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Virological response among patients with available outcome testing after sofosbuvir plus ravidasvir in Malaysia's decentralised hepatitis C programme: A national registry-based observational cohort study

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ABSTRACT

Objective: To evaluate the real-world effectiveness of sofosbuvir plus ravidasvir (SOF/RDV) for chronic hepatitis C in Malaysia.

Methods: This is a national registry-based observational cohort study using programme data from public hospitals and primary care clinics. Adults with confirmed active hepatitis C virus infection who received SOF/RDV from 2018 to 2024 were included. Patients without cirrhosis received 12 weeks of therapy and those with compensated cirrhosis received 24 weeks. Sustained virological response at 12 weeks was assessed using hepatitis C virus RNA or core antigen testing. Variables were summarised using frequencies, percentages, and medians with interquartile ranges. Assessed variables included demographic characteristics, injection-drug-use history, HIV co-infection, cirrhosis, treatment duration, treatment setting, treatment status, and sustained virological response 12 weeks after treatment (SVR12). Group comparisons used *Chi*-square, Fisher's exact, or Mann-Whitney *U* tests. Multivariable logistic regression assessed factors associated with failure to achieve SVR12.

Results: A total of 1 143 patients were included. Their median age was 48 years (IQR 41.0–56.5), 1 055 (92.3%) were male, 815 (71.3%) were people who inject drugs, and 49 (4.3%) had HIV co-infection. SVR12 testing was available for 504 patients (44.1%); 469/504 achieved SVR12 (93.1%). SVR12 was achieved by 336/358 people who inject drugs (PWID) (93.9%, 95% *CI* 90.9%–95.9%) and 133/146 non-PWID (91.1%, 95% *CI* 85.4%–94.7%). The exploratory multivariable model did not identify statistically significant predictors, but precision was limited by the small number of failures.

Conclusions: Among the 44.1% of treated patients with available post-treatment virological testing, SOF/RDV was associated with a high SVR12 rate. Substantial incomplete outcome ascertainment prevents a definitive estimate of programme-wide effectiveness and

limits generalisability to the full treated population. Strengthening treatment-cascade documentation and post-treatment testing is necessary for reliable monitoring of cure and elimination progress.

KEYWORDS: Hepatitis C; Antiviral agents; Sofosbuvir; Ravidasvir; Sustained virological response; Primary health care; Malaysia

Summary

Question: What is the real-world virological response to sofosbuvir plus ravidasvir (SOF/RDV) in Malaysia's decentralised hepatitis C programme?

Findings: In this national registry cohort of 1 143 adults, post-treatment virological results were available for 504 (44.1%), of whom 469 (93.1%) achieved sustained virological response 12 weeks after treatment. Response was not significantly associated with injecting drug use.

Meaning: SOF/RDV achieved a high virological response among patients with documented follow-up, although incomplete outcome ascertainment limits estimation of programme-wide effectiveness.

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1. Introduction

Hepatitis C virus (HCV) infection remains a major global public health challenge, with an estimated 50 million people living with chronic infection worldwide[1]. Chronic HCV infection is a leading cause of progressive liver disease, including cirrhosis, hepatic decompensation, and hepatocellular carcinoma. Despite advances in diagnosis and treatment, HCV transmission persists and disproportionately affects marginalized populations such as people who inject drugs (PWID), men who have sex with men, and individuals with limited access to healthcare services[2]. These populations often experience barriers to specialist care, highlighting the importance of expanding access to treatment through decentralised healthcare systems.

The introduction of direct-acting antivirals (DAAs) has transformed the management of chronic HCV infection. Unlike interferon-based therapies, DAAs are well tolerated, orally administered, and directly inhibit viral proteins essential for HCV replication. Modern DAA regimens routinely achieve sustained virological response (SVR) rates exceeding 95% in clinical trials, effectively making hepatitis C a curable infection[3]. These therapeutic advances have enabled simplified treatment strategies that can be delivered outside specialist hepatology centres. Building on these therapeutic advances, the World Health Organization (WHO) has set ambitious targets to eliminate viral hepatitis as a public health threat by 2030 through expanded testing, treatment, and prevention strategies[4].

However, most evidence supporting DAA effectiveness originates from randomized clinical trials or cohorts managed in tertiary hepatology centres. Such settings often involve highly selected patient populations, structured monitoring, and specialist care that may not reflect the realities of routine healthcare delivery. Real-world effectiveness may therefore differ from clinical trial efficacy due to variations in patient characteristics, adherence, comorbidities, and health system factors[5-9]. In addition, access to DAAs remains constrained in many low- and middle-income countries due to cost and procurement barriers, highlighting the need for affordable, scalable therapeutic options.

