A Population Approach to Disease Management: Hepatitis C Direct-Acting Antiviral Use in a Large Health Care System

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ABSTRACT

BACKGROUND: The introduction of the first direct-acting antiviral agents (DAAs) for the treatment of hepatitis C virus (HCV), telaprevir and boceprevir, marked a unique event in which 2 disease-changing therapies received FDA approval at the same time. Comparative safety and effectiveness data in real-world populations upon which to make formulary decisions did not exist.

OBJECTIVE: To describe the implementation, measurement, and outcomes of an enduring population-based approach of surveillance of medication management for HCV.

METHODS: The foundation of the population approach to HCV medication management used by the Department of Veterans Affairs (VA) relied upon a basic framework of (a) providing data for effective regional and local management, (b) education and training, (c) real-time oversight and feedback from a higher organization level, and (d) prompt outcome sharing. These population-based processes spanned across the continuum of the direct-acting antiviral oversight process. We used the VA's HCV Clinical Case Registry—which includes pharmacy, laboratory, and diagnosis information for all HCV-infected veterans from all VA facilities—to assess DAA treatment eligibility, DAA uptake and timing, appropriate use of DAAs including HCV RNA monitoring and medication possession ratios (MPR), nonconcordance with guidance for adjunct erythropoiesis-stimulating agent (ESA) and granulocyte colony-stimulating factor (GCSF) use, hematologic adverse effects, discontinuation rates, and early and sustained virologic responses. Training impact was assessed via survey and change in pharmacist scope of practice.

RESULTS: One year after FDA approval, DAAs had been prescribed at 120 of 130 VA facilities. Over 680 VA providers participated in live educational training programs including 380 pharmacists, and pharmacists with a scope of practice for HCV increased from 59 to 110 pharmacists (86%). HCV RNA futility testing improved such that only 1%-3% of veterans did not have appropriate testing compared with 15%-17% 6 months earlier. By facility, the median proportion of veterans with MPR ≥ 0.95 remained 80% for those prescribed boceprevir; for telaprevir, the median proportion was 75% and improved to 80% 6 months later. Nonconcordance with VA medication guidance was as follows: receipt of an ESA without dose reducing ribavirin, 30% boceprevir, 45% telaprevir; ESA initiated with a hemoglobin >10 g/dL, 42% boceprevir, 25% telaprevir; receipt of GCSF with absolute neutrophil count above the criteria threshold, 84%.

CONCLUSIONS: This clinically focused, comprehensive, population-based medication management approach affected real-time change in health services, practice, and outcomes evidenced by widespread and rapid DAA uptake, improved HCV RNA monitoring, attention to adherence, and more appropriate management of DAA-related anemia. Timely outcome sharing provided decision makers and clinicians evidence to support current HCV practices.

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What is already known about this subject

- The first 2 direct-acting antiviral agents (DAAs) for hepatitis C virus (HCV) were approved by the FDA within several days' time, in May 2011, and quickly became the standard of care for genotype 1 HCV infection.
- Compared with peginterferon/ribavirin dual therapy, clinical trials of boceprevir- or telaprevir-based triple drug regimens showed substantially improved sustained virologic response rates and shortened treatment durations.

What this study adds

- A comprehensive population-based hepatitis C medication management process affected real-time change in health services, practice, outcomes, and policy.
- Identifying potentially eligible patients to receive boceprevir- or telaprevir-based regimens (range 133 to 2,358 patients per facility) allowed facilities to plan for utilization and expenditures. In this large national health care system, drug uptake was rapid with 72% of 130 facilities prescribing DAAs within 6 months and 92% of sites prescribing DAAs within 1 year after approval.
- Focused training resulted in an increase in the number of pharmacists acquiring a scope of practice for hepatitis C care from 59 to 110—an increase of 86%.
- Timely outcome sharing improved HCV RNA monitoring, attention to adherence, contributed to more appropriate management of DAA-related anemia, and provided decision makers and clinicians evidence to support current HCV practices.

