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Streamlining Screening to Treatment: The Hepatitis C Cascade of Care at Kaiser Permanente Mid-Atlantic States

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Hepatitis C virus (HCV) screening is recommended for patients at risk and/or born during 1945–1965, but screening gaps persist. This new program screens target populations and enhances care linkage for chronically HCV-infected patients. Kaiser Permanente Mid-Atlantic States created a comprehensive HCV screening pathway, supported by a HCV care coordinator. The testing pathway includes HCV antibody (Ab), automatic HCV RNA for Ab-positive patients, coinfection and liver health tests, vibration-controlled transient elastography (VCTE), and a physician referral. A total of 11 200 patients were screened; 3.25% were HCV Ab positive, and 100% of Ab-positive patients received HCV RNA testing. Of HCV Ab-positive patients, 75.9% had chronic HCV, of which 80.8% underwent VCTE. HCV diagnosis was communicated to 94% of patients, and 70.9% had HCV documented in the electronic health record. The pathway shows promise in closing gaps, including improving HCV RNA testing, communicating diagnoses, and assessing liver fibrosis. Improved testing and linkage could increase curative treatment access.

Keywords. hepatitis C virus; HCV; cascade of care; screening; linkage to care.

The National Health and Nutrition Examination Survey (NHANES) estimates that approximately 3–4 million individuals in the United States are chronically infected with hepatitis C virus (HCV). An estimated 50%–80% are unaware of their infection, and may infect others and suffer disease progression [1, 2]. Approximately 50% of those with chronic HCV will develop cirrhosis, and 33% (1 000 000 nationwide) will die from liver-related complications if left untreated [1]. HCV is the leading cause of liver transplant and hepatocellular carcinoma [3]. Costs associated with HCV-related advanced liver disease continue to rise [4].

To stem the rising morbidity and mortality related to HCV, patients should enter a cascade of care that begins at screening and ends with effective HCV treatment and the opportunity for "cure," as defined by sustained viral response at least 12 weeks after the cessation of therapy [5]. Several barriers limit screening, diagnosis, and treatment. Provider knowledge about HCV and its associated risk factors is low [6–9]. NHANES data suggest that only 3.7% of follow-up survey respondents report that they had been tested because they or their doctor thought they were at risk for HCV infection, and <50% were notified of their positive infection status [2]. Information from the Chronic Hepatitis Cohort Study (CHeCS) indicates that gaps in care exist at every step along the HCV screening and care cascade [10]. In the CHeCS, 38% of HCV antibody (Ab)–positive patients had no follow-up HCV RNA testing documented in the electronic database; 62% had no liver biopsy between 2001 and 2010 [10–12]. Even larger gaps exist for patients coinfected with human immunodeficiency virus (HIV) and HCV [13]. Furthermore, HCV treatments have been historically less effective and/or intolerable for many patients. Until 2013, HCV treatments have underperformed, with efficacy only as good as 50% in genotype 1 (the predominant genotype in the United States) [14–17]. Without effective and tolerable treatments available, physicians have been less aggressive in screening at-risk patients. As a result, patients have historically delayed engagement with health systems and have not entered the HCV care cascade until late in the course of the disease, presenting with liver complications in the late stage of infection [2].

Since 2013, several factors have increased the focus on HCV screening, diagnosis, and treatment. The US Preventive Services Task Force (USPSTF) elevated 1-time HCV Ab screening for patients born during 1945–1965 to a "B" grade. Several pharmaceutical agents used in combination, called direct-acting antiviral agents, have demonstrated >90% efficacy across most genotypes, even among patients with cirrhosis [5, 18–20]. Noninvasive liver stiffness assessment technologies were approved by the US Food and Drug Administration, including vibration-controlled transient elastography (VCTE; FibroScan); these noninvasive tests obviate the need for liver biopsy in many cases.

