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Article type : Original

Title: A Digital Case-Finding Algorithm for Diagnosed but Untreated Hep C: A Tool for Increasing Linkage to Treatment and Cure

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Key words: hepatitis C virus, direct acting antiviral drug, care coordination, digital, algorithm, fibrosis, phenotyping algorithm

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Abbreviations

Alanine aminotransferase (ALT)
Centers of Disease Control and Prevention (CDC)
Diagnosed-but-untreated (DBU)
Direct acting antiviral drug (DAA)
Electronic medical record (EMR)
Fibrosis-4 (FIB-4) score
Hepatitis C virus (HCV)
Hepatocellular carcinoma (HCC)
International classification of diseases (ICD)
Negative predictive value (NPV)
New York City Department of Health and Mental Health (NYC DOHMH)
Positive predictive value (PPV)
Soft computer corporation (SCC)
Short message service (SMS)
Structured query language (SQL)
Sustained virological response (SVR)
United States Preventive Task Force (USPTF)

Funding: Supported, in part, by a grant from Gilead Sciences and from NIOSH/CDC.

ABSTRACT

Background and Aims: Although chronic hepatitis C virus (HCV) infection increases mortality, thousands of patients remain diagnosed-but-untreated (DBU). We aimed to a) develop a DBU phenotyping algorithm, b) use it to facilitate case finding and linkage to care, and c) identify barriers to successful treatment.

Approach and Results: We developed a phenotyping algorithm using JAVA and SQL and applied it to ~2.5 million EPIC electronic medical records (EMRs) (data entered 1/2003–12/2017). Approximately 72,000 EMRs contained an HCV international classification of diseases code and/or diagnostic test. The algorithm classified 10,614 cases as DBU (HCV RNA-positive and alive). Its positive and negative predictive values were 88% and 97%, respectively, as determined by manual-review of 500 EMRs randomly selected from the ~72,000. Navigators reviewed the charts of 6,187 algorithm-defined DBUs and they attempted to contact potential treatment candidates by phone. By 6/2020, 30% (n=1,862) had completed an HCV-related appointment. Outcomes analysis revealed that DBU patients enrolled in our care coordination program were more likely to complete treatment—72% (n=219) vs. 54% (n=256), p<0.001—and to have a verified sustained virological

response—67% vs. 46%, p<0.001—than other patients. Forty-eight percent (n=2,992) of DBU patients could not be reached by phone, which was a major barrier to engagement. Nearly half of these patients had fibrosis-4 scores ≥2.67, indicating significant fibrosis. Multivariable logistic regression showed that DBUs who could not be contacted were less likely to have private insurance than those who could: 18% vs. 50%, p<0.001. **Conclusions**: The digital DBU case-finding algorithm efficiently identified potential HCV treatment candidates, freeing resources for navigation and coordination. The algorithm is portable and accelerated HCV elimination when incorporated in our comprehensive program.

INTRODUCTION

Hepatitis C virus (HCV) infection remains a major public health threat. Highly effective direct-acting antiviral (DAA) treatments have been available since 2014; however, 1–3 million people in the United States (U.S.) remain infected, and about 50,000 new infections occur every year (1). HCV is the leading cause of hepatocellular carcinoma (HCC)–related death in the U.S. and in many other parts of the world (2-5). HCV is reported to cause about 20,000 deaths annually in the U.S., but the actual death rate could be up to five-fold higher and exceed 80,000 per year (6). The World Health Organization (WHO) and other agencies have set goals to reduce HCV infections and premature deaths (7,8); however, the U.S. appears unlikely to meet its WHO 2030 impact targets (9).

As a first step toward reducing the HCV-related disease burden, public health agencies have issued a series of screening guidelines. Early advisories focused on patients with specific risk factors (4). In 2012, the Centers for Disease Control and Prevention (CDC) expanded screening recommendations to include all baby boomers, i.e., persons born 1945–1965. In early 2020, the CDC and the U.S. Preventive Services Task Force (USPSTF) further expanded guidelines to include nearly all adults (10,11).

To be effective, screening must lead to treatment, but this often fails to occur. According to the New York City Department of Health and Mental Hygiene (NYC DOHMH), only 62% of residents who had a positive test for HCV RNA in 2015 had received HCV treatment by 2019 (12) . A recent study conducted in Bronx, NY, found that 80% of the HCV RNA–positive samples were collected from patients whose medical record already contained a positive HCV RNA test (13), highlighting the large gap between diagnosis and treatment. Similarly, CDC data indicate that 60% of the 2.4 million people with chronic HCV in the U.S. are aware of their positive HCV status, but remain untreated (1). Sizable populations of diagnosed-but-untreated (DBU) HCV-infected persons have also been described in Europe, Asia, Central and South America, and Africa (5). These findings establish that millions of DBU patients exist and require case finding and outreach (3-5,14,15).

Electronic medical record (EMR) usage has expanded in recent years (16), providing an opportunity to systematically identify DBU HCV patients on a large scale. We previously developed and used phenotyping algorithms to subtype non-alcoholic fatty liver disease and to identify patients with HCC (17). Phenotyping algorithms are widely used in research to identify patients with specific diseases (17-19) and they have the

potential to improve healthcare delivery. The PheKB website provides an extensive repository of phenotyping algorithms; however, it does not have an algorithm for HCV (20), revealing an unmet need.

To facilitate HCV clinical case finding, we developed a high-quality phenotyping algorithm to automatically identify DBU HCV RNA-positive patients based on EMR data in EPIC, the most-widely used platform in the U.S. (21). The algorithm included elements previously used by the NYC DOHMH (22) and additional structured and unstructured data fields. Medical record numbers of algorithm-defined HCV treatment candidates were given to patient navigators who manually reviewed charts and reached out to treatment candidates, offering care coordination. We compared outcomes of patients enrolled in our care coordination program to patients who were not enrolled and found a positive association with enrollment. Our project demonstrates the usefulness of computer-assisted HCV case finding. To help others eliminate HCV, we posted the phenotyping algorithm on GitHub.

METHODS

Project Description and Setting

This project was carried out to enhance the HCV elimination program in the Mount Sinai healthcare network. This network provides clinical care at ten main sites in the greater New York metropolitan area and serves over 7 million children and adults. Our program assisted patients receiving liver care at six of these sites (Fig. 1). A computer algorithm was developed to identify living, DBU HCV-infected adults. Four hundred and seventy-five patients were enrolled in a nested observational study that evaluated clinical outcomes, including the rate of HCV treatment initiation. All study procedures were conducted in compliance with the Helsinki accord; the project was approved by the Institutional Review Board of the Icahn School of Medicine at Mount Sinai.