Among newer DAA combinations, sofosbuvir plus ravidasvir (SOF/RDV) represents a distinct therapeutic innovation developed through a non-profit, access-oriented drug development model led by the Drugs for Neglected Diseases initiative (DNDi) in collaboration with public and private partners. Unlike conventional pharmaceutical development pathways, this model prioritises affordability, accessibility, and public health impact in low- and middle-income countries. Sofosbuvir is a nucleotide polymerase inhibitor that forms the backbone of several highly effective antiviral combinations, while ravidasvir is a potent NS5A inhibitor with activity across multiple

HCV genotypes[10,11]. Importantly, SOF/RDV has been included in the WHO Model List of Essential Medicines, recognising its clinical efficacy, safety, and strategic importance for global hepatitis C elimination efforts. Clinical trial data, including the STORM-C-1 study conducted in Malaysia and Thailand, have demonstrated high efficacy of the SOF/RDV regimen in patients with and without compensated cirrhosis[12-14]. However, evidence on its large-scale implementation within national programmes, particularly in decentralised care models central to elimination strategies, remains limited.

Malaysia has implemented a national strategy to expand hepatitis C treatment through public hospitals and primary care clinics, including facilities providing methadone maintenance therapy where HCV prevalence is high among key populations. This decentralised treatment model enables direct-acting antiviral therapy to be delivered through both specialist and primary care services, creating an opportunity to evaluate treatment outcomes under routine programmatic conditions. In the context of global hepatitis C elimination, therapies that combine high efficacy with affordability and programmatic feasibility are critical. SOF/RDV is one of the few regimens specifically developed to address these gaps. Evaluating its performance in real-world national programmes is therefore essential not only for clinical validation but also for informing policy adoption and scale-up in resource-constrained settings.

2. Methods

2.1. Study design and data source

This study was a national registry-based observational cohort study using data from the My HIV Care Cascade (MyHCC) registry. The MyHCC registry is maintained by the Ministry of Health Malaysia and collects programmatic data on patients receiving hepatitis C care across participating public hospitals and primary care clinics across Malaysia. Data are entered by trained healthcare personnel using standardised reporting forms and undergo periodic data verification as part of routine programme monitoring.

2.2. Study population

All patients with active hepatitis C infection treated with DAAs in participating hospitals or health clinics were eligible. The study population comprised adult patients aged 18 years and above, of either sex, who had been diagnosed with active hepatitis C infection, received DAA treatment, and completed at least 12 weeks of follow-up at the respective hospitals or clinics between 2018 and 2024.

Patients were excluded if they did not complete the prescribed DAA regimen, were lost to follow-up, or died during the treatment or follow-up period.

2.3. Diagnosis, treatment, and outcome assessment

Since 2018, DAA therapy has been decentralised to family medicine specialists in primary care clinics, many of which provide methadone maintenance therapy where HCV prevalence is high among key populations. In accordance with the Malaysian Clinical Practice Guideline for the Management of Chronic Hepatitis C, all patients with a positive screening test (anti-HCV antibody, performed by rapid diagnostic test or laboratory-based immunoassay) underwent confirmatory testing^[10]. Before initiation of SOF/RDV, active HCV infection was confirmed using either HCV RNA polymerase chain reaction (PCR) testing or, where resources were limited, HCV core antigen (HCVcAg) testing through the laboratory service supporting the treating hospital or health clinic. Patients were entered into the treatment cohort after confirmation of active infection.

Patients without cirrhosis received 12 weeks of SOF/RDV therapy, while those with compensated cirrhosis received 24 weeks of treatment according to Malaysian Clinical Practice Guidelines for Chronic Hepatitis C. SVR12 was defined as an undetectable HCV RNA result obtained at least 12 weeks after completion of DAA treatment, in accordance with the Malaysian Clinical Practice Guidelines for Chronic Hepatitis C. The Clinical Practice Guidelines recommend HCV RNA assessment at 12 weeks and recognizes nucleic acid testing at either 12 or 24 weeks after treatment as a test of cure; therefore, tests performed later than 12 weeks were also accepted as valid sustained virological response assessments. Tests obtained before 12 weeks were not considered SVR12. Indeterminate, equivocal, or non-interpretable results were treated as missing outcome data rather than as virological failure. Detectable HCV RNA at or after 12 weeks was classified as failure to achieve SVR.

Records of patients treated for hepatitis C in primary care or hospitals from 2018 to 2024 were extracted from the MyHCC registry. Each patient record was screened for eligibility based on predefined inclusion and exclusion criteria. Eligible patients were included, and sociodemographic, clinical, and laboratory data were collected using a standardised data collection form for analysis. Because the MyHCC registry reflects routine programmatic monitoring rather than a research-driven follow-up protocol, post-treatment viral testing was not available for all treated patients. This reflects real-world service delivery conditions rather than loss to follow-up within a controlled study setting. No patients included in

the registry were clinical trial participants. Patients treated up to 2021 received SOF/RDV through an early-access programme. Thereafter, treatment was provided through routine Ministry of Health care in hospitals and participating health clinics. To assess whether inclusion of earlier-access patients influenced the results, a sensitivity analysis was performed restricting the cohort to patients who initiated SOF/RDV from August 2023 onward.