Kaiser Permanente Mid-Atlantic States (KPMAS)—comprised of Kaiser Foundation Health Plan and the Mid-Atlantic Permanente Medical Group (MAPMG)—is an integrated delivery and financing system providing care to members in Maryland,

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Virginia, and the District of Columbia. Prior to the 2013 USPSTF guidelines, only 14.4% of KPMAS patients within the 1945–1965 birth cohort were screened (15.8% of all adults aged ≥18 years) [21]. Updating these data through 2014 improved screening rates to 17.1% among this birth cohort (18.6% of all adults) [22]. Among those screened, 84% received a confirmatory HCV RNA test. These numbers are higher compared to similar cohorts [10], but represent less-than-universal screening. Motivated by the opportunity to identify HCV-infected patients and connect these patients to treatment efficiently and earlier, KPMAS designed a new HCV screening pathway, with a HCV care coordinator at its core (Table 1; Figure 1). The pathway is specifically designed to improve the carriage of patients through each step of the HCV care cascade, including screening, detection, and notification of HCV (and other associated infectious diseases) infection status, fibrosis staging and monitoring, and linkage to care via a physician referral.

METHODS

Eligible Patient Identification in the USPSTF Birth Cohort (1945–1965)

We developed an algorithm to drive a best-practice alert within the Kaiser Permanente electronic medical record (EMR) [23]. This algorithm flags patients born between 1945 and 1965 (the "birth cohort") who are eligible for HCV Ab screening and without documentation in the EMR of prior HCV testing.

Table 1. Patients Who Entered the Hepatitis C Virus Screening Pathway

Characteristic	HCV Antibody Positive	HCV Antibody Negative
Patients, No.	365	10 835
Age at enrollment, y, mean (SD)	57.5 (9.5)	58.2 (8.2)
Race, %		
Black	62.6	38.8
American Indian/Alaska Native	0.0	0.2
Asian/Pacific Islander	9.1	11.6
Hispanic	3.2	13.1
Multiracial	2.1	1.4
White	23.0	35.0
Sex		
Female	158 (43.3)	6122 (56.5)
Male	207 (56.7)	4713 (43.5)
Mean income (SD)	$75 269 ($33 391)[a]	$91 473 ($41 271)[a]
HCV RNA positive	277 (75.9)	NA
HBsAg positive	2 (0.5)	NA
HIV infected	4 (1.1)	NA
Men who have sex with men	0 (0)	122 (1.13)
Medical record documentation of hepatitis C	259 (70.9)	NA

Data are presented as No. (%) unless otherwise specified. Demographic characteristics of patients screened (N = 11 200) for HCV antibody, as well as characteristics of patients positive for HCV antibody.

Abbreviations: HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus: HIV, human immunodeficiency virus; NA, not applicable; SD, standard deviation.

[a] Significant at $P < .0001$.

Detailed inclusion/exclusion criteria are available in the Supplementary Material.

New HCV Screening Pathway Orders

Physicians place one order set that grants authorization for the complete pathway, obviating the need for signing/co-signing of additional testing orders. The order set has 2 components:

1. Hepatitis C antibody screen with reflex to HCV RNA, hepatitis B surface antigen (HBsAg), and HIV antibody tests: This order initiates a group of laboratory tests that automatically reflex—which means that positive test results trigger additional downstream testing of multiple specimens collected at a single laboratory visit. (See Figure 1 for a complete list of included laboratory tests.) The order includes a button to document verbal consent for HIV testing, to comply with local statutes [24–26].
2. Initiate protocol for HCV viral load detected: This order component is comparable to inpatient care nursing protocols. This protocol grants approval for a nonphysician support staff member (at MAPMG, the HCV care coordinator), to execute a physician order if upstream HCV RNA tests return positive results.

When the HCV screening order is placed, an EMR "after-visit summary" prints for the patient, outlining the screening steps, providing HCV information, introducing the HCV care coordinator, and providing contact information for questions.

Laboratory Testing

The clinic-based laboratory draws 1 ethylenediaminetetraacetic acid (EDTA) tube and 1 serum separator tube (SST) from each patient. The EDTA specimen is immediately processed for HCV Ab testing. If positive or indeterminate, the sample is tested for HBsAg and HIV type 1/2 Abs. The SST specimen is used for quantitative HCV RNA testing. Patients testing positive for HCV Ab and HCV RNA return for a second blood collection. This specimen is used for the HCV Assessment Labs set (see Figure 1 for a complete list of laboratory tests).

Results Routing

The ordering physician automatically receives all laboratory test results in the EMR inbox. Certain results are also routed to the HCV care coordinator EMR inbox, to enable patient tracking (see next section).