Outcomes of Interest

The four outcomes of interest are: 1) the positive and negative predictive values (PPV and NPV, respectively) of the phenotyping algorithm, 2) the number (percent) of algorithm-defined HCV DBU patients who started HCV treatment before 6/2020, 3) factors associated with failure to initiate treatment, 4) treatment outcomes of patients enrolled in the program's care coordination program.

The Digital HCV Case-Finding Algorithm

The digital phenotyping algorithm uses Java and structured query language (SQL). It was applied to data entered or migrated into our main EMR, EPIC, from 1/2003–12/2017. The algorithm recognizes all FDA-approved HCV RNA tests recorded in Mount Sinai's EPIC and/or Soft Computer Corporation (SCC) clinical laboratory records, all drugs used to treat HCV (Supplemental Table 1), and all ICD9/10 codes for HCV infection (B17.10, B17.11, B18.2, B19.10, B19.20, B19.21, K73.2, K74.60, K74.69, R76.8, Z86.19). It uses natural language processing (NLP), accesses the Mount Sinai death registry, calculates fibrosis-4 (FIB-4) scores (23) and infers HCV status using serial alanine aminotransferase (ALT) measurements.

The algorithm selected adults ≥18 years of age with an HCV-related entry (HCV-specific ICD-9 or -10 code and/or a clinical laboratory test for HCV antibody and/or RNA). It then selected living DBU HCV-infected patients, defined as either patients whose most recent HCV RNA test was positive and who had no prescription for an HCV medication, and no record of being deceased, or patients with a positive HCV RNA test dated after the last prescription for an HCV medication. Because DAAs are highly effective and many patients do not obtain HCV RNA testing after the end of treatment (24-27), the algorithm classified patients who had a prescription for HCV treatment as HCV RNA-negative (cured) unless the EMR had a positive post-treatment RNA test. Of those classified as HCV RNA-positive, it also identified DBU patients at high risk for rapid disease progression, defined as FIB-4 score ≥ 2.67, HIV-positive, and/or diabetic; and it distinguished between patients whose most recent HCV RNA test was before and after 1/2014. Patients with ALT ≥40 IU were considered to have transaminitis, in accordance with the ALT upper limit of normal defined by others (35). The algorithm also identified subgroups of patients, such as patients who previously achieved a sustained virological response (SVR) to HCV treatment and patients with positive tests for HCV antibodies and no indication that follow-up HCV RNA testing was performed.

Because HCV RNA tests are performed less frequently than ALT measurements, we classified patients as "likely to have an ongoing HCV infection" based on ALT measurements recorded before and after the date of the last recorded HCV RNA test. Based on our data showing that ALT values decreased by ≥50% in >80% of patients who achieved an SVR, we considered patients to be chronically infected if their last HCV RNA test was positive and ALT values after that test were within 50% of the ALT values obtained prior to the positive HCV RNA test. This method was only applied to patients who had ALT measurements at least 30 days before the RNA test and at least 30 days after the RNA test. If not, they were considered still infected by default.

Evaluation of the Case-Finding Algorithm's Performance by Blinded Chart Review

A random number generator was used to select EMRs of 500 patients from among the ~72,000 EMRs with an HCV-related entry. Four trained patient navigators each reviewed 250 EMRs (each record was reviewed twice, with conflicts adjudicated). HCV infection and treatment status were determined by laboratory values and/or physician documentation. Manual review was considered the gold standard. Current HCV infection was indicated by one or more of the following: a) HCV RNA recorded in the most recent laboratory data; b) HCV RNA documented in a physician note or media section, with no record of treatment; or c) HCV infection documented in a physician note. Conversely, cured infection was indicated by a record of an SVR, defined as a negative HCV RNA test after the end of treatment or HCV cure documented in a physician note. Patients were classified as either a) being alive and having evidence of current HCV infection, or b) not having evidence of current HCV infection and/or not being alive. The algorithm's performance was evaluated by comparing its classifications to the gold standard, expressed as percentages. The algorithm's precision (PPV) equaled the number of living HCV RNA-positive patients identified by manual review divided by the number the algorithm assigned to this category. The NPV equaled the true negatives (i.e. the number of living patients whose last HCV RNA test was negative, plus the number of patients with no HCV RNA test, plus the number of deceased patients according to manual review), divided by the number the algorithm classified as negative (i.e., patients

who were deceased and/or had no record of a positive HCV RNA test or evidence that the final test was negative). Specificity equaled the patients (living or deceased) who were no longer eligible for treatment who were correctly classified by the algorithm divided by all patients no longer eligible for treatment as determined by chart review. Recall (sensitivity) equaled the HCV RNA-positive patients correctly classified by the algorithm divided by the HCV RNA-positive patients identified by chart review. Accuracy equaled the percentage of cases the algorithm classified correctly.

Patient Navigation and Care Coordination

Navigators reviewed the EMRs of 6,187 algorithm-defined DBUs; starting with patients with HCV RNA tests obtained after 2014 and those with risk factors for liver disease progression (HIV infection and/or diabetes). They attempted to phone treatment candidates, dialing all phone numbers at least three times at varying hours of the day on different days of the week over several weeks, leaving voicemail messages when possible. Navigators did not send short message service (SMS) communications because recipients may be charged for them. Letters were sent to 619 patients at their last documented address in the EMR after three unsuccessful phoning attempts; however, the yield was too low, and mailing was discontinued. Navigators offered assistance scheduling an initial appointment with an HCV specialist, using procedures previously shown to be effective (28-30), and offered linkage to the project's care coordinators who served six sites (Fig 1). Navigators also conducted one round of follow-up outreach to likely treatment candidates who were lost to care after they initially engaged at Mount Sinai sites not served by the project's care coordinators. All patients enrolled in care coordination had at least one in-person or remote session with a coordinator. Coordinators identified barriers that might impede initiating or completing treatment via a structured psychosocial assessment and open conversations. They tailored a care plan and provided services through SVR12. Services included scheduling appointments; providing pharmacy and insurance coordination; referring to mental health, substance use disorder, and social services; and contacting patients at weekly/biweekly intervals to check in, provide treatment adherence and alcohol counseling, as well as tailored health education. Coordinators also conferenced weekly with providers and reported patients' complaints of side effects or difficulties obtaining and/or taking medication. Coordinators continue to contact patients who have not completed treatment twice yearly to re-engage them.