Chronic hepatitis C virus (HCV) infection is a major global health problem leading to chronic liver disease, cirrhosis, and hepatocellular carcinoma. In the United States, it is the principal cause of death from liver disease and the leading cause of liver transplantation.[1] The Department of Veterans Affairs (VA) is the largest provider of health care to HCV-infected individuals in the United States, caring for approximately 170,000 veterans, representing nearly 5% of all individuals in the United States with chronic HCV.[2,3] The availability of boceprevir and telaprevir—the first approved direct-acting antiviral agents (DAAs) by the U.S. Food and Drug Administration (FDA)—offered the possibility of substantial improvement in the treatment of HCV genotype 1 when used

in combination with peginterferon and ribavirin.[4-7] Despite advances in efficacy, evidence suggested that boceprevir- or telaprevir-based regimens would be more difficult to manage because of complex treatment algorithms, higher pill burden, complicated drug interactions, and adverse effects, particularly anemia.[8-9] Safety and effectiveness data in real-world populations, such as veterans, with comorbidities or relative contraindications upon which to make formulary decisions did not exist. Demand for these agents was great given the landmark changes in response, yet the baseline characteristics of the clinical trial populations in whom these agents were evaluated were substantially different from those of the VA HCV-infected population. Furthermore, no comparative efficacy data were available for the 2 agents. In response to the immediate need for more effective HCV treatment among the veteran population, in whom sustained virologic response (SVR) rates had been historically lower, an expedited formulary review began within 2 weeks after FDA approval.

The release of telaprevir and boceprevir marked a unique event in which 2 disease-changing therapies received FDA approval at virtually the same time. Such an event provides large health care organizations with the opportunity to gather information and data on how new therapies are adopted, alter existing uptake and utilization, and impact therapeutic outcomes.[10] The availability of HCV DAAs was expected to have substantial impact on the health care system with regards to HCV management and characterized a "treatment trifecta" involving high utilization, high cost, and the requirement of intensive monitoring for effectiveness and safety. In response, the VA Office of Public Health/Population Health—the VA program office responsible for overseeing the VA National Hepatitis C Program and assessing and reporting on populations of veterans and the factors and interventions influencing their health—in collaboration with the VA Pharmacy Benefits Management Services undertook a prospective plan to evaluate the use of these new treatments in the VA. In this article, we describe the implementation, measurement, and outcomes of an enduring population-based approach of surveillance of medication management for HCV.

Methods

The foundation of the population approach to HCV medication management used by the VA relied upon a basic framework of (a) providing data and tools for effective regional and local management, (b) education and training, (c) real-time oversight and feedback from a higher organization level, and (d) prompt outcome sharing. These population-based processes spanned across the continuum of the DAA oversight process.

Treatment Eligibility and Uptake

Planning and preparation for the new HCV therapies started 12 months prior to FDA approval and began with providing VA-specific data for national, regional, and local forecasting and decision making. The initial step in preparing the system for these agents was assessing the current status of the VA HCV-infected population by identifying and describing the target population for treatment. The VA's Clinical Case Registry for HCV (CCR:HCV), maintained by the Office of Public Health/Population Health, is an extract of the VA electronic medical record that contains prescription, laboratory, diagnosis, and inpatient and outpatient visit information for HCV-infected veterans seen at all 130 VA medical facilities.[11] We used CCR:HCV as the data source for all reporting and evaluations.

Using CCR:HCV laboratory and prescription data from all 130 VHA facilities, we produced reports of facility, regional (the VA system is divided into 21 regions, or veterans integrated service networks), and national level populations identifying the number of veterans with HCV genotype 1 infection who were in need of treatment as determined by a detectable HCV viral load, as well as those who appeared to be eligible candidates based on the indication for therapy and expected contraindications.[8] Using pharmacy records to track historical use of peginterferon plus ribavirin, we constructed models of drug uptake using historical caseloads for VA HCV treatment and projected rates of new treatment caseloads over time. The models assumed the following: the numbers of veterans with HCV in care would remain stable; only genotype 1 HCV-infected patients would be eligible for treatment; both treatment naïve and experienced patients would be eligible; patients with contraindications to peginterferon or ribavirin (based on VA comorbidity data in HCV-infected veterans) would remain ineligible for treatment; and yearly HCV treatment rates would range from 5% to 25% of those eligible based on historical VA treatment rates. Additional reports were constructed to identify veterans with advanced liver disease—using *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes (see Appendix, available in online article) and calculations of model end-stage liver disease (MELD) scores—and determine the prevalence among those in VA care nationally and at a region and facility level. Together, these reports helped construct a view of historical, current, and future HCV care in the VA that was shared with fiscal and operational leadership and with local clinical providers of HCV care. Cost projections detailing HCV medication and adjunct therapy estimates and consequences of HCV disease progression were compiled and presented to VHA leadership to prepare the system for the potential changes in workload and associated costs. Adjunct erythropoietin-stimulating agent (ESA) use and granulocyte colony-stimulating factor (GCSF) use estimates were derived from usage in prior years, which had been approximately 25% and 7%, respectively. DAA cost projections were provided for both boceprevir and telaprevir, and drug prices were estimated from available peginterferon/ribavirin regimen pricing and potential high (2.5-fold) and low (1.5-fold) estimates.