Support Staff: HCV Care Coordinator

The HCV care coordinator, a research nurse, closes gaps in the HCV screening pathway by tracking progress and managing patient follow-up (Figure 1). The HCV coordinator supports HCV-monoinfected patients and HCV/hepatitis B virus (HBV)–coinfected patients. Patients coinfected with HIV are immediately referred to the Department of Infectious Diseases for follow-up by the MAPMG HIV multidisciplinary care team [27, 28]. Newly identified HIV-infected patients are also tested for HCV; prior data indicate 96% HCV testing rates among KPMAS HIV-infected patients [27].

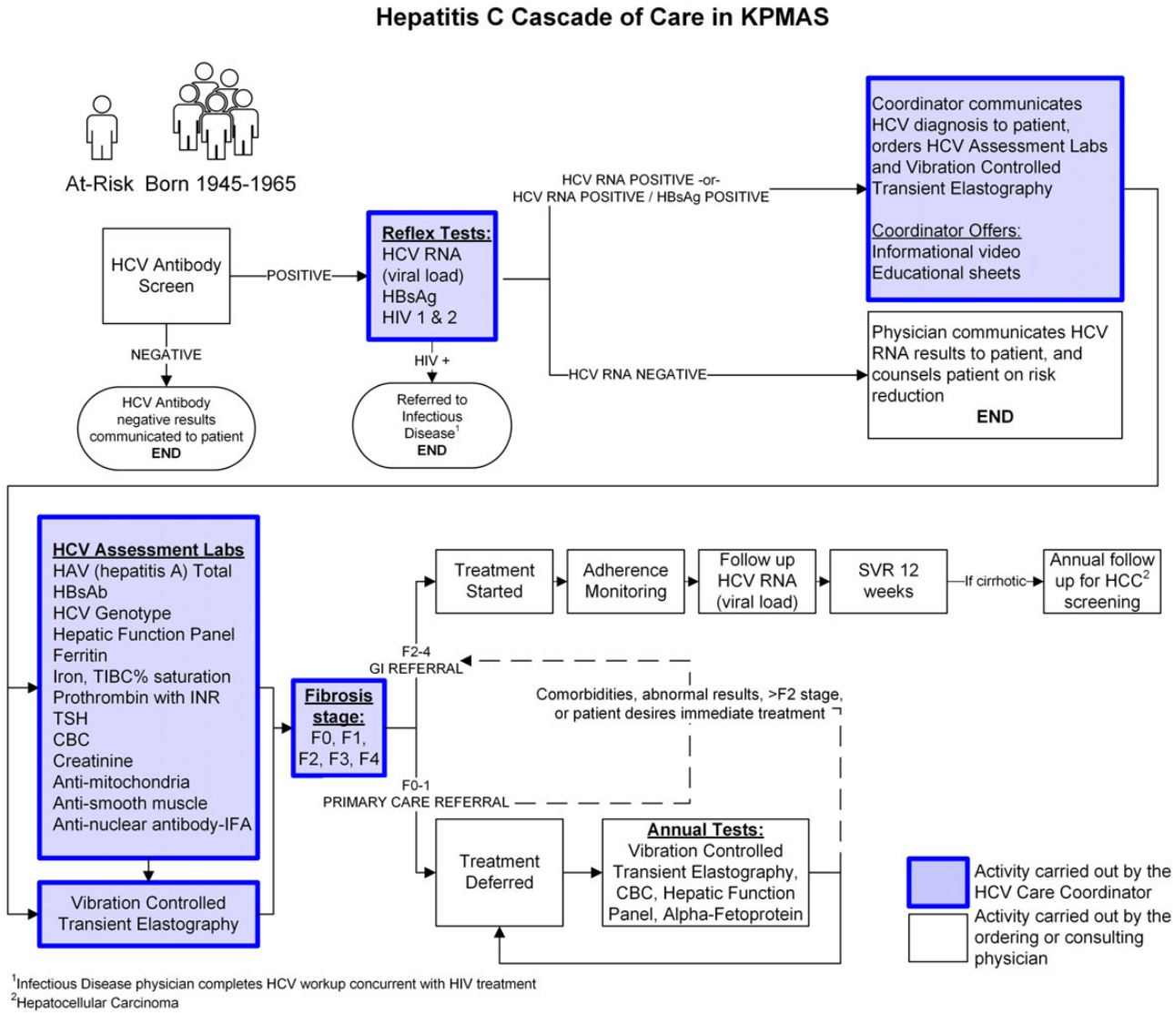

Figure 1. The new hepatitis C virus (HCV) screening pathway in Kaiser Permanente Mid-Atlantic States. Thick outlined/shaded/blue boxes indicate activities carried out by the HCV care coordinator. Abbreviations: CBC, complete blood count; HAV, hepatitis A virus; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HCC, hepatocellular carcinoma; HIV, human immunodeficiency virus; IFA, immunofluorescent assay; INR, international normalized ratio; KPMAS, Kaiser Permanente Mid-Atlantic States; SVR, sustained virologic response; TIBC, total iron binding capacity; TSH, thyroid-stimulating hormone.

The coordinator does not manage HCV Ab–negative patients. The ordering provider communicates HCV Ab–negative results to the patient, using standardized response text developed for this program. Additionally, the coordinator does not manage patients who have spontaneously cleared the virus (HCV Ab positive, HCV RNA negative). The coordinator reminds the ordering provider to communicate these results. The patient receives a different standardized text, which includes recommendations for healthy behaviors. These patients do not need to proceed further through the screening pathway.

Test results are automatically routed to the coordinator's EMR inbox. The coordinator communicates and explains chronic HCV (HCV Ab and RNA positive) results to the patient. Patients are offered informational sheets and a KPMAS-produced HCV educational video (informational sheets available upon request by contacting the corresponding author). The coordinator orders the HCV Assessment Labs and instructs the patient to return for a second blood draw. The coordinator schedules the VCTE test and provides test preparation