Data Analysis

Weighted one-sample chi-square tests were used to compare the 6,187 patients whose HCV status has been determined to the entire population of algorithm-defined DBU patients. Bivariate and multivariable logistic regressions were used to identify barriers to starting HCV treatment. Two-sample t-tests were performed to assess differences between patients enrolled or not enrolled in care coordination for continuous variables, chi-square for categorical, using IBM SPSS Statistics 25 software (31).

RESULTS

Design and Evaluation of the HCV Case-Finding Algorithm

A phenotyping algorithm was developed to identify DBU HCV-infected patients according to structured and unstructured data entered into EPIC EMRs between 1/2003 and 12/2017. It also identified patients who had no record of HCV screening and patients who tested positive for HCV antibodies but had no record of HCV RNA testing (Fig. 2). Of the ~2.5 million EMRs analyzed, the algorithm classified ~72,000 EMRs as having at least one HCV-related entry (an ICD-9/10 code for HCV and/or a clinical laboratory test result for HCV antibody or RNA) and of these, it classified 10,614 as DBU) (Fig. 3). Living patients whose last recorded HCV RNA test was positive were considered DBU unless they had a prescription for an HCV medication and no subsequent positive test for HCV RNA. Most algorithm-defined DBU patients had no record of HCV treatment (Fig. 2, orange box, “Chronically Infected”), but some failed treatment or became re-infected (Fig. 2, orange box, “”Positive RNA”).

To evaluate the algorithm’s performance, 500 EMRs were randomly selected from the group of ~72,000 EMRs with an HCV-related entry. According to manual review, the 500 EMRs included 85 living HCV RNA-positive patients and 425 patients who were deceased and/or not HCV RNA-positive. The algorithm identified 84 EMRs as representing living HCV RNA-positive patients (DBUs); 74 were confirmed by manual review and 10 were HCV RNA-negative at last follow-up according to chart notes (Fig. 4). All 10 misclassifications resulted from entries stored in the media section in a format the algorithm could not interpret. The algorithm’s precision (PPV) was 88% (74/84) and its sensitivity was 87% (74/85). The algorithm identified 416 patients as not being DBU HCV-infected patients. According to the algorithm, these patients were either deceased, their final HCV RNA test was negative, they had a prescription for an HCV medication that was not followed by a positive HCV RNA test, or they did not have any HCV RNA test result. Manual review confirmed the algorithm’s classification in 405 of 416 cases. The algorithm misclassified 11 HCV RNA positive patients as RNA-negative. The most common causes of misclassification were chart notes that used idiosyncratic language to report HCV RNA-positive test results or data from scanned documents stored in the EMR’s media section. The algorithm’s NPV was 97% (405/416); its specificity was 98% (405/415); and its overall accuracy was 96% (percentage of correctly classified cases; [74+405]/500). These results show that the digital phenotyping algorithm is a highly effective case-finding tool that can be used to reduce the human resources needed to find DBU patients based on existing EMR data.

Characteristics of the DBU HCV Treatment Candidates

The mean age of the 10,614 algorithm-defined DBU HCV-infected patients was 60 years [standard deviation (SD) of 12.6] (Table 1). Many had advanced liver disease: 50% had a FIB-4 score ≥2.67, indicating that at least half of the population had significant fibrosis (32-34). By 6/2020, navigators had manually reviewed 6,187 charts and attempted to contact potential treatment candidates by phone. Weighted chi-square tests showed that these 6,187 patients are generally similar to the total group in terms of the percentages of patients in various subgroups with FIB-4 score ≥2.67 and ALT ≥40 IU/mL (Table 1). Efforts are underway to contact the remaining 4,427 patients (Fig. 3). The algorithm inferred the HCV RNA status of these patients, as described in

Methods. Most (77%) are likely to remain HCV-infected, as ALT measurements had not decreased by ≥50% since the last available test for HCV RNA. These patients average 63 years in age; 47% have a FIB-4 score ≥2.67; and 51% have ALT values ≥40 IU/mL, indicating fibrosis and transaminitis.

The Greatest Barrier: Our Inability to Contact DBU HCV Patients by Phone or Mail

Among the 6,187 algorithm-defined DBU patients, 48% (N=2,992) could not be reached by phone (Fig. 3). Compared to the others, the patients who could not be reached by phone were younger (mean age 56 vs. 61 years), less likely to have a FIB-4 score ≥2.67 (46% vs 59%), and less likely to have private insurance (18% vs 50%), p<0.001 for all comparisons. As determined by multivariable logistic regression, the factors associated with our inability to contact patients include: no record of an appointment with a liver specialist (OR, 2.5), HIV infection (OR, 2.08), HIV and diabetes (OR, 1.79), sex recorded as other/unknown (OR, 1.54), Medicaid as the only type of insurance (OR, 1.49), homelessness (OR, 1.31), and sex recorded as male (OR,1.25) (Table 2). Letters were sent to 619 of these patients, but only one engaged in care as a result, indicating that mailing is not effective in this setting. The great majority (83%) of the patients who could not be contacted by phone are likely to remain HCV-infected, as they had no record of HCV treatment and ALT had not decreased by 50% or more.

Entry into the HCV Treatment Pipeline

By 6/2020, 31% of the 6,187 algorithm-defined DBU patients had kept at least one HCV-specific appointment (N=1,862) at our institution or elsewhere, or expressed an interest in HCV treatment (N=39) (Fig. 3). We analyzed outcomes in 475 patients who expressed an interest in HCV care and had not started treatment prior to 12/2017. By 4/2020, 325 of these patients had initiated HCV treatment. Logistic regression analysis revealed that the odds of starting treatment were inversely related to the number of reasons for treatment delay [p<0.001; OR, 0.48 per cause of delay; 95% confidence interval (CI): 0.38, 0.61], (Table 3). Thirty percent of the 325 patients who started treatment had a positive test for HCV RNA that had been in their EMR >12 months, highlighting the need for pro-active programs to identify DBU patients with chronic HCV infection and to provide them support services.

