | 90.9% | 99.5% |
| Transgender | 100.0% | – | – | – | – |
| Age | | | | | |
| 12–19 | 84.5%† | 100.0% | 50.0%† | – | 100.0%† |
| 20–29 | 87.5% | 94.6% | 93.9% | 100.0%† | 100.0% |
| 30–39 | 93.4% | 97.7% | 93.0% | 90.0% | 99.0% |
| 40–49 | 94.4% | 95.2% | 89.0% | 100.0%† | 99.5% |
| 50–59 | 94.4% | 95.9% | 89.5% | 100.0% | 100.0% |
| 60–69 | 93.7% | 97.6% | 91.2% | 66.7%† | 100.0% |
| 70+ | 94.3% | 98.1% | 90.2% | 100.0%† | 96.0% |
| Missing | 93.6% | 95.5% | – | – | – |
| Family history of HCV | | | | | |
| Yes | 97.9% | – | 91.4% | 100.0%† | – |
| None Reported | 92.4% | – | 90.1% | 92.1% | – |
| History of injecting drugs | | | | | |
| Yes | 84.6% | 96.0% | 86.1% | 92.3% | 99.6% |
| None reported | 92.6% | 96.8% | 90.8% | – | 99.1% |
| Known HIV coinfection | | | | | |
| Yes | 83.2% | 97.0% | 89.7% | 100.0%† | 99.6% |
| No | 92.5% | 96.4% | 90.6% | 92.1% | 99.1% |
| Known HBV coinfection | | | | | |
| Yes | – | – | 92.1% | 66.7%† | 98.2% |
| No | 92.4% | – | 90.2% | 94.4% | 99.4% |
| Cirrhosis | | | | | |
| Compensated | 93.0% | – | 90.0% | – | 99.2% |
| Decompensated | 93.7% | – | 86.4% | – | 100.0% |
| Cirrhotic (no additional information) | 91.5% | 97.0% | – | 100.0%† | |
| Non-cirrhotic | 92.4% | 96.4% | 90.7% | 91.7% | 99.3% |
| Missing | – | 100.0%† | – | – | – |
| Treatment regimen | | | | | |
| SOF/DCV | 92.1% | 96.5% | 90.3% | 92.3% | 99.5% |
| SOF/DCV+RBV | 81.0% | 97.7% | – | – | 99.0% |
| SOF/VEL | 91.7% | – | – | – | – |
| SOF/VEL+RBV | 94.4% | – | – | – | – |
| Other | 86.4% | 96.7% | – | – | – |
| Treatment duration | | | | | |
| 12 weeks | 92.2% | 96.4% | 90.1% | 91.7% | 99.3% |
| 24 weeks | 93.9% | 97.0% | 90.5% | 100.0%† | 100.0% |
| Other | 94.2% | | – | – | 100.0%† |

Continued

Table 4 Continued

| | India (Punjab State only) | Indonesia | Myanmar | Nigeria (Nasarawa State only) | Vietnam |
|---|---|---|---|---|---|
| | % cured | % cured | % cured | % cured | % cured |
| Year of treatment initiation | | | | | |
| 2016 | 94.2% | – | – | – | – |
| 2017 | 91.4% | 97.8% | 90.1% | 100.0%† | 99.1% |
| 2018 | 93.4% | 95.6% | 91.2% | 87.5% | 99.5% |
| 2019 | 90.8% | 96.7% | – | 100.0%† | 100.0%† |
| 2020 | 90.8% | 96.7% | – | – | – |
| 2021 | 76.9% | 96.1% | – | – | – |

*Among those who completed SVR12 testing.
†Sample size was <10 people in this category.
DCV, daclatasvir; HBV, hepatitis B virus; HCV, hepatitis C virus; RBV, ribavirin; SOF, sofosbuvir; VEL, velpatasvir.

may need additional support to ensure that they are able to complete treatment.

In general, strong outcomes were seen in both PLHIV and PWID, two vulnerable patient groups. In Indonesia, Myanmar and Vietnam, a high proportion of both PLHIV and PWID completed treatment and were confirmed cured. Vietnam's initial HCV programme targeted these groups for support, and Myanmar and Indonesia's programmes prioritised PWID, PLHIV and cirrhotic patients for the limited courses of free treatment available through the public sector. In these country programmes, a high proportion of patients treated were PLHIV and/or PWID, and HCV care was integrated with other health services. In Punjab, India, where these groups recently have become more of a focus as the programme has expanded, HCV treatment completion was significantly lower among PWID. Of note, the vast majority of PWID in Punjab, India's treatment programme were male and in younger age groups. In some programme contexts, PWID may need additional support to complete treatment.

A lower proportion of patients completed treatment in more recent years of programmes. With greater volumes of patients treated in more facilities over time, individuals may be receiving less support from health workers for adherence and education. This may be a training issue as services are decentralised to lower cadres of health workers; as programmes grow, additional support around patient education and counselling may be needed to encourage all patients to complete treatment.