2.4. Statistical analysis

All data were de-identified and analyzed as a cohort using IBM SPSS Statistics version 30 (IBM, Somers, NY, USA). Categorical variables were summarised as frequencies and percentages. Group comparisons were performed using the *Chi-square* test or Fisher's exact test, as appropriate. Continuous variables were not normally distributed (Shapiro-Wilk test) and were expressed as median [interquartile range (IQR)], comparison was conducted using the Mann-Whitney *U* test. Because the MyHCC registry reflects routine programmatic monitoring, post-treatment SVR testing was not available for all treated patients. Analyses were therefore conducted among patients with available outcome data. Missing data were handled using listwise deletion. SVR12 analyses were restricted to patients with documented outcome results; missing or indeterminate results were excluded rather than imputed. Because outcome availability may be related to patient, facility, or programme characteristics, estimates are subject to selection and ascertainment bias.

To identify independent factors associated with failure to achieve SVR12, a multivariable logistic regression model was constructed with failure to achieve SVR12 as the dependent variable. Variables with a *P*-value <0.25 in univariate analysis were entered simultaneously into the model. Collinearity was assessed prior to inclusion of covariates. Model fit was evaluated using the Hosmer–Lemeshow test. Given the relatively small number events of failure to achieve SVR12 (*n*=35), the number of variables included in the model was limited to reduce the risk of overfitting. Effect estimates are reported as adjusted odds ratios (aOR) with 95% confidence intervals. A two-sided *P*-value of <0.05 was considered statistically significant.

The final exploratory logistic regression included all 504 patients with documented SVR12 results because the three selected covariates (blood or blood-product transfusion exposure, HIV co-infection, and sexual exposure) were complete in this analytic cohort. Variables associated with failure to achieve SVR12 at *P*<0.25 in univariable analysis were entered simultaneously. With 35 failures and three predictors, the model provided approximately 11.7 failure events per predictor; estimates remain exploratory because the event count was small and confidence intervals were wide.

2.5. Ethical approval

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Medical Research and Ethics Committee, National Institutes of Health (NIH), Malaysia, prior to study initiation (NMRR ID-25-00302-RMA (IIR), approval date: 17 March 2025). The analytic dataset was de-identified, access was restricted to authorised personnel, and use was governed by Ministry of Health procedures. The requirement for informed consent was waived due to the use of de-identified registry data.

3. Results

3.1. Baseline characteristics

A total of 1 143 patients with chronic hepatitis C were included in the analysis (Figure 1). The cohort included patients from 218 contributing facilities across 15 states and federal territories, with geographic contribution varying substantially across regions ($P<0.001$) (Supplementary Table 1). The median age was 48 years (IQR: 41.0–56.5), and the cohort was predominantly male (92.3%). Malay patients comprised 81.8% of the cohort; the remaining 18.2% comprised Chinese, Indian, Sarawakian, and other recorded ethnicities.

