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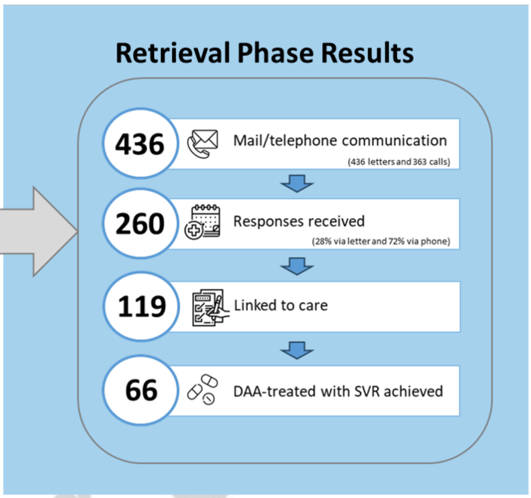
Reconnecting Hepatitis C Patients Lost to Follow-Up: A targeted Strategy

- A substantial fraction of HCV diagnosed patients never link to care.
- **Objective:** To evaluate the effectiveness of a dual-modality retrieval strategy—mailed invitations followed by telephone outreach—in re-linking HCV-diagnosed patients lost to the health system within a defined health area.
- **4816** serologies reviewed (2010-2018), identifying **677** patients lost to follow-up (449 anti-HCV+ y 228 PCR RNA-HCV+)
- **436** personalized letters were sent, followed by telephone contact to nonresponders (several attempts at different times) offering a hepatology consultation.

Active retrieval combining mailed invitations and telephone outreach effectively re-links lost HCV patients to care.



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Reconnecting hepatitis C patients lost to follow-up –A targeted strategy

Short Title: Reconnecting Lost Hepatitis C Patients

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AO, SC, IA, PC, MR, JGS, AG and MA study design and data acquisition. RDH writing original draft. AO and RDH drafted the manuscript. All authors reviewed and approved the final version of the manuscript.

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List of abbreviations:

HCV-RNA: Hepatitis C Virus Ribonucleic Acid

FIB-4: FIB-4 Index of Liver Fibrosis

PCR: Polymerase Chain Reaction

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2)

HCV: Hepatitis C Virus

Conflict of interest

RDH is an employee of PORIB who received fees from Gilead Sciences for consulting services for the development of this work. JGS consulting for Gilead; grants from Gilead; presentations for Abbvie and Gilead. All other authors declare no conflict of interest.

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ABSTRACT

Background: Hepatitis C virus (HCV) infection remains a major contributor to liver-related morbidity and mortality worldwide. Although direct-acting antivirals (DAAs) achieve cure rates exceeding 95%, a substantial fraction of diagnosed patients never link to care.

Objectives: To evaluate the effectiveness of a dual-modality retrieval strategy—mailed invitations followed by telephone outreach—in re-linking HCV-diagnosed patients lost to the health system within a defined health area.

Methods: From 2010 to 2018, 4,816 anti-HCV serologies were reviewed and 677 patients (449 anti-HCV positive; 228 HCV RNA positive) were identified as lost to follow-up. An administrative team sent 436 personalized letters inviting patients to contact a dedicated phone line, then placed up to three calls (n = 363) to nonresponders during varied days and times. Respondents were offered expedited hepatology consultation (diagnostic confirmation, fibrosis staging) and DAA therapy.

Results: Of 436 patients contacted, 260 (60%) responded (28% via letter and 72% via phone). Among these, 119 (47%) enrolled in follow-up (exclusion reasons: 65 declined further care, 51 were already treated/cured elsewhere, 13 had relocated, and 12 were deceased). A total of 119 patients attended hepatology consultation and underwent HCV RNA testing; 66 (55%, 66/119) initiated DAAs and all achieved sustained virological response at 12 weeks post-therapy completion, representing 10% of the original cohort, and 25% of contacts.

Conclusions: Active retrieval combining mailed invitations and telephone outreach effectively re-links lost HCV patients to care, enabling DAA treatment and supporting national elimination goals.

Keywords: Hepatitis C. Missing in the system. System binding.

INTRODUCTION

Hepatitis C virus (HCV) infection inflicts a heavy burden on healthcare systems as a leading cause of cirrhosis, hepatocellular carcinoma, and liver-related mortality(1). Early infection is often asymptomatic, delaying diagnosis until advanced liver damage develops (1,2). The advent of direct-acting antivirals (DAAs) has transformed HCV management, offering cure rates surpassing 95% with minimal adverse effects and preventing progression to cirrhosis, hepatocellular carcinoma, and liver-related mortality (3).