instructions. At the conclusion of the testing pathway, the coordinator reports final results to the patient and explains next steps. Patients are referred for ongoing care based on the fibrosis (F) score determined by VCTE and the overall clinical picture (see "Management Post–Fibrosis Scoring" section below). The coordinator also supports the ordering physician by sending reminder messages to act on specific, time-sensitive abnormal

laboratory tests, including thyroid-stimulating hormone and complete blood count.

Hepatic VCTE

Patients with positive HCV Ab and HCV RNA tests are referred for VCTE. Gastroenterologists interpret the F-score by comparing kilopascal (kPa) values to F-score ranges, using previously published tables (Figure 2) [29, 30].

FIB-4 Scoring

The gastroenterologist calculates the FIB-4 score (an additional noninvasive measure of liver disease stage) using alanine and aspartate aminotransferase levels, age, and platelet count [31, 32], using the following F-score ranges: F0–F1, FIB-4 <1.45; F3–F4, FIB-4 >3.25) [32].

Management Post–Fibrosis Scoring

Patients are referred for ongoing care based on the VTCE F-score and the overall clinical picture. Once testing is complete, HCV and associated diagnoses are added to the EMR Problem List. Patients with F-scores of 0–1 are referred to primary care for continued monitoring—including annual follow-up VCTE, α-fetoprotein, complete blood count, and liver function tests. F0–F1 patients may receive a referral to gastroenterology if comorbidities are present, if requested, or if results change (Figure 1). Patients with F-scores of 2–4, those who are symptomatic, or those with comorbidities are referred to a gastroenterologist for an in-person consult [33]. F4 patients are also enrolled in the hepatocellular carcinoma sonography monitoring program once seen in gastroenterology. Patients coinfected with HBV are referred to gastroenterology for an in-person consult, regardless of the F-score. Patients under primary care management are tracked through an internally developed EMR tracking tool that provides reminders for annual follow-up care.

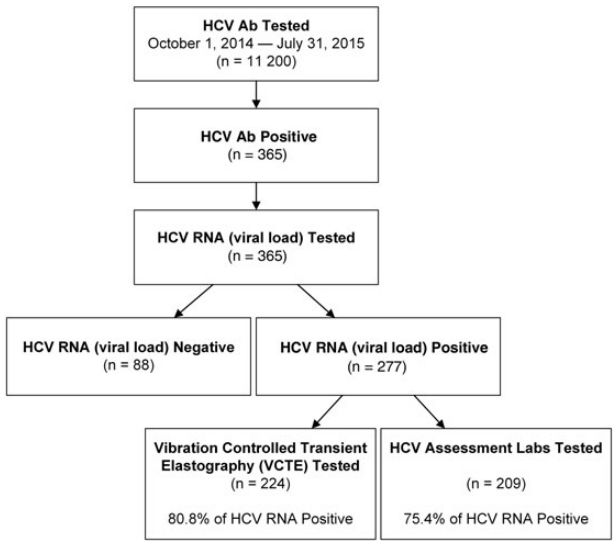

Figure 2. Patients completing each step of the hepatitis C virus (HCV) screening pathway. Abbreviations: Ab, antibody; VCTE, vibration-controlled transient elastography.