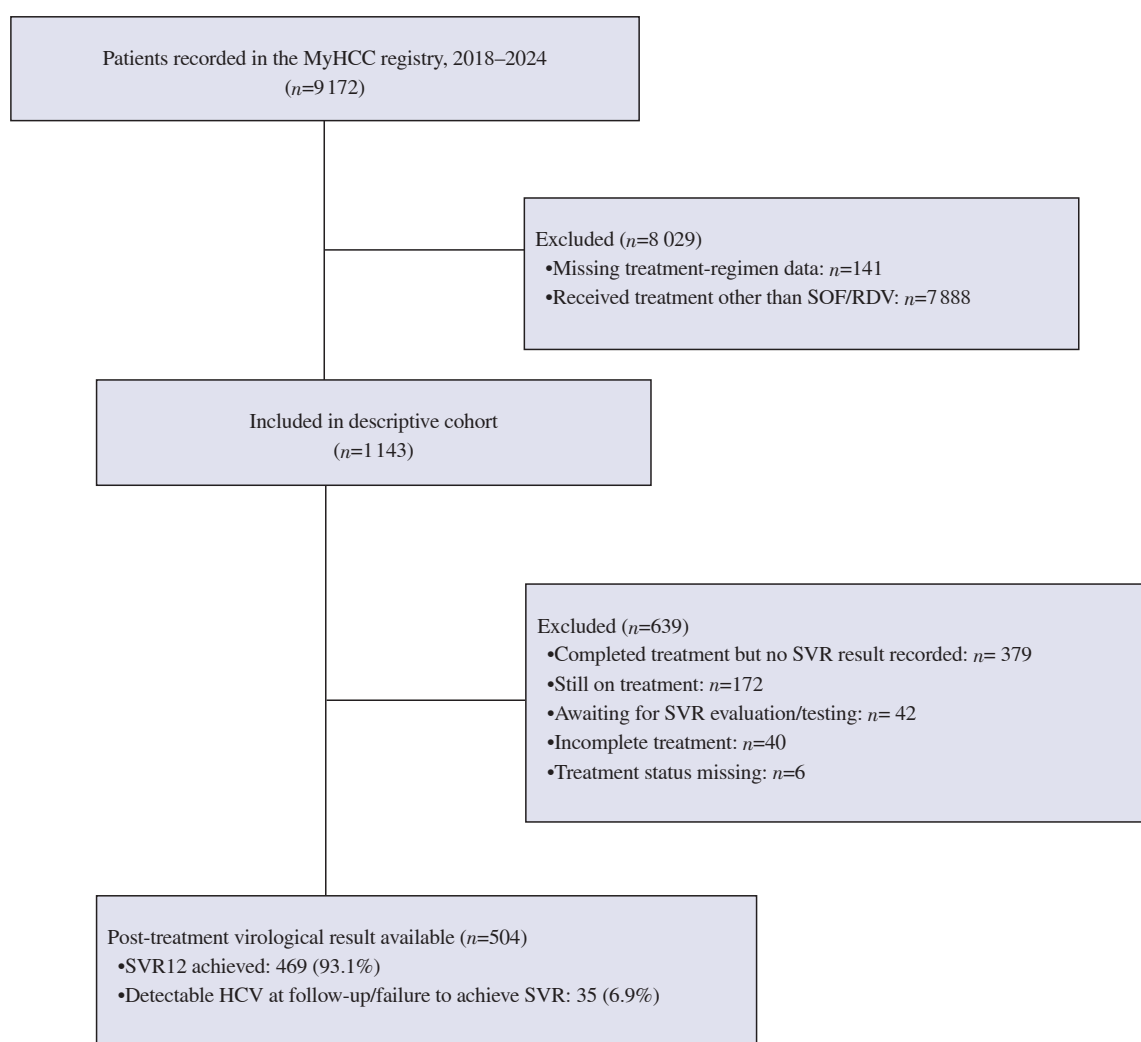


Figure 1. Flow diagram of the study. MyHCC: My HIV Care Cascade; SVR12: Sustained virological response 12 weeks after treatment; HCV: Hepatitis C virus.

Most patients belonged to high-risk populations, with people who inject drugs (PWID) accounting for 71.3% of the cohort. Other reported risk factors included sexual exposure (9.4%), tattooing (6.9%), blood or blood product transfusion (3.0%), and body piercing (1.9%), while 11.9% had no identifiable risk factor. HIV co-infection was present in 4.3% of patients.

Cirrhosis status was available for 702/1 143 patients; 159/702 (22.6%) had cirrhosis and 543/702 (77.4%) did not. Treatment duration was available for 1 068/1 143 patients; 789/1 068 (73.9%) received 12 weeks and 279/1 068 (26.1%) received 24 weeks. Among the 159 patients with recorded cirrhosis, treatment duration was available for 157: 139/157 (88.5%) received 24 weeks and 18/157 (11.5%) received 12 weeks; while treatment duration was missing for two patients. Ribavirin use was recorded in 10 patients among 718 with available ribavirin data.

Table 1. Sociodemographic characteristics of patients ($n=1\,143$).

Characteristics	Data
Age, years, median (IQR)	48.0 (41.0-56.5)
Sex [†] , n (%)	
Male	1055 (92.3)
Female	87 (7.6)
Ethnicity, n (%)	
Malay	935 (81.8)
Chinese	98 (8.6)
Indian	53 (4.6)
Sarawakian	26 (2.3)
Others	31 (2.7)
Risk factor, n (%)	
People who inject drugs	815 (71.3)
Blood/blood product transfusion	34 (3.0)
Organ transplant	3 (0.3)
Needle stick injury	7 (0.6)
Sexual exposure	108 (9.4)
Tattooing	79 (6.9)
Body piercing	22 (1.9)
Hemodialysis	4 (0.3)
Vertical transmission	4 (0.3)
Unknown	136 (11.9)
Co-infection with HIV	49 (4.3)
Cirrhosis status [‡] , n (%)	
Yes	159 (22.6)
No	543 (77.4)
Treatment duration [#] , n (%)	
12-weeks	789 (73.9)
24-weeks	279 (26.1)
Added ribavirin	10 (1.4)

[†]: Sex was missing for one patient. [‡]Cirrhosis status available for 702 patients; 441 patients had missing cirrhosis data. [#]Treatment duration data available for 1 068 patients; 75 patients contained missing data. IQR: interquartile range.

3.2. Treatment outcomes

Treatment status and virological testing were recorded as separate programme fields and were not mutually exclusive. Of 1 143 initiators, 863 (75.5%) were coded as treatment-completed, 42

(3.7%) as incomplete, 184 (16.1%) as still receiving treatment, 45 (3.9%) as awaiting SVR testing, and 9 (0.8%) had missing treatment status. Among the 504 patients with a recorded SVR result, 484 were coded as completed, 2 as incomplete, 12 as still on treatment, 3 as awaiting testing, and 3 had missing treatment status. Tested patients were slightly older (median 47 *vs.* 46 years; $P=0.009$) (Supplementary Table 2). This discordance probably reflects delayed or incomplete registry updating and prevents construction of a strictly mutually exclusive clinical cascade from the available fields (Supplementary Table 3).