TABLE 1 *VA Criteria for Use of Boceprevir, Telaprevir, Erythropoiesis-Stimulating Agents and Granulocyte Colony-Stimulating Factor*

Medication	Inclusion Criteria for Use
Boceprevir and telaprevir	❑ Will receive boceprevir or telaprevir in combination with peginterferon and ribavirin. ❑ Under care of and/or in collaboration with an experienced VA HCV practitioner. ❑ Provider has discussed with patient the potential risks and benefits of HCV therapy and progression of HCV disease and a shared decision has been made for use. ❑ Adherence counseling performed and documented understanding by patient. AND ❑ Chronic infection with HCV genotype 1 with no previous treatment (i.e., treatment-naïve). OR ❑ Chronic infection with HCV genotype 1 who have previously received peginterferon and ribavirin but did not achieve a sustained virologic response (i.e., treatment-experienced). ❑ For women of childbearing potential (this applies to female patients or in female partners of male patients): Because boceprevir or telaprevir must be used in combination with ribavirin therapy (pregnancy category X), it should not be started unless a report of a negative pregnancy test has been obtained immediately prior to initiation of therapy. Systemic oral contraceptives may not be as effective in women taking boceprevir or telaprevir; hence, it is recommended that 2 alternative effective methods of contraception, including intrauterine devices and barrier methods, should be used in women during treatment with boceprevir or telaprevir and concomitant ribavirin, and for 6 months after treatment has concluded. ❑ Careful virologic monitoring is required to assess when treatment is futile and should be halted to avoid the emergence of resistance. Prompt assessment of HCV RNA levels and treatment response is necessary to avoid resistance.
Erythropoiesis-stimulating agents	❑ Patient receiving hepatitis C therapy (peginterferon, ribavirin, with or without boceprevir or telaprevir). ❑ Patient underwent evaluation for other causes of anemia (e.g., bleeding, nutritional deficiency) and has been treated appropriately. ❑ Patient develops anemia defined as Hgb < 10 g/dL (or as clinically indicated for significant anemia-related signs and symptoms) and persists for at least 2 weeks after reducing the ribavirin dose to 600 mg/day (either through 200 mg incremental dose reductions or 1-time dose reduction to 600 mg/day). ❑ Provider has discussed with patient the potential risks and benefit of ESA therapy and a shared decision has been made for use.
Granulocyte colony-stimulating factor	❑ Patient receiving hepatitis C therapy (peginterferon, ribavirin, with or without boceprevir or telaprevir). ❑ Patient develops neutropenia defined as either (a) ANC < 250/mm^3; OR (b) ANC < 500/mm^3 with 1 of the following risk factors for developing infection: (1) cirrhosis, biopsy proven or clinically evident; (2) pre- or postliver transplant; (c) HIV/HCV coinfection. ❑ Patient has failed to respond (i.e., neutropenia persists) despite at least 2 weeks of peginterferon dose reduction (i.e., peginterferon alfa-2a reduction from 180 mcg/week to 135 mcg/week or peginterferon alfa-2b reduction from 1.5 mcg/kg/week to 1 mcg/kg/week).

ANC = absolute neutrophil count; ESA = erythropoiesis-stimulating agent; g/dL = grams per deciliter; Hgb = hemoglobin; HCV = hepatitis C virus; HIV = human immunodeficiency virus; kg = kilogram; mcg = microgram; mg/day = milligram per day; mm^3 = cubic millimeter; VA = Department of Veterans Affairs.

To assist with local population management, we enhanced the functionality of the local CCR:HCV reporting tools to provide clinicians customizable means to identify candidates for HCV treatment (i.e., HCV viremic with genotype 1 infection, prior treatment history, comorbidities), to calculate MELD scores, and to identify veterans with HCV and advanced liver disease or cirrhosis. The availability and customizability of the information obtained from local CCR reports provided the means to better prepare local facilities for DAA uptake in terms of patient numbers and costs, not only of medications but other resources including laboratory services and clinic staff, based on their targeted HCV treatment population.