In 2023, the World Health Organization set a global target to eliminate HCV by 2030 (4). Efforts have focused on broadening serological screening and prompt initiation of DAAs (4,5). Nevertheless, between 40% and two-thirds of diagnosed patients are lost to follow-up at some point, most commonly immediately after diagnosis (6,7). These "lost" patients constitute a a known barrier for achieving WHO-defined HVC elimination benchmarks and require proactive, systematic retrieval (7–9).

Our prior work identified 667 lost HCV patients among 4,816 anti-HCV positives (2010–2018), one-third of whom were viremic (10). While various national and international retrieval initiatives have since been launched (6–9,11–13), data remain scarce on optimal outreach methods and treatment outcomes. This study assesses the effectiveness of a dual-modality retrieval protocol—postal invitation followed by telephone outreach—to re-link lost HCV patients to care and achieve cure.

METHODS

Study Design and Population

A retrospective cohort of 677 patients identified as lost to follow-up (449 anti-HCV positive without HCV RNA testing; 228 HCV RNA positive) between 2010 and 2018 was assembled from the hospital's serology database and electronic medical records. Exclusion criteria were death prior to outreach. Both detection and retrieval phases were approved by the Hospital Universitario La Paz Ethics Committee, with the contact protocol specifically authorized.

Retrieval Protocol

Postal Invitation: A personalized letter, crafted in clear, non-alarming language, informed recipients of a possible HCV infection and provided a dedicated phone number for scheduling an expedited hepatology consultation. A one-month response window was allowed.

Telephone Outreach: Patients who did not respond to mail were called—up to three attempts per patient—using all available contact numbers at varied times (morning and afternoon) on different weekdays. Calls reiterated the invitation and offered prompt appointments.

Retrieval occurred in two waves, concluding in March 2023 and October 2023. An administrative coordinator managed addresses, letter dispatches, and calls; clinicians provided follow-up calls for clinical clarifications when needed.

Evaluation and Treatment

Respondents were scheduled for hepatology consultation, where diagnosis was confirmed with full labs for all patients, disease staging performed (including FIB-4 calculation), and DAAs prescribed per standard clinical guidelines. Treatment response was assessed by sustained virological response at 12 weeks post-therapy completion.

RESULTS

Patient Disposition

Of the 677 lost patients, 52 (8%) were deceased, 99 (15%) had emigrated, and 90 (13%) had incomplete or outdated contact information, leaving 436 reachable by mail. Postal invitations elicited 73 responses (17%). Telephone retrieval to the remaining 363 patients achieved contact with 187 (52%) after an average of 2.6 calls each. Overall retrieval success was 60.8% (265/436).

Enrollment and Treatment Outcomes

Among the 260 contacted, 65 (25%) declined follow-up, 51 (20%) had already been treated elsewhere, 13 (5%) had relocated and 12 (5%) were deceased.

Ultimately, 119 (46% of contacts) attended hepatology appointments. Of these, 38 were nonviremic on repeat testing, 15 (12.6%) failed to attend despite booking, and 66 (55%) initiated DAAs and achieved sustained virological response—100% cure rate. These 66 patients represent 10% of the original lost cohort (66/677), 15% of reachable patients (66/436) and 25% of contacted individuals (66/260)

Patient Characteristics

Among those treated (n = 66), 47 (71.2%) were men, with a mean age of 58.8 years at consultation, 19 (28.8%) had normal transaminases and 17 (25.8%) had a FIB-4 score >3.25 indicating advanced liver disease risk.

DISCUSSION

This dual-modality retrieval strategy achieved a 60.8% outreach success rate and re-linked 66 patients to DAA therapy, fully curing them. Telephone outreach proved substantially more effective than postal invitations (72% vs. 28% of contacts), aligning with other similar prior studies carried out in other regions (6–9,11–13) highlighting phone calls as the primary driver of successful retrieval.

The absolute treatment effectiveness of the initial seropositive or viremic group was 10% or 11,5% if we do not consider previously treated patients, migrated, dead or HCV RNA negative, and 25% calculated on the total number of patients contacted. Although these data may be interpreted as modest, compared to the findings of a recent study conducted in Germany, which identified 1,965 patients with chronic hepatitis C, of whom only 100 could be contacted, 10 had started treatment and 5 were pending (15% of those contacted and 1% of the total number lost), the results are representative (14) . In addition, compared with other screening modalities, it underscores the efficiency of database-driven retrieval. Llaneras et al. screened 17,560 emergency patients, of whom 128 were viremic and 45 treated (15), while Gómez et al. screened 2,895 SARS-CoV-2–positive inpatients, finding only three active infections and treating none (16).Our targeted approach yielded a significantly higher treatment rate relative to the size of the screened population.

Despite two outreach waves, the second contributed only one additional enrollee, suggesting diminishing returns and the need for ongoing maintenance of updated contact data. Offering teleconsultations improved access, though 12.6% of booked patients still defaulted—highlighting the need for reinforcing patient education on HCV's risks and DAA benefits. The COVID-19 pandemic likely impeded timely contact and clinic attendance (9).

Preventable losses—mainly outdated contact details—could be mitigated by automated alerts in electronic health records and routine data verification (17,18). Integration with primary care and shared minimal-dataset registries across hospitals would facilitate referrals, especially for patients residing outside the central catchment. Another initiative to continue avoiding losses would be the ProLINK strategy based on the automation of laboratory systems to generate daily lists of patients with previous positive HCV serology results and with serum samples available in microbiology laboratories after having performed an analysis for any reason (19).

Historically, interferon-based regimens limited treatment eligibility; today's DAAs can be administered to nearly all patients, supporting the argument for proactive retrieval. Notably, one-quarter of treated patients had elevated FIB-4 scores, underscoring the critical need to identify and treat advanced-disease cases.

Finally, this strategy required the assistance of an administrative coordinator to manage patient contact, in addition to the involvement of the microbiology and hepatology departments. Although the cost or cost-effectiveness of the recovery strategy was not evaluated, studies show that implementing similar strategies to search for patients lost in the system are cost-effective (9,12).

CONCLUSION

Active retrieval of HCV-positive patients lost to follow-up—combining personalized mailed invitations with systematic telephone outreach—effectively re-links a significant number of individuals to hepatology care and DAA therapy, advancing national HCV elimination targets.

Data Availability

The datasets generated during this study are available from the corresponding author upon reasonable request.

Artificial Intelligence Declaration

The authors confirm that no artificial intelligence or AI-assisted technologies were used in manuscript preparation.

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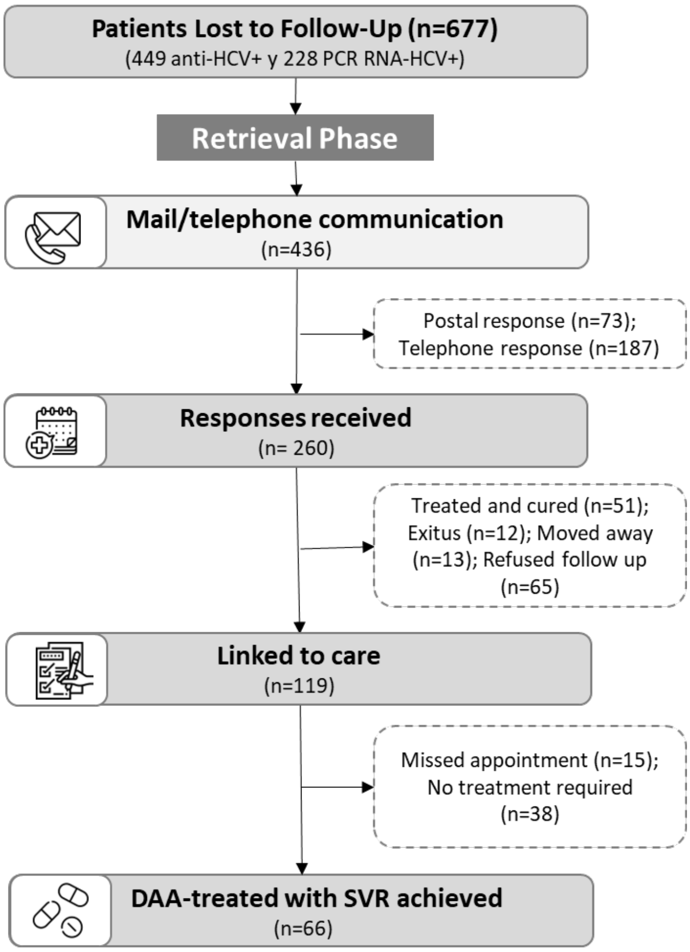
FIGURE



DAA, Direct-acting antivirals; SVR: Sustained virological response

Figure 1. Flow of re-engaged HCV patients through follow-up and treatment pathway