Post-treatment virological testing was available for 504/1 143 patients (44.1%). Among these, 469/504 achieved SVR12 (93.1%) and 35/504 had detectable virus at follow-up (6.9%). The crude extreme bounds for cure among all 1 143 initiators range from 41.0% if none of the 639 patients without recorded results achieved SVR12 to 96.9% if all did; these deliberately extreme assumptions illustrate the uncertainty created by incomplete ascertainment and are not estimates of the true programme cure rate. Among 159 patients with cirrhosis, treatment duration was available for 157; 139 (88.5%) received 24 weeks and 18 (11.5%) received 12 weeks. Mortality status was available for 780 patients, among whom nine deaths were recorded (1.2%); mortality was not an effectiveness endpoint and is interpreted cautiously because vital-status data were incomplete (Table 2).

Table 2. Outcomes of patients treated with sofosbuvir/ravidasvir.

Outcomes	n/N	Percentage (%)
Status of treatment		
Completed treatment	863/1 143	75.5
Incomplete treatment	42/1 143	3.7
Still on treatment	184/1 143	16.1
Awaiting SVR test	45/1 143	3.9
Done SVR test	504/1 143	44.1
SVR among those tested	469/504	93.1
Death [*]	9/780	1.2

^{*}Treatment-status and SVR-testing fields may overlap and are not presented as a mutually exclusive cascade. Mortality data were available for 780 patients; data were missing for the remaining patients. SVR: Sustained virological response.

3.3. Factors associated with sustained virological response

Among 504 patients with documented SVR12 results, subgroup-specific response was 336/358 among PWID (93.9%, 95% *CI* 90.9%-95.9%) and 133/146 among non-PWID (91.1%, 95% *CI* 85.4%-94.7%; $P=0.33$). SVR12 was observed in 20/23 patients with HIV co-infection (87.0%, 95% *CI* 67.9%-95.5%) and 449/481 without HIV co-infection (93.3%, 95% *CI* 90.8%-95.2%; $P=0.21$). Among patients with recorded cirrhosis status, SVR12 was 77/84 (91.7%, 95% *CI* 83.8%-95.9%) with cirrhosis and 285/306 (93.1%, 95% *CI* 89.7%-95.5%) without cirrhosis ($P=0.64$). Response was 347/372 (93.3%, 95% *CI* 90.3%-95.4%) after 12 weeks and 113/123

(91.9%, 95% CI 85.7%-95.5%) after 24 weeks ($P=0.69$). These available-case subgroup findings should not be extrapolated to patients without outcome testing (Supplementary Table 4).

Within the tested cohort, HIV co-infection and selected exposure histories were numerically more frequent among patients without SVR12, but confidence intervals were wide and differences were not statistically significant. The small HIV-positive subgroup and absence of antiretroviral regimen, adherence, and drug-interaction data preclude firm conclusions (Table 3).

Table 3. Characteristics of patients treated with sofosbuvir/ravidasvir according to sustained virological response ($n=504$).

Variables	SVR		P-value
	Yes ($n=469$)	No ($n=35$)	
Age, years, median (IQR)	49.0 (38.0-56.0)	48.5 (37.5-59.0)	0.72
Sex [^]			
Male	425 (90.8)	31 (88.6)	0.56
Female	43 (9.2)	4 (11.4)	
Ethnicity			
Malay	378 (80.6)	29 (82.9)	0.74
Non-Malay	91 (19.4)	6 (17.1)	
Risk factor			
People who inject drugs	336 (71.6)	22 (62.9)	0.27
Blood/blood product transfusion	16 (3.4)	3 (8.6)	0.14 [*]
Organ transplant	2 (0.4)	0 (0.0)	>0.99 [*]
Needle stick injury	5 (1.1)	0 (0.0)	>0.99 [*]
Sexual exposure	51 (10.9)	7 (20.0)	0.11 [*]
Tattooing	18 (3.8)	1 (2.9)	>0.99 [*]
Body piercing	5 (1.1)	0 (0.0)	>0.99 [*]
Hemodialysis	2 (0.4)	0 (0.0)	>0.99 [*]
Vertical transmission	3 (0.6)	0 (0.0)	>0.99 [*]
Unknown	59 (12.6)	5 (14.3)	0.79 [*]
Co-infection with HIV	20 (4.3)	3 (8.6)	0.21
Cirrhosis status ($n=390$) [#]			
Yes	77 (21.3)	7 (25.0)	0.64
No	285 (78.7)	21 (75.0)	
Treatment duration ($n=495$) [#]			
12-weeks	347 (75.4)	25 (71.4)	0.60
24-weeks	113 (24.6)	10 (28.6)	
Added ribavirin	4 (1.2)	1 (3.6)	0.34 [*]

[^]: Sex was missing for one patient. Data were expressed as n (%) unless otherwise indicated. ^{*}Fisher's exact test; [#]Within the tested cohort, cirrhosis status was available for 390 patients (114 missing) and treatment duration for 495 patients (9 missing). Percentages are column percentages unless subgroup-specific SVR12 rates are explicitly stated. SVR: Sustained virological response.