### SVR12 testing coverage and cure

There was room for improvement in the coverage of SVR12 testing (approximately 70% of all patients). Coverage was lowest in Nasarawa, Nigeria, Indonesia and Vietnam. Nigeria and Vietnam are countries with out-of-pocket payment models, although other factors may have contributed. However, overall among patients with SVR12 results, 92% of patients were cured. DAAs are effective in curing most people of HCV, regardless of whether they receive an SVR12 test to confirm this. For initial programmes operating with limited budgets, it is more cost-effective to focus spending on HCV diagnosis and treatment efforts rather than on SVR12 confirmation. Thus, SVR12 should not necessarily be the primary focus for resource-limited settings. However, mechanisms to confirm treatment completion should be in place.

### Treatment outcomes across health facilities

Treatment completion and cure rates varied substantially across health facilities. Strong outcomes were seen across different types of facilities, indicating that programme decentralisation is possible to lower-level health facilities with strong results. However, the variability in outcomes across facilities and over time indicate that there were other factors at the facility and/or patient level that influenced outcomes. On the facility side, this could include differences in staff training and mentorship leading to varying effectiveness of patient education and counselling, impacting outcomes. Staff attitudes towards patients, high staff turnover and/or heightened stigma could have played a role in outcomes at some facilities. Patients seeking care at certain facilities may have had lower incomes on average, and therefore more financial barriers to travelling to the facility, paying for services (depending on the payment model in each country), and ultimately completing treatment. While this analysis looked at patient factors associated with treatment completion, it was limited to characteristics included in patient medical records. Many personal reasons may contribute to treatment discontinuation. Self-perceived reasons for lost to follow-up reported in other studies include limited knowledge and education about HCV,[5 19] challenges in accessing HCV services,[5 19] and personal belief that follow-up was not needed.[19] These significant differences in outcomes across health facilities underscore the importance of public sector programmes routinely reviewing programme data by facility to identify health facilities that may need additional support, through refresher trainings and/or other strategies.

### Strategies to improve treatment outcomes

A number of evidence-based strategies may be implemented to improve treatment completion and reduce lost to follow-up from HCV programmes. Updated 2022 WHO guidelines recommend simplified service delivery through decentralisation, integration and task sharing, strategies to improve programme outcomes, as well as offering reflex VL testing and point-of-care as an alternative to centralised VL testing.[20] In many programmes, excessive visits are required for testing and treatment. Simplifying algorithms to minimise the number of times patients must come to health facilities for care will be an important strategy. This may be done through same day screening and confirmatory VL; support via telemedicine[21–23]; and multimonth prescription dispensations, a strategy that has been used effectively in Cambodia to streamline number of visits for HCV patients,[24 25] demonstrated strong SVR12 outcomes across five countries in the MINMON trial,[26] and has also been used to streamline ART services for PLHIV. In addition, decentralising care to lower tier health facilities and additional cadres of HCW will improve access and has been shown to have equivalent SVR12 rates compared with care by specialists.[27] Clear and comprehensive training materials and a regular training schedule will be necessary to successfully decentralise care to lower tier facilities in the longer term. Integration of services may also improve patient outcomes; in this analysis, programmes that prioritised PLHIV and PWID demonstrated strong outcomes in these groups. A recent meta-analysis reported that integrating HCV care with primary care and harm reduction services/decentralisation of care may improve linkage to care and treatment access and thus could be an important way to improve follow-up.[28] In addition, while many programmes have already built strong data systems, it will be important for systems to track all patients through the testing and treatment process, identifying in real time those who do not come for appointments and prescription refills for follow-up by health facility staff. Some programmes, such as in Punjab, India are already doing this. Automated SMS appointment/treatment refill pickup reminders/results delivery have been effective in other disease programmes such as HIV.[29] Programmes in Punjab, India are currently employing this strategy to improve treatment adherence and completion. Myanmar's programme has used automated reporting tools through OpenMRS to create easy-to-access lists of patients for follow-up or SVR12 scheduling that are facilitating efficient HCW phone follow-up. Supportive interventions such as adherence clubs and community-based support have been successful to improve retention in care for PLHIV on ART[30] and have been used successfully in HCV programmes in Myanmar[31] and Vietnam.[32 33] Finally, ensuring adequate programme financing, including minimal out-of-pocket costs/user fees for testing and treatment and financing to implement these evidence-based policies will be critical to close gaps in service utilisation.

## CONCLUSION

Across five LMIC, early public sector programme data demonstrated high treatment completion and cure rates across demographic and clinical groups. These findings are positive and suggest that investments in HCV programmes have strong potential to cure many PLHCV. Males, younger individuals, those with cirrhosis/on longer treatment regimens, and PWID may need additional support in certain contexts to complete their treatment. Decentralised, integrated, and simple HCV diagnosis and treatment programmes, with adequate funding, community engagement, and strong routine data systems to enable real-time programme monitoring and strengthening, will be essential to scale programmes and achieve HCV elimination.

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