Education and Training

A multipronged approach was used for provider education and training. As part of the formulary requirement, treatment criteria and prescribing guidance was developed for the use of boceprevir, telaptevir, and adjunct treatments (i.e., ESAs and GCSF) to educate providers and promote appropriate use (Table 1). Likewise, extensive multidisciplinary provider education and training occurred systemwide on HCV care and treatment via live or virtual conferences. Clinical tools, such as dashboards, local CCR:HCV report functions, clinician discussion boards, and note templates, were developed to support HCV management. More intensive training focused on

expanding pharmacists' roles in HCV management as a means to increase treatment capacity. A survey was administered to pharmacists after training to assess knowledge and confidence in HCV management as a result of the training. The change in the number of VA pharmacists with a scope of practice in HCV was measured before and after training.

Appropriate Use and Clinical Outcomes

Shortly after FDA approval, when the decision was made to add boceprevir to the VA National Formulary and to make telaprevir available to providers by nonformulary request, the VA Office of Public Health began an ongoing evaluation of comparative effectiveness and safety to inform and guide formulary review and region oversight. The intent was to provide simultaneous safety, effectiveness, and quality surveillance reporting, which was supported by ongoing internal analyses of the HCV-infected veteran population receiving boceprevir or telaprevir treatment, as part of the operational commitment to provide real-time oversight and monitoring of the national formulary decision. Data from these analyses were updated approximately quarterly and presented to the VA's National Pharmacy Benefit Management Services, including region pharmacy leaders on the national formulary committee, to share information, identify needs, and address key issues that may require re-evaluation or re-review of the existing national criteria for use of these agents. These analyses were conducted as part of the ongoing administrative activities of the Office of Public Health/Population Health Program to ensure safe, effective, and efficient care for veterans with chronic HCV and did not require international review board approval.

To assess hematologic adverse effects, HCV RNA monitoring, discontinuation rates, and early and SVR, veterans were prospectively identified from the CCR:HCV and included in the cohort if they were infected with HCV genotype 1 and had initiated VA-prescribed peginterferon, ribavirin, and either boceprevir or telaprevir prior to January 1, 2012. CCR:HCV prescription dispense dates and days' supply were used to calculate boceprevir, telaprevir, and peginterferon/ribavirin treatment durations and medication possession ratios (MPR). Prescription data were also used to identify ESA or GCSF use. CCR:HCV laboratory data included HCV RNA levels to assess appropriate monitoring in accordance with criteria for use and package labeling; early virologic responses and SVR; and hemoglobin, absolute neutrophil counts, and platelet values to assess hematologic adverse effect rates and appropriate thresholds for ESA or GCSF initiation.[12,13] As data accumulated, they were shared with the VA Pharmacy Benefits Management and the national formulary committees.

Real-time oversight was provided by several methods. First, daily uptake reports were reviewed to track trends in utilization at each site across the system. Sites with no or low treatment rates, despite large numbers of potentially eligible patients, and sites with high nonformulary telaprevir use were contacted directly by a member of the National Hepatitis C Program to address barriers to access and facility-specific issues related to nonformulary use. Second, for the first 6 months after addition to the formulary, each prescription was reviewed electronically for proper dose, frequency, and food instructions, and prescribing providers were alerted to resolve any discrepancies. This consistency check was performed as a centralized process as a tertiary check that the prescriber and the validating pharmacist approved the correct patient instructions as approved by the FDA. Third, important safety and treatment issues originating from either within the VA or from the FDA were summarized and disseminated via timely e-mail communication to an updated list of field HCV providers. Key subject matter experts associated with the Hepatitis C Program office were identified for providers to address HCV treatment-related questions.

The fourth component of the population approach involved prompt outcome sharing. This was accomplished generally quarterly via presentation; virtual live webcasts; web posting; and/or e-mail distribution of national, regional, and local uptake and use patterns, adherence rates, and treatment outcomes data on DAA use in the VA system. To describe medication uptake, we reported the overall number of veterans in VA care who were prescribed a DAA in 2011 and 2012 and the number of veterans receiving boceprevir- and telaprevir-based treatment, by week, from the date of FDA approval. We also reported the percentage of veterans receiving a DAA by region and facility. Drug utilization evaluation to assess accordance with ESA and GCSF criteria for use, particularly thresholds for initiation, was reported as was early virologic and SVR rates.

Results