Table 4. Exploratory multivariable analysis of failure to achieve SVR12 with sofosbuvir/ravidasvir.

Variables	aOR (95% CI)	Wald statistics (df)	P-value
Blood / blood transfusion exposure	3.00 (0.82, 10.96)	2.748	0.10
HIV co-infection	2.23 (0.62, 7.98)	1.508	0.22
Sexual exposure	2.13 (0.88, 5.15)	2.787	0.10

The final model included three covariates and only 35 failure events; adjusted estimates are exploratory and imprecise. The model demonstrated good fit (Hosmer Lemeshow test: $\chi^2=0.001$; $P=0.975$); model assumptions were met; no significant interactions and multicollinearity problem; model explained between 1.1% (Cox and Snell R^2) and 2.8% (Nagelkerke R^2) of the variance in failure to achieve SVR12. Statistical significance at $P<0.05$; aOR: adjusted odds ratio; CI: confidence interval.

The cohort included 291 hospital patients and 852 patients treated in primary or community clinics, based on facility names recorded in the registry. SVR12 testing was documented for 132/291 hospital patients (45.4%) and 372/852 primary/community clinic patients (43.7%; $P=0.66$). Among tested patients, SVR12 was 122/132 (92.4%, 95% CI 86.6%-95.8%) in hospitals and 347/372 (93.3%, 95% CI 90.3%-95.4%) in primary/community clinics ($P=0.70$). Treatment-completed status was recorded for 203/291 hospital patients (69.8%) and 660/852 primary/community clinic patients (77.5%; $P=0.01$); however, status fields were not mutually exclusive with SVR fields and may reflect differential updating. These findings do not demonstrate causality but show comparable available-case virological response and testing ascertainment across settings (Supplementary Table 5).

The dataset contained 260 treatment initiations before August 2023 and 883 from August 2023 onward. SVR testing was more frequently recorded before August 2023 (181/260, 69.6%) than in the later period (323/883, 36.6%; $P<0.001$), whereas available-case SVR12 was similar: 170/181 (93.9%) before August 2023 and 299/323 (92.6%) from August 2023 onward ($P=0.72$) (Supplementary Table 6). Because the registry does not identify whether earlier patients were trial, early-access, or routine-care participants, this period analysis is descriptive and cannot resolve programme provenance. The principal programme implication is the need to strengthen outcome monitoring through active recall, automatic flags for due and overdue SVR12 tests, transfer-of-care documentation, and facility-level dashboards.

3.4. Multivariable analysis of failure to achieve SVR12

The exploratory multivariable logistic regression included 504 patients and three predictors. Blood or blood-product transfusion exposure (aOR 3.00, 95% CI 0.82-10.96; $P=0.10$), HIV co-infection (aOR 2.23, 95% CI 0.62-7.98; $P=0.22$), and sexual exposure (aOR 2.13, 95% CI 0.88-5.15; $P=0.10$) had adjusted odds ratios above 1, but all confidence intervals were wide and crossed the null. With only 35 failures, the analysis had limited power and should be viewed as descriptive and hypothesis-generating. Non-significance does not establish absence of association (Table 4).

4. Discussion

This registry study observed SVR12 in 469/504 (93.1%) patients with available post-treatment virological testing after SOF/RDV. Comparison of tested and untested patients showed similar distributions of sex, ethnicity, PWID status, HIV co-infection, cirrhosis, treatment duration, and facility type. Thus, selection related to geography or local programme processes remains plausible even though several measured patient characteristics were similar.

Unlike many DAA regimens developed through traditional commercial pathways, SOF/RDV represents a novel paradigm in drug development by prioritising affordability, public health need, and low- and middle-income country accessibility. Its inclusion in the WHO Model List of Essential Medicines underscores its global strategic importance, particularly for countries seeking cost-effective, scalable solutions for hepatitis C elimination. Our findings provide real-world evidence supporting the implementation of access-oriented treatment strategies[13,15,16].

The SVR rate observed in this study is broadly consistent with previously reported clinical trial outcomes. The STORM-C-1 study conducted in Malaysia and Thailand reported SVR rates approaching 97% among patients treated with SOF/RDV, including those with compensated cirrhosis[13]. The slightly lower effectiveness observed in this real-world cohort is expected and likely reflects challenges encountered in routine practice, including variations in treatment adherence, comorbidities, and healthcare access.

These findings are also comparable with real-world outcomes reported for other DAA regimens. Observational studies evaluating various DAA combinations have reported SVR rates ranging from 88% to 95%[8,17], while cohorts including patients with advanced liver disease treated with sofosbuvir-based therapies have demonstrated SVR rates approaching 90%[18]. Collectively, these findings suggest that the effectiveness of SOF/RDV observed in this national programme aligns with global benchmarks for modern DAA therapy.