RESULTS

Pathway Performance to Date

From 1 October 2014 through 31 July 2015, 11 200 patients initiated the new HCV screening pathway (Table 1). HCV antibody was detected in 365 (3.25%) patients, of whom 100% received a confirmatory HCV RNA test and 75.9% were RNA positive. The mean income of HCV Ab–positive and HCV Ab–negative patients was significantly different, with HCV Ab–positive patients having a lower income. The total number of chronic HCV cases defined in this timeframe was 2.46% (277 patients), in which 80.8% (214) underwent VCTE to assess liver stiffness (Table 2). Zero patients opted out of HIV screening. Among HCV Ab–positive patients, 1.1% (4 patients) were coinfected with HIV and 0.5% (2 patients) with HBV; 75.4% of chronic HCV patients returned for the second HCV Assessment Labs set. Diagnosis was conveyed to 94% of chronic HCV-monoinfected patients and HCV/HBV-coinfected patients during a visit or via telephone, and HCV diagnosis was documented in the EMR Problem List for 70.9% (259 patients, Table 2; the remaining 29.1% had HCV-related laboratory results in the EMR, but did not have an HCV diagnosis on the Problem List). Infectious disease or primary care physicians communicated an HIV diagnosis. All chronic HCV patients are added to the HCV registry. Provider, pharmacist, and summary reports are generated to identify trends in the KPMAS HCV-infected population that may affect care and prompt appropriate follow-up.

Table 2. Clinical Characteristics of Patients Diagnosed With Chronic Hepatitis C Virus (HCV) Through the HCV Screening Pathway

Characteristic	No. (%)
HCV genotype results (n = 209)	
1	174 (83.3)
2	17 (8.1)
3	8 (3.8)
4	5 (2.3)
5	0
6	5 (2.3)
Vibration-controlled transient elastography, kPa (n = 224)	
0–5.4	70 (31.2)
5.5–7.0	51 (22.7)
7.1–9.4	53 (23.6)
9.5–11.9	15 (6.6)
≥12.0	35 (15.6)
Hepatitis A antibody testing (n = 195)	
Antibody positive, No. (%)	108 (55.3)
Antibody negative, No. (%)	87 (44.6)
Patients notified of chronic HCV diagnosis (monoinfected, HCV/HBV coinfected) via telephone or visit	94%

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; kPa, kilopascal.

Additionally, the pathway was used to obtain necessary diagnostics for patients with preexisting HCV already on the MAPMG HCV registry (identified by comparing medical record numbers from the registry during a prelaunch time period with medical record numbers from patients completing the new pathway). A total of 174 HCV registry patients were retested, of whom 61% (107) were previously missing needed tests. Through the new pathway, 100% of these patients received HCV RNA testing.

DISCUSSION

Health systems and clinicians now have an unprecedented opportunity to close the gaps in HCV screening and care. New recommendations and new curative treatments support the redesign of HCV screening and linkage-to-care pathways. KPMAS has redesigned the HCV screening pathway to address specific gaps in care, including HCV RNA testing rates, patient diagnosis communication, and assessment of liver fibrosis. As of October 2014, KPMAS has addressed these gaps by implementing (1) an automated EMR best-practice alert to notify providers that a patient is recommended for HCV screening; (2) automated confirmatory HCV RNA laboratory testing (100% of HCV Ab–positive patients); (3) an HCV care coordinator to assist in ordering follow-up labs, scheduling VCTE, and informing patients of their infection status; and (4) offering a noninvasive alternative for measuring liver damage (VCTE).