Among the 475 patients, 219 enrolled in our care coordination program. About 30% of them requested or accepted referrals to support services such as primary care, mental health care, transportation, detoxification/rehabilitation, and housing management. We compared outcomes between these 219 patients and 256 patients who were not enrolled in our program during the same period. The two groups were similar in baseline FIB-4 scores and, among those who started treatment, in the time from initial evaluation to treatment start. However, a higher percentage of enrolled patients started treatment (81% vs 58%, p < 0.001), completed treatment (72% vs 54%, p < 0.001), and achieved an SVR, defined as a negative HCV RNA test ≥ four weeks after the end of treatment (67% vs 46%, p<0.001) (Table 3). The reasons for not starting and not completing treatment are presented in Supplemental Tables 2 and 3, respectively.

DISCUSSION

We built an algorithm that uses two standard programming languages, Java and SQL, to identify HCV treatment candidates. It is a useful tool for finding DBU patients with chronic HCV infection and can be widely applied to EPIC EMRs. Based on the measured sensitivity, the algorithm identified approximately 87% of all living adults whose EMRs contained a most recent HCV RNA test that was positive. The algorithm reduced the number of charts requiring manual chart review from ~2.5 million to 10,614, a 235-fold enrichment, freeing resources for outreach and care coordination. Additional features include its ability to risk-stratify patients based on factors such as persistent ALT elevations, the FIB-4 score, and medical history, including diabetes and HIV infection. The demographics of the DBU patients (mean age 60 years, 60% male) are consistent with U.S. national data showing that individuals born between 1945 and 1969 account for 72% of chronic HCV infections, and that chronic infection is higher in men (36,37). It is concerning that 50% of the DBU patients had a FIB-4 score ≥2.67, indicating many had advanced fibrosis/cirrhosis and are in urgent need of HCV treatment and evaluation for liver cancer surveillance (32-34).Our study revealed the need for additional innovative strategies for engaging DBU patients in HCV care. Only about 30% received treatment according to our data. The greatest barrier to linking DBU patients to care was our inability to reach them by phone. The NYC DOHMH reported similar findings. Their navigators were only able to reach 42% of the 1,096 patients with viral hepatitis they attempted to contact in 2019 (12). We are currently developing new IT-based approaches to contact individuals via direct, secure electronic messages in EPIC (MyChart) and to deliver messages to providers with whom these patients are actively engaged.

Fragmentation of the U.S. healthcare system is an additional barrier to HCV elimination. Information technology (IT) can reduce this barrier by using surrogate data (i.e., persistence of ALT elevations in patients with prior positive tests for HCV RNA) to bridge gaps in EMRs that may arise because patients obtain care in multiple networks. We created a subprogram that analyzes ALT measurements, which are obtained far more frequently, to manage the frequent absence of the recent HCV RNA data. Our DBU case-finding algorithm can be adapted for use on other EMRs, providing a tool that can be bring a degree of uniformity to HCV case finding.

Our study underscores the importance of active case management. Thirty percent of 325 patients who started treatment in our nested study had a positive HCV RNA test result that had been in their medical record for over 12 months. Many DBU patients had competing medical, financial, psychosocial, and life priorities (such as caregiver obligations) that we attempted to address by providing comprehensive services, including referrals to social services and help coordinating transportation and insurance. Our findings emphasize the value of navigation and care coordination for HCV treatment, as we (14,28,38) and others (39-42) have demonstrated, and has been demonstrated in other settings (43,44). After starting treatment, patients face challenges to completing it that need to be addressed (24,45).

As illustrated in Fig. 5, a multifaceted approach is needed to eliminate HCV within a network like ours. Complementary initiatives are needed: a) to contact and engage DBU patients who are identified based on historical data in the EMR, b) to provide a user-friendly digital portal for receiving referrals, and c) to identify previously undiagnosed patients through screening. The CDC's recommendation to screen nearly all adults was released just as the COVID-19 pandemic was devastating communities around the globe, which likely

reduced awareness of the new guidelines. We examined screening data collected during the final quarter of 2020 at primary care clinics at Mount Sinai Hospital. Only 13% of previously unscreened adults who attended at least one appointment received HCV screening (unpublished data). The DOHMH estimates that 40% of HCV cases remain undiagnosed in New York City (12), consistent with CDC data indicating that 39% of infections have not been diagnosed (1). Automated best practice alerts, smart order sets, and health maintenance messages can promote HCV screening (46-49). We are currently building HCV-related directives into our EMR.

Strengths and Limitations: A main strength of our study is the portability of the algorithm. The Mount Sinai EPIC EMR includes data from multiple campuses and serves a wide variety of providers who use the EMR in different ways. Data were sourced from SCC software embedded within the EMR, which further diversified the data formats the algorithm is designed to accommodate. As a result, the phenotyping algorithm can be readily adapted for other EPIC EMRs and potentially even non-EPIC EMRs. Moreover, the algorithm can be modified to parse in-coming data; we are currently using it to identify newly diagnosed patients. In addition, the algorithm can be used to identify patients stalled at various points in the HCV care pipeline, including patients who have not received HCV screening and patients with positive HCV antibody tests and no confirmatory HCV RNA testing. We deposited our algorithm on GitHub (50) so that it can be accessed by other healthcare groups.

Regarding weaknesses, applying the algorithm is low-cost and scalable, but it does require the involvement of informatics experts. That said, nearly all U.S.-based healthcare practices now use EMRs and have IT personnel, making application feasible, and benefiting health systems that are accountable care organizations with full responsibility for the care of their patients. Incomplete medical records were a limitation of this real-world study, as was the inability of navigators to contact many of the treatment candidates by phone. Automated methods to update phone numbers (e.g., when patients make new appointments) may be helpful.

In conclusion, the digital case-finding algorithm is an efficient tool for identifying patients who are HCV RNA-positive and likely treatment candidates and for stratifying based on risk factors for more successful linkage. Once the algorithm is written for a specific EMR, its use is essentially free of cost. Prototypic HCV micro-elimination projects such as this one are especially important in the U.S. given the lack of a robust, federally funded plan for the country (3,37). The approach used here to support an HCV elimination program can be applied to other diseases, such as HBV and metabolic fatty liver disease.

Acknowledgements:
Many thanks to our care coordination and navigation team members, Priscilla Agyeman, Lidia Funes, Daryin Hummel, De Shaunda Page-Cook, Glyn Singleton and Colleen Stapleton.