PWID comprised more than 70% of the cohort. The high proportion of PWID in this cohort reflects the established epidemiology of HCV in Malaysia, where pre-decentralisation studies reported HCV prevalence of approximately 40%-90% among PWID and identified substantial barriers to testing and linkage to care under more centralised service models[19,20]. Among tested patients, 93.9% of PWID and 91.1% of non-PWID achieved SVR12 ($P=0.33$). Importantly, testing availability itself was similar among PWID and non-PWID (43.9% *vs.* 44.5%; $P=0.91$). These results support offering treatment without exclusion based on injecting history, while the registry remains unable to assess reinfection, ongoing injecting, adherence, or harm-reduction engagement. The integration of HCV care into primary care may be particularly relevant for PWID, as recent Malaysian data indicate that primary-

care practitioners frequently encounter patients with substance-use disorders, while experience and training in their management remain variable[21]. Greater clinical exposure, including experience with methadone maintenance therapy, has been associated with more favourable attitudes towards this population.

Among the small number of tested patients with HIV co-infection, 20/23 achieved SVR12. The subgroup was too small for precise inference, and the registry did not capture antiretroviral regimens, adherence, or potential drug-drug interactions[22]. Firm conclusions regarding comparative effectiveness in HIV co-infection are therefore not possible.

A numerically higher odds of failure to achieve SVR12 was also observed among patients with a history of blood transfusion exposure, although this finding was not statistically significant. This observation may reflect longer duration of infection or more advanced liver disease in this subgroup. Larger studies with detailed fibrosis staging may help clarify potential clinical explanations for this association.

Approximately one-quarter of patients with available data in our cohort had cirrhosis. Notably, cirrhosis did not significantly reduce treatment effectiveness, indicating that SOF/RDV remains effective across different stages of liver disease. This observation is consistent with evidence showing that modern pan-genotypic DAA regimens have largely overcome the reduced treatment responses historically observed in cirrhotic patients[23]. In this cohort, most patients with cirrhosis received extended 24-week therapy according to national treatment guidelines, which may have contributed to the favourable outcomes observed.

From a global health perspective, these findings are particularly relevant for low- and middle-income countries, where decentralised and simplified hepatitis C care models are increasingly recognised as necessary to expand access beyond specialist services[20,24]. The present results support primary care-led HCV treatment by aligning with evidence that community and primary care pathways can achieve effective treatment delivery and improve linkage to care in routine practice[20,25]. They also strengthen the case for SOF/RDV as an access-oriented regimen, because the STORM-C-1 trial showed that this combination is effective and well tolerated across diverse patient groups, including those with compensated cirrhosis[13]. This is especially important because ravidasvir has been advanced through a DNDi-led model specifically framed as an alternative pharmaceutical innovation pathway for equitable access in hepatitis C[26].

The Malaysian experience therefore provides real-world support for the broader policy logic behind WHO Essential Medicines inclusion, namely that effective and affordable therapies should be implementable at national scale within routine health systems[26,27]. The finding that cirrhosis did not significantly compromise outcomes is also consistent with prior evidence that decentralised HCV

programmes can retain effectiveness across clinically heterogeneous populations[13,24]. Although post-treatment SVR testing was incomplete, this pattern is common in real-world decentralised programmes because patient mobility, service fragmentation, and laboratory access can limit outcome ascertainment outside trial settings[28,29]. Taken together, these data indicate that DNDi-developed therapies can be feasibly delivered through decentralised primary care systems and can contribute meaningfully to scalable national hepatitis C elimination strategies.

This study has several strengths, including its large national cohort, inclusion of patients treated across both hospital and primary care settings, and high representation of key populations such as PWID. The use of a national registry improves external validity and supports the relevance of the findings to similar healthcare systems. However, several limitations should be acknowledged. A key limitation of this study is that SVR data were available for only 44.1% of the cohort. This incomplete outcome ascertainment may introduce selection or ascertainment bias, as patients who underwent post-treatment testing may differ systematically from those who did not. This reflects real-world programmatic conditions rather than controlled study settings but should be considered when interpreting effectiveness estimates. The cohort spans different implementation phases of SOF/RDV access. Earlier patients included those treated through the early-access programme up to 2021, whereas later patients were managed through routine hospital and health-clinic services; none were trial participants. Restricting the analysis to patients treated from August 2023 onward yielded a similar available-case SVR12 estimate, although post-treatment HCV RNA ascertainment was substantially lower in the later routine-programme period. The registry also lacked detailed information on genotype; therefore, genotype-specific effectiveness could not be assessed. Although genotype 3 predominates in Malaysian studies, those external distributions may not reflect this cohort[13,30]. Fibrosis characterisation was incomplete because cirrhosis status was missing for a substantial proportion of patients and detailed fibrosis measures were not consistently available. Direct adherence measures were also unavailable; treatment-completion status should not be interpreted as equivalent to medication adherence.

Overall, this study provides important real-world evidence supporting the effectiveness of SOF/RDV in a national hepatitis C treatment programme. Beyond clinical effectiveness, the findings highlight the value of therapeutics developed through alternative innovation models that prioritise access, affordability, and scalability. The Malaysian experience demonstrates that a WHO-endorsed, DNDi-developed regimen can be successfully deployed through decentralised healthcare systems, supporting progress toward hepatitis C elimination by 2030.