An automated EMR best-practice alert flags patients based on birthdate and screening eligibility, prompting physicians to test the at-risk baby boomer population, a group often unaware of their HCV infection. Ensuring that 100% of HCV Ab–positive samples are automatically tested for HCV RNA closes a significant gap in comprehensive HCV testing [10, 12]. Automatic confirmatory HCV RNA testing avoids a patient blood draw visit and enables physicians to correctly diagnose chronic HCV and plan care accordingly. Interestingly, although the pathway was designed to screen undiagnosed patients, it has also been helpful in comprehensively diagnosing and staging previously diagnosed HCV patients who may have lacked 1 or more diagnostic tests (for example, HCV Ab–positive patients who lacked an HCV RNA test). Because HCV Ab–positive samples are automatically tested for HCV RNA, 100% of these previously diagnosed patients have received HCV RNA testing—giving physicians an updated and comprehensive clinical picture. Future work will analyze the percentage of previously diagnosed patients who completed each pathway step.

The pathway addresses other gaps as well. Implementing the noninvasive VCTE test enables gastroenterology providers to test patients more frequently, and potentially monitor disease progression more closely. Physicians report that some previously diagnosed patients who had declined biopsy in the past were willing to undergo VCTE, resulting in an updated clinical picture (personal communication with Bradley J. Winston, Jacquelyn Redd and Dana A. Sloane June 2015).

NHANES data indicate that more than half of HCV–positive patients are not notified of their infection status [12]. Early data suggest this pathway is closing this gap; 94% of monoinfected chronic HCV and HCV/HBV-coinfected patients tested through this new pathway were informed of their diagnosis via telephone by the HCV care coordinator. The remaining 6% were notified by letter, so we could not definitively confirm receipt of information. Interestingly, there were no negative consequences to having a coordinator communicate an HCV diagnosis. In fact, coordinators spend between 15 and 45 minutes in patient discussion—saving physician time and enabling top-of-license staff practice. Infectious disease or primary care physicians informed patients of an HIV diagnosis and linked 100% of newly diagnosed HIV-infected patients to care. Furthermore, the new pathway encourages appropriate HCV clinical documentation, addressing gaps in HCV diagnosis documentation [12]. At the conclusion of the testing pathway, the HCV infection is documented in the EMR Problem List; this is the most visible place for a diagnosis, and is considered best-practice documentation. Because all HCV-related laboratory results are automatically captured in the EMR, even the remaining 29.1% had HCV infection documentation somewhere in the record—but not in the most prominent location. To date, 70.9% of pathway patients had correct Problem List documentation; the HCV coordinator will assist with this step to reach 100%.

Program evaluation has identified areas for improvement. The percentage of patients who return for VCTE (80.8%) and the HCV Assessment Labs (75.4%) is lower than goal. The 19.2% missing VCTE includes ineligible patients (due to weight, pacemakers/defibrillators, or pregnancy), those whose physicians recommended biopsy, and those nonresponsive to coordinator outreach. A slightly lower percentage of patients return for the HCV Assessment Labs (75.4%). These laboratory tests are necessary, as many physicians simultaneously review the HCV Assessment Labs for results that may skew VCTE results, such as inflammation [34]. Patients lacking these laboratory results may have their care decisions delayed, because gastroenterologists use the HCV genotype to determine a course of treatment. In 2016, the coordinator will pursue more aggressive outreach to ensure that all clinically eligible patients complete the VCTE and all laboratory tests.

There are several initiatives in progress to improve the KPMAS HCV pathway. Most importantly, upcoming analysis will outline the treatment paths for newly diagnosed patients, including which medications were prescribed, and follow-up care for patients whose treatment was deferred. Obstetric/gynecologic (OB/GYN) providers will also start seeing the HCV screening alert. Opening the pathway to OB/GYN providers will present new challenges, as both VCTE and the curative medications are not presently indicated for pregnant women.

Therefore, the HCV care coordinator will track pregnant patients as far as testing allows, and reengage them after the pregnancy has concluded.

There are several considerations for groups looking to replicate this work. Implementing such a comprehensive and ambitious screening process required the commitment of KPMAS leaders and champions, including an executive champion, a lead physician champion, gastroenterology and infectious disease specialists, primary care physicians, and a senior project manager (see Supplementary Material for details on roles).