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Table 1. Characteristics of 10,614 algorithm-defined HCV treatment candidates compared to characteristic of 6,187 algorithm-defined HCV treatment candidates whose EMRs were manually reviewed

	Total 10,614						Reviewed 6,187						P-value**	
Group	**n**	**Age Mean (SD)**	**FIB-4* ≥ 2.67 n (%)**	**FIB-4* Median (IQR)**	**ALT (IU/L) Median (IQR)**	**ALT ≥ 40 n (%)**	**n**	**Age Mean (SD)**	**FIB-4* ≥ 2.67 n (%)**	**FIB-4* Median (IQR)**	**ALT (IU/L) Median (IQR)**	**ALT ≥ 40 (IU/L) n (%)**	**P FIB-4 ≥ 2.67**	**P ALT ≥ 40**
Total		60.2 (12.6)	4,196 (50%)	2.6 (1.5, 6.1)	45 (28, 75)	5,484 (57%)		58.9 (12.8)	2,212 (50%)	2.7 (1.5, 6.1)	44 (27, 73)	3,303 (57%)	0.78	0.27
Men	6,667	59.5 (12.1)	2,628 (51%)	2.7 (1.5, 6.4)	48 (30, 80)	3,985 (61%)	4,144	58.3 (12.2)	1,433 (50%)	2.7 (1.5, 6.2)	47 (30, 77)	2,484 (61%)	0.38	0.95
Women	3,050	61.5 (13.5)	1,223 (49%)	2.6 (1.4, 5.9)	40 (25, 67)	1,496 (50%)	1,780	60.5 (14.0)	649 (49%)	2.5 (1.4, 5.8)	37 (23, 62)	819 (47%)	0.8	**0.01**
Birth cohort														
Before 1945	1,238	79.7 (5.8)	795 (73%)	4.4 (2.6, 8.9)	42 (25, 69)	652 (53%)	649	79.7 (6.0)	381 (73%)	4.4 (2.5, 8.8)	38 (22, 66)	313 (49%)	0.94	**0.02**
1945-1965	6,515	62.1 (5.3)	2,810 (52%)	2.8 (1.7, 6.5)	44 (27, 74)	3,610 (56%)	3,905	61.8 (5.3)	1,542 (52%)	2.83 (1.7, 6.4)	43 (27, 70)	2,109 (55%)	0.90	0.07
1966-1986	1,759	43.1 (6.0)	246 (24%)	1.2 (0.8, 2.3)	50 (30, 83)	1,080 (63%)	1,207	42.9 (6.1)	157 (24%)	1.3 (0.9, 2.5)	51 (31, 83)	766 (65%)	0.27	0.18
1987-2000	207	26.8 (2.8)	2 (3%)	0.6 (0.4, 0.7)	61.5 (36, 119)	140 (70%)	161	26.7 (2.8)	2 (3%)	0.6 (0.4, 0.9)	66 (38, 127)	113 (73%)	0.55	0.43
Risk Factors														

HIV	1,495	56.7 (10.3)	572 (47%)	2.42 (1.5, 5.0)	42 (26, 69)	792 (53%)	1,226	56.7 (10.4)	481 (47%)	2.5 (1.5, 5.2)	43 (26, 69)	659 (54%)	0.34	0.57
Diabetes	1,194	65.0 (9.3)	561 (50%)	2.7 (1.6, 5.7)	38 (22, 63)	558 (47%)	751	65.1 (9.3)	335 (50%)	2.6 (1.6, 5.6)	37 (22, 63)	346 (47%)	0.39	0.77
HIV/Diabetes	256	61.1 (7.7)	111 (51%)	2.6 (1.8, 5.2)	37 (21.5, 62)	120 (47%)	225	60.8 (7.2)	99 (51%)	2.7 (1.8, 5.2)	38 (223, 61)	106 (47%)	0.79	0.94
Insurance														
Medicaid & Medicare	206	65.2 (9.3)	120 (58%)	3.5 (1.9, 8.0)	46 (26, 65)	111 (54%)	107	64.5 (8.1)	65 (61%)	3.8 (2.0, 8.3)	46 (28.5, 66.5)	60 (56%)	0.48	0.58
Medicare	1,457	69.1 (10.8)	836 (57%)	3.6 (1.9, 7.6)	37 (22, 64)	645 (44%)	898	68.3 (10.9)	515 (57%)	3.6 (1.9, 7.7)	37 (21, 62)	395 (44%)	0.56	0.06
Medicaid	3,174	58.6 (10.8)	1,345 (42%)	2.4 (1.4, 5.5)	43 (26, 72)	1,518 (48%)	1,739	57.6 (11.0)	752 (43%)	2.5 (1.5, 5.8)	43 (26, 70)	875 (50%)	0.28	**<0.001**
Private and/or Medicaid and Medicare	5,540	58.6 (12.9)	1,826 (33%)	2.6 (1.4, 6.0)	48 (30, 82)	3,087 (56%)	3,307	57.1 (13.1)	844 (26%)	2.5 (1.4, 5.7)	47 (30, 79)	1893 (57%)	0.14	**<0.001**
Uninsured/ Other	238	55.8 (12.4)	69 (29%)	1.6 (1.1, 4.4)	49 (34, 73)	123 (52%)	136	54.9 (12.4)	36 (26%)	1.6 (1.0, 4.7)	47 (32, 71)	80 (59%)	0.92	0.18

*The FIB-4 score was calculated using the last laboratory data collected prior to 12/2017

**Comparing Reviewed vs Total Population Proportions with weighted One-Sample Chi-square test.

Table 2: Bivariate and multivariable analysis of factors associated with our inability to reach patients by phone								
			Bivariate logistic regression			**Multivariable model***		
	Reached n=3185 n(%)/ M(SD)	**Unreachable n=3002 n(%)/ M(SD)**	**P value**	**OR**	**CI**	**P value**	**OR**	**CI**
Insurance			<0.001			<0.001		
Private and/or Medicaid and Medicare (ref)	718 (30.6%)	387 (23.6%)						
Medicaid	880 (37.6%)	859 (52.3%)	<0.001	1.8	(1.55, 2.11)	<0.001	1.49	(1.25, 1.78)
Medicaid & Medicare	70 (3%)	37 (2.3%)	0.93	0..98	(0.65, 1.49)	0.96	0.99	
Medicare	613 (26.2%)	285 (17.4%)	0.12	0.86	(0.72, 1.04)	0.57	0.94	
Uninsured/Other	62 (2.6%)	74 (4.5%)	<0.001	2.21	(1.55, 3.17)	0.39	1.22	
Sex			<0.001			0.006		
Females (ref)	1,022 (32%)	758 (25%)						
Males	2,034 (64%)	2,110 (70%)	<0.001	1.4	(1.25, 1.56)	0.007	1.25	(1.06, 1.47)
Other/Unknown	129 (4%)	134 (5%)	0.11	1.4	(1.08, 1.82)	0.02	1.54	(1.08, 2.21)
HIV/Diabetes			<0.001			<0.001		
none (ref)	1986 (62%)	1,999 (67%)						
HIV	558 (17.5%)	668 (22%)	0.008	1.2	(1.05, 1.4)	<0.001	2.08	(1.74, 2.48)
Diabetes	531 (17%)	220 (7%)	0.001	0.41	(0.35, 0.49)	0.006	0.735	(0.59, 0.92)
Both	110 (3.5%)	115 (4%)	0.78	1.04	(0.79, 1.36)	<0.001	1.79	(1.29, 2.49)
Homelessness	484 (15%)	552 (18%)	0.001	1.26	(1.10, 1.44)	0.007	1.31	(1.08, 1.59)
Intravenous drug use	1,750 (55%)	1,318 (44%)	<0.001	0.64	(0.58, 0.71)	0.11	0.87	
FIB- 4 >2.67	1,387 (59%)	825 (46%)	<0.001	0.75	(0.67, 0.85)	0.21	0.91	

FIB- 4	5.1 (5.4)	4.3 (4.7)	<0.001	0.97	(0.96, 0.98)			
ALT	63.2 (65.6)	65.6 (81.8)	0.4	1.0	(1.0, 1.001)			
Age	61.3 (12.2)	56.5 (13.0)	<0.001	0.97	(0.96, 0.97)			
Number of phone numbers on file	2.4 (1.8)	2.3 (1.6)	0.001	0.95	(0.92,0.98)	0.05	0.96	
Number of addresses on file	1.8 (1.3)	1.9 (1.4)	<0.001	1.07	(1.03, 1.11)	0.01	1.08	(1.02, 1.15)
No Liver care at Sinai	697 (22%)	1,620 (54%)	<0.001	4.2	(3.75, 4.67)	<0.001	2.5	(2.18, 3.05)
Abbreviations: ALT= Alanine transaminase; OR = Odds Ratio; CI = Confidence Interval								

Table 3: Analysis of 475 patients who were deemed eligible for HCV treatment as of 12/2017			
	Enrolled in our care coordination program (n=219)	Not enrolled in our care coordination program (n=256)	**P-Value***
FIB-4 at baseline Median (IQR)	2.5 (1.5, 4.7)	2.1 (1.3, 3.6)	0.76
Time from HCV evaluation to treatment initiation median (IQR) days	52 (30.8, 100)	71 (40.5, 147.8)	0.58
Number (percentage) initiating treatment	177 (81%)	148 (58%)	**<0.001**
Number (percentage)completing treatment	157 (72%)	137 (54%)	**<0.001**
Number (percentage) achieving SVR 4 or later	146 (66%)	118 (46%)	**<0.001**
*Two sample T-test for continuous variables and chi-square for categorical variable Abbreviations: Interquartile range (IQR)			

Figure 1. Mount Sinai Liver Disease HCV Services Map

Figure 2. Logic of the HCV digital case-finding algorithm

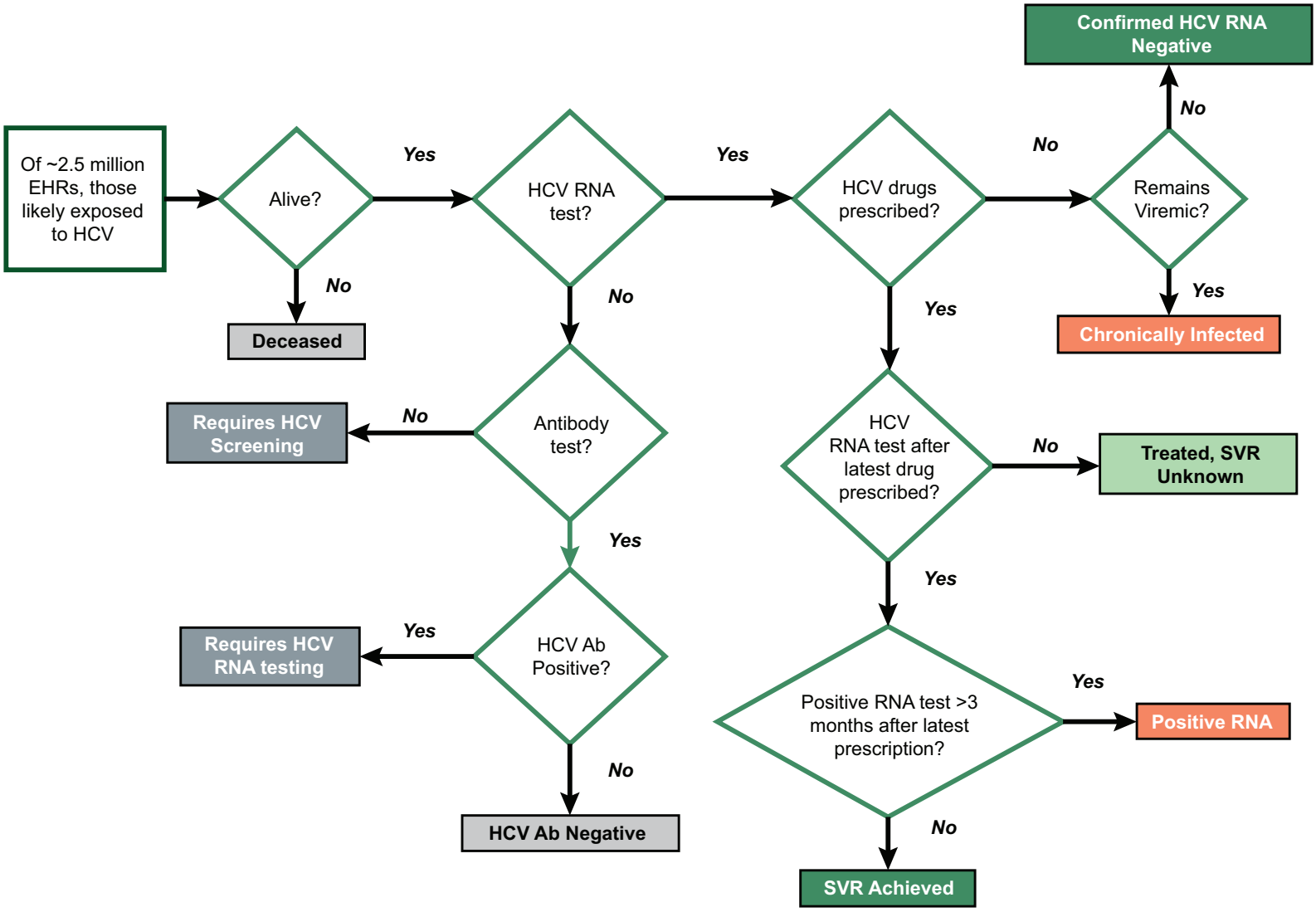

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Figure 3. Flow chart showing the HCV status of ~2.5 million adults with data entered into the Mount Sinai Network EMR 2003-2017.

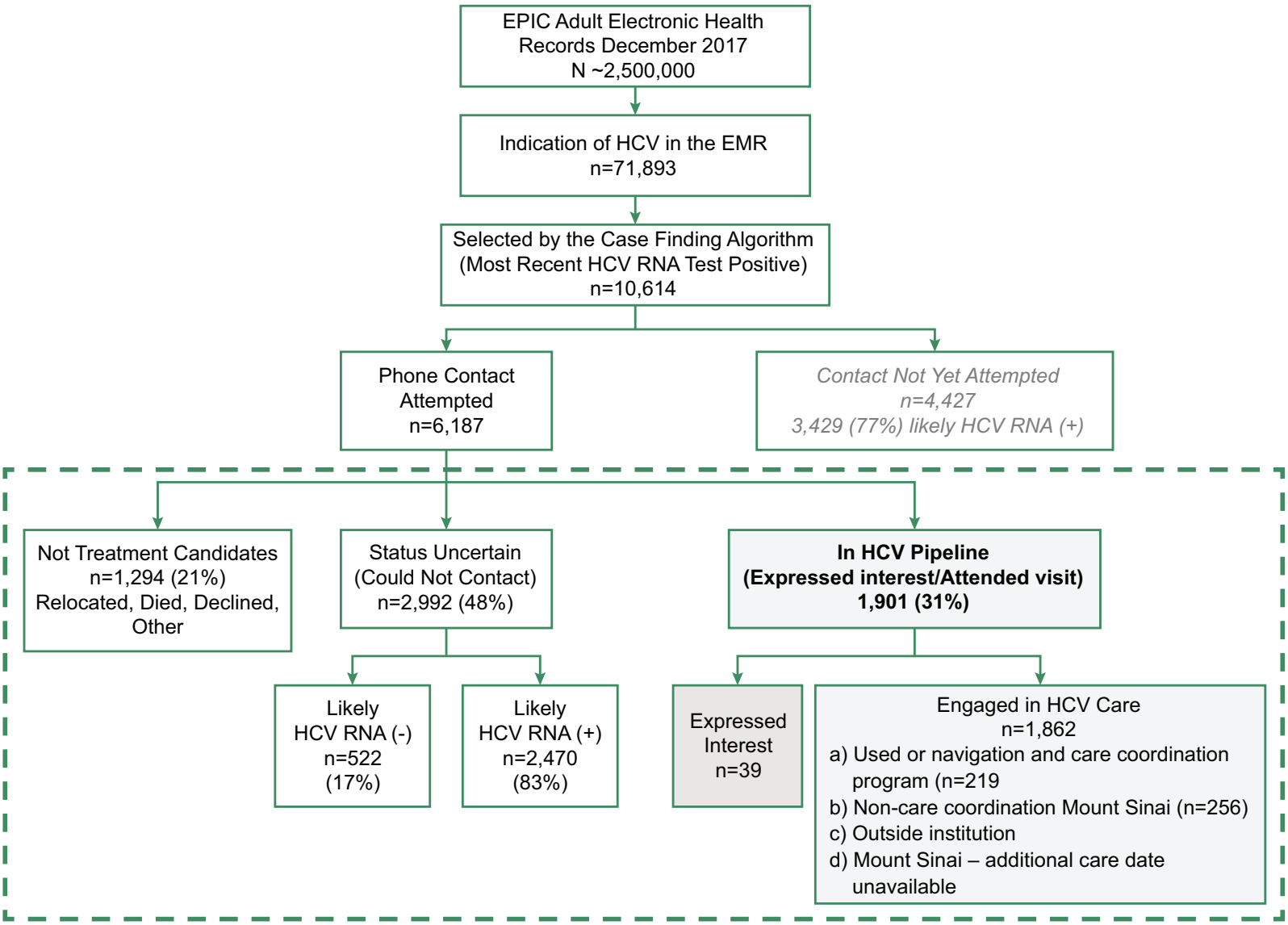

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Figure 4. Evaluation of the Phenotyping Algorithm

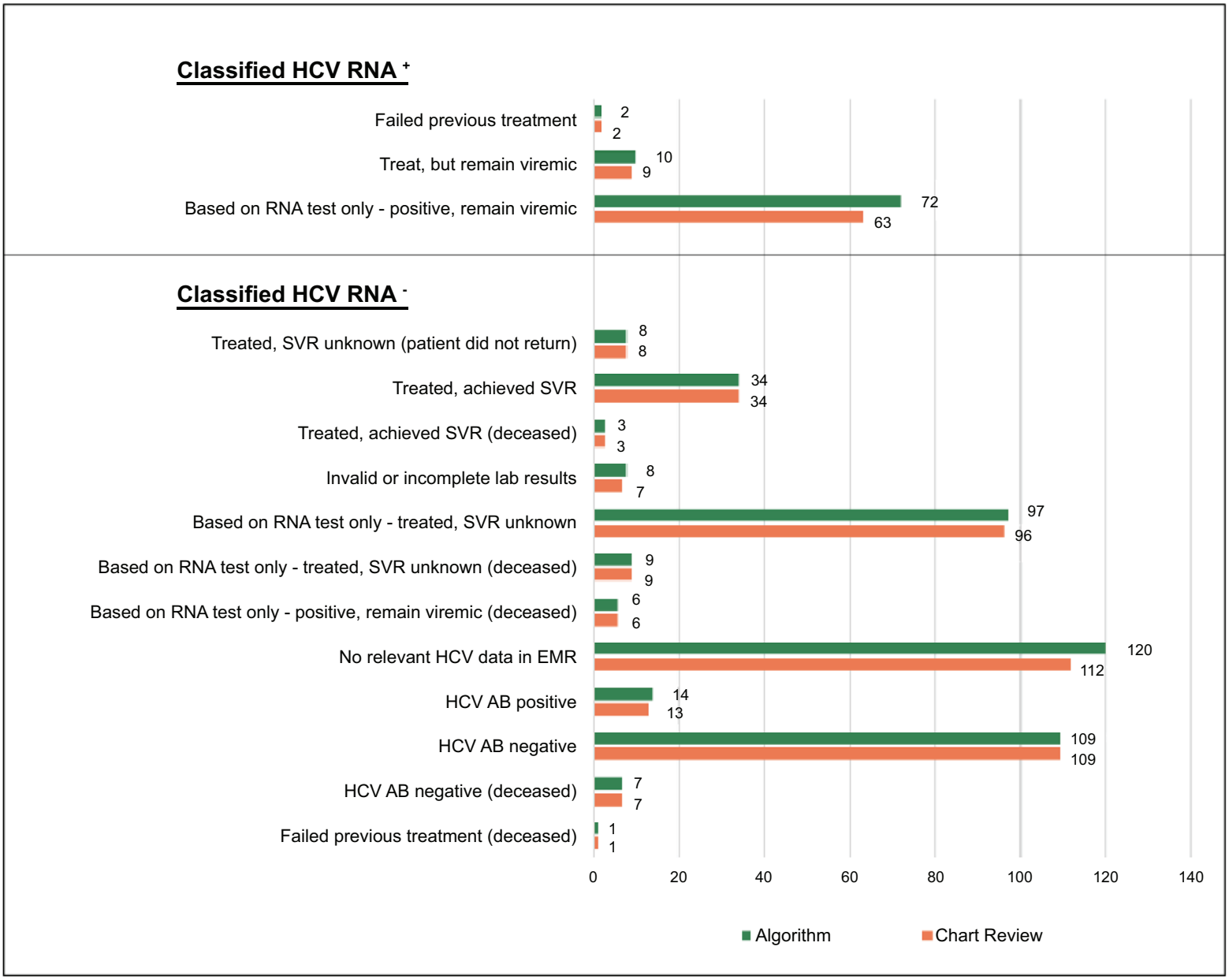

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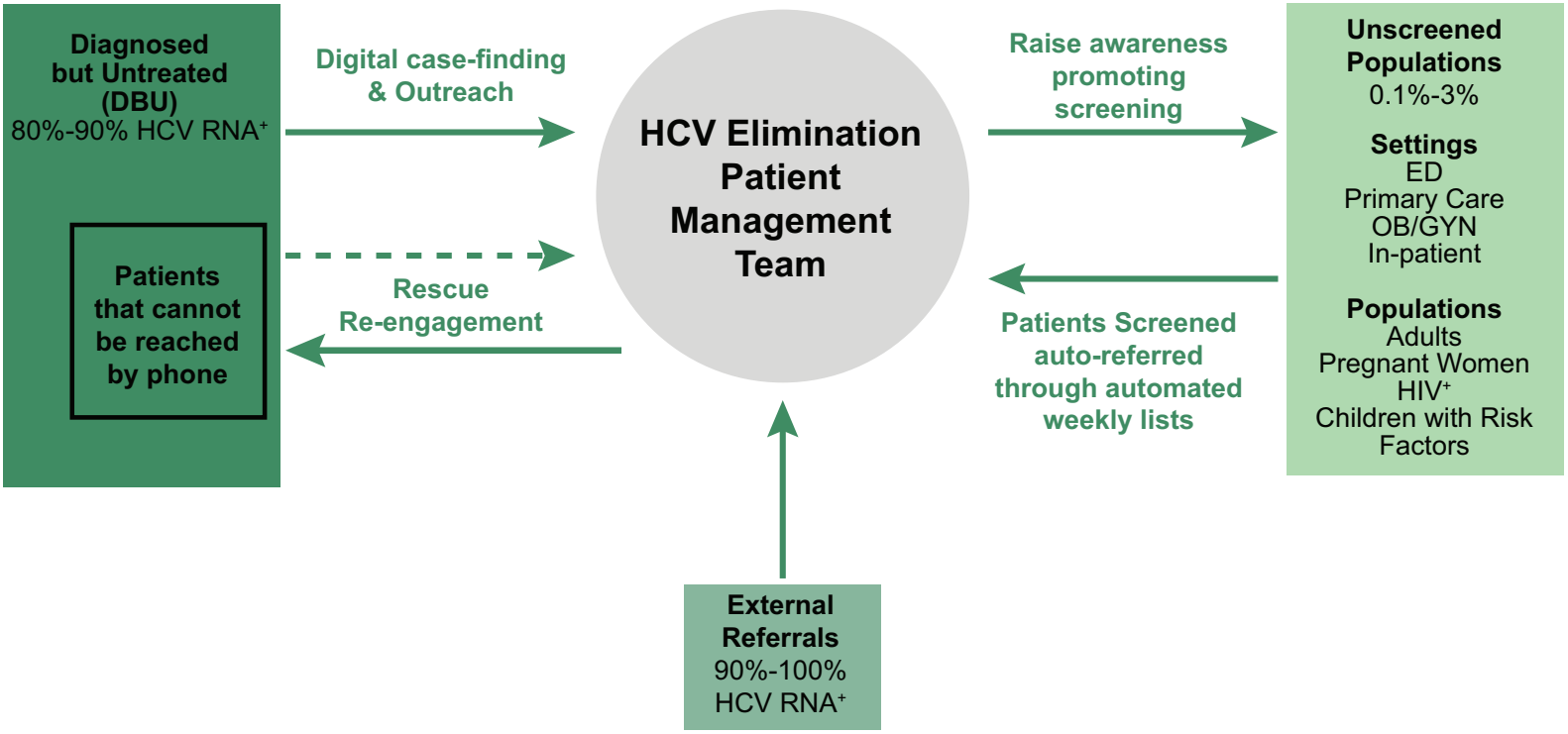
Figure 5. Comprehensive HCV Elimination Across a Healthcare



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