Conflict of interest statement

The authors declare no conflicts of interest.

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Authors' contributions

JJ and WLC contributed to the study conception and design, definition of intellectual content, literature search, data and statistical analyses, manuscript preparation, editing, and review, and served as guarantors. DH and ZA contributed to the study design, definition of intellectual content, data acquisition, manuscript editing, and manuscript review.

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Supplementary Table 1. Geographic coverage of patients included.

State/Federal Territory	Patients	% cohort	Contributing facilities
Melaka	232	20.3	26
Negeri Sembilan	170	14.9	31
Kedah	128	11.2	18
Sarawak	128	11.2	13
Perak	118	10.3	27
Pahang	94	8.2	32
Selangor	64	5.6	14
Pulau Pinang	50	4.4	7
WP Kuala Lumpur	49	4.3	6
Johor	45	3.9	19
Terengganu	43	3.8	14
Kelantan	15	1.3	7
Sabah	4	0.3	2
WP Putrajaya	2	0.2	1
WP Labuan	1	0.1	1
Total	1143	100.0	218

Supplementary Table 2. Comparison of patients with and without documented SVR12 testing.

Characteristic	No SVR12 result (<i>n</i> =639)	SVR12 result available (<i>n</i> =504)	<i>P</i> -value
Age, median (IQR), years	46 (19)	47 (18)	0.01
Male sex	599/639 (93.7)	456/504 (90.5)	0.07
Malay ethnicity	528/639 (82.6)	407/504 (80.8)	0.46
People who inject drugs	457/639 (71.5)	358/504 (71.0)	0.91
HIV co-infection	26/639 (4.1)	23/504 (4.6)	0.79
Cirrhosis	75/312 (24.0)	84/390 (21.5)	0.49
24-week treatment	156/573 (27.2)	123/495 (24.8)	0.42
Hospital	159/639 (24.9)	132/504 (26.2)	0.66
Primary/community clinic	480/639 (75.1)	372/504 (73.8)	0.66

Percentages use available denominators. The state comparison used the 15 recorded numeric state codes. Facility type was derived from the recorded site name. Significant state-level variation indicates possible geographic or programme-level ascertainment differences.

Supplementary Table 3. Treatment status versus SVR result.

Treatment-status code	<i>N</i>	No SVR result	SVR12	Failure
Missing status	9	6	2	1
Completed	863	379	455	29
Incomplete	42	40	0	2
Still on treatment	184	172	11	1
Awaiting SVR test	45	42	1	2

This table demonstrates that the programme fields are not mutually exclusive or synchronised. It should be presented as a data-quality finding, not forced into a conventional participant flow.

Supplementary Table 4. SVR12 among tested patients by clinical subgroup and treatment setting.

Subgroup	SVR12 (<i>n/N</i>)	SVR12 (%)	95% <i>CI</i>
PWID	336/358	93.9	90.9-95.9
Non-PWID	133/146	91.1	85.4-94.7
HIV-positive	20/23	87.0	67.9-95.5
HIV-negative	449/481	93.3	90.8-95.2
Cirrhosis	77/84	91.7	83.8-95.9
No cirrhosis	285/306	93.1	89.7-95.5
12-week treatment	347/372	93.3	90.3-95.4
24-week treatment	113/123	91.9	85.7-95.5
Hospital	122/132	92.4	86.6-95.8
Primary/community clinic	347/372	93.3	90.3-95.4

Pairwise *P* values: PWID versus non-PWID, 0.33; HIV-positive versus HIV-negative, 0.21; cirrhosis versus no cirrhosis, 0.64; 12 versus 24 weeks, 0.69; hospital versus primary/community clinic, 0.695. Confidence intervals are Wilson intervals.

Supplementary Table 5. Recorded treatment and outcome fields by facility type.

Facility	Hospital (<i>n</i> =291)	Primary/ community clinic (<i>n</i> =852)
Completed	203	660
Incomplete	23	19
Ongoing	47	137
Awaiting	16	29
Status missing	2	7
SVR tested	132	372
SVR12	122	347
Failure	10	25

SVR testing availability did not differ by facility type (*P*=0.66). Completed-treatment coding was more frequent in primary/community clinics when all initiators were compared (*P*=0.01) and among records coded as either completed or incomplete (*P*<0.001). Because treatment-status and SVR fields were not mutually exclusive, these comparisons should be interpreted as registry-field completeness and status patterns rather than a definitive retention cascade.

Supplementary Table 6. Descriptive comparison by treatment initiation period.

Period	August 2023 onward (<i>n</i>=883)	Before August 2023 (<i>n</i>=260)
Primary/ community clinic	667	185
Completed	633	230
SVR tested	323	181
SVR12	299	170
Failure	24	11
SVR12 among tested (95% <i>CI</i>)	92.6% (89.2-95.0)	93.9% (89.4-96.6)

SVR testing availability differed by period ($P<0.001$); available-case SVR12 did not ($P=0.72$). The registry does not identify early-access, or routine-care provenance for the earlier records.