Although this work was completed in an integrated delivery system, there are many aspects which can be replicated by independent physicians or health systems without an associated health plan. A coordinator can be used by any group to assist patients through HCV screening, saving physician time. Using coordinator preauthorization for further testing reduces physician-related delays. EMR automated alerts to notify physicians of patients eligible for USPSTF-recommended HCV screening helps ensure that patients are tested. MAPMG utilized gastroenterologists and infectious disease specialists for HCV follow-up care, but hepatologists can also manage these patients. Furthermore, accountable care organizations with close relationships between primary care and specialists (infectious disease and gastroenterology in particular) can begin to coordinate the management of chronic HCV patients, with primary care managing lower-acuity patients and specialists managing higher acuity cases. Any provider could adopt noninvasive liver fibrosis tests, such as VCTE or FIB-4, to supplement or replace biopsy for certain patients.

Many challenges with HCV screening and care remain. Most notably, the high cost of curative drugs on the market today can reduce drug access [35]. However, advanced liver disease costs are also high [4]. Healthcare systems that maintain long-term relationships with patients, as is the case with KPMAS, must create processes that enable the treatment of all eligible patients in a timely manner. The new HCV care pathway enables broad HCV screening and an efficient process to move large volumes of patients through the HCV care cascade. Streamlined laboratory testing and noninvasive tests such as VCTE help physicians monitor the progression of liver damage more carefully—and act quickly when clinical changes occur. As more curative treatments become available, providers and health plans nationwide must coordinate to create pathways that create opportunities for eligible patients to access treatments.

Supplementary Data

Supplementary materials are available at http://cid.oxfordjournals.org. Consisting of data provided by the author to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the author, so questions or comments should be addressed to the author.

Notes

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References

1. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. Ann Intern Med **2006**; 144:705–14.
2. Denniston MM, Klevens RM, McQuillan GM, Jiles RB. Awareness of infection, knowledge of hepatitis C, and medical follow-up among individuals testing positive for hepatitis C: National Health and Nutrition Examination Survey 2001–2008. Hepatology **2012**; 55:1652–61.
3. Ward JW. The epidemiology of chronic hepatitis C and one-time hepatitis C virus testing of persons born during 1945 to 1965 in the United States. Clin Liver Dis **2013**; 17:1–11.
4. Xu F, Tong X, Leidner AJ. Hospitalizations and costs associated with hepatitis C and advanced liver disease continue to increase. Health Aff **2014**; 33:1728–35.
5. Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. N Engl J Med **2013**; 368:1878–87.
6. Clark EC, Yawn BP, Galliher JM, Temte JL, Hickner J. Hepatitis C identification and management by family physicians. Fam Med **2005**; 37:644–9.
7. Jacobson IM, McHutchison JG, Dusheiko G, et al. Telaprevir for previously untreated chronic hepatitis C virus infection. N Engl J Med **2011**; 364: 2405–16.
8. Committee on the Prevention and Control of Viral Hepatitis Infection;Board on Population Health and Public Health Practice; Institute of Medicine. Hepatitis and liver cancer: a national strategy for prevention and control of hepatitis B and C. Colvin HM, Mitchell AE, eds. Washington, DC: National Academies Press, **2010**.
9. Leverence RR, Williams RL, Pace W, et al. Context of clinical care: the case of hepatitis C in underserved communities—a report from the Primary Care Multiethnic Network (PRIME Net) Consortium. J Am Board Fam Med **2009**; 22:638–46.
10. Moorman AC, Gordon SC, Rupp LB, et al. Baseline characteristics and mortality among people in care for chronic viral hepatitis: the Chronic Hepatitis Cohort Study. Clin Infect Dis **2013**; 56:40–50.
11. Highleyman L. Hepatitis C cascade studies show gaps in testing and treatment. Available at: http://www.hivandhepatitis.com/hepatitis-c/hepatitis-c-topics/hcv-treatment/4693-hepatitis-c-cascade-studies-show-gaps-in-testing-and-treatment. Accessed 10 May 2015.
12. Holmberg SD, Spradling PR, Moorman AC, Denniston MM. Hepatitis C in the United States. N Engl J Med **2013**; 368:1859–61.
13. Graham CS. Hepatitis C and HIV co-infection: closing the gaps. JAMA **2015**; 313:1217–8.
14. Manns MP, McHutchison JG, Gordon SC, et al. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. Lancet **2001**; 358:958–65.
15. Fried MW, Shiffman ML, Reddy KR, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. N Engl J Med **2002**; 347:975–82.
16. Hadziyannis SJ, Sette H Jr., Morgan TR, et al. Peginterferon-alpha2a and ribavirin combination therapy in chronic hepatitis C: a randomized study of treatment duration and ribavirin dose. Ann Intern Med **2004**; 140:346–55.
17. Fried MW. Side effects of therapy of hepatitis C and their management. Hepatology **2002**; 36(5 suppl 1):S237–44.
18. Lawitz E, Sulkowski MS, Ghalib R, et al. Simeprevir plus sofosbuvir, with or without ribavirin, to treat chronic infection with hepatitis C virus genotype 1 in non-responders to pegylated interferon and ribavirin and treatment-naive patients: the COSMOS randomised study. Lancet **2014**; 384:1756–65.
19. Jacobson IM, Gordon SC, Kowdley KV, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med **2013**; 368:1867–77.
20. Afdhal N, Reddy KR, Nelson DR, et al. Ledipasvir and sofosbuvir for previously treated HCV genotype 1 infection. N Engl J Med **2014**; 370:1483–93.

21. Linas BP, Hu H, Barter DM, Horberg M. Hepatitis C screening trends in a large integrated health system. Am J Med **2014**; 127:398–405.
22. Rodriguez CV, Hu H, Rubenstein K, Linus BMH. Increasing hepatitis C virus (HCV) screening and confirmatory testing in a large integrated health system. In: 2015 National Summit on HCV and HIV, Arlington, VA, June 2015.
23. Chen C, Garrido T, Chock D, Okawa G, Liang L. The Kaiser Permanente electronic health record: transforming and streamlining modalities of care. Health Aff **2009**; 28:323–33.
24. Maryland Health General Code. §18-202.1. Available at: http://mgaleg.maryland.gov/webmga/frmStatutesText.aspx?article=ghg&section=18-202.1&ext=html&session=2015RS&tab=subject5. Accessed 25 February 2016.
25. Code of Virginia, Title 32.1 Health. §32.1-37.2. Available at: http://law.lis.virginia.gov/vacode/32.1-37.2/. Accessed 25 February 2016.
26. Centers for Disease Control and Prevention. State HIV laws. Available at: http://www.cdc.gov/hiv/policies/law/states/index.html#DC. Accessed 25 February 2016.
27. Horberg M, Hurley L, Towner W, et al. HIV quality performance measures in a large integrated health care system. AIDS Patient Care STDS **2011**; 25:21–8.
28. Horberg MA, Hurley LB, Towner WJ, et al. Determination of optimized multidisciplinary care team for maximal antiretroviral therapy adherence. J Acquir Immune Defic Syndr **2012**; 60:183–90.
29. Bonder A, Afdhal N. Utilization of FibroScan in clinical practice. Curr Gastroenterol Rep **2014**; 16:372.
30. Cha SW, Jeong WK, Kim Y, et al. Nondiseased liver stiffness measured by shear wave elastography: a pilot study. J Ultrasound Med **2014**; 33:53–60.
31. Martinez SM, Crespo G, Navasa M, Forns X. Noninvasive assessment of liver fibrosis. Hepatology **2011**; 53:325–35.
32. Vallet-Pichard A, Mallet V, Nalpas B, et al. FIB-4: an inexpensive and accurate marker of fibrosis in HCV infection. comparison with liver biopsy and fibrotest. Hepatology **2007**; 46:32–6.
33. American Association for the Study of Liver Diseases/Infectious Diseases Society of America HCV Guidance Panel. Hepatitis C guidance: AASLD-IDSA recommendations for testing, managing, and treating adults infected with hepatitis C virus. Hepatology **2015**; 62:932–54.
34. Chan HL, Wong GL, Choi PC, et al. Alanine aminotransferase-based algorithms of liver stiffness measurement by transient elastography (Fibroscan) for liver fibrosis in chronic hepatitis B. J Viral Hepat **2009**; 16:36–44.
35. Somashekhar S. Costly hepatitis drug Sovaldi rattles industry. Available at: http://www.washingtonpost.com/national/health-science/costly-hepatitis-drug-sovaldi-rattles-industry/2014/03/01/86cab0b4-a091-11e3-9ba6-800d1192d08b_story.html. Accessed 25 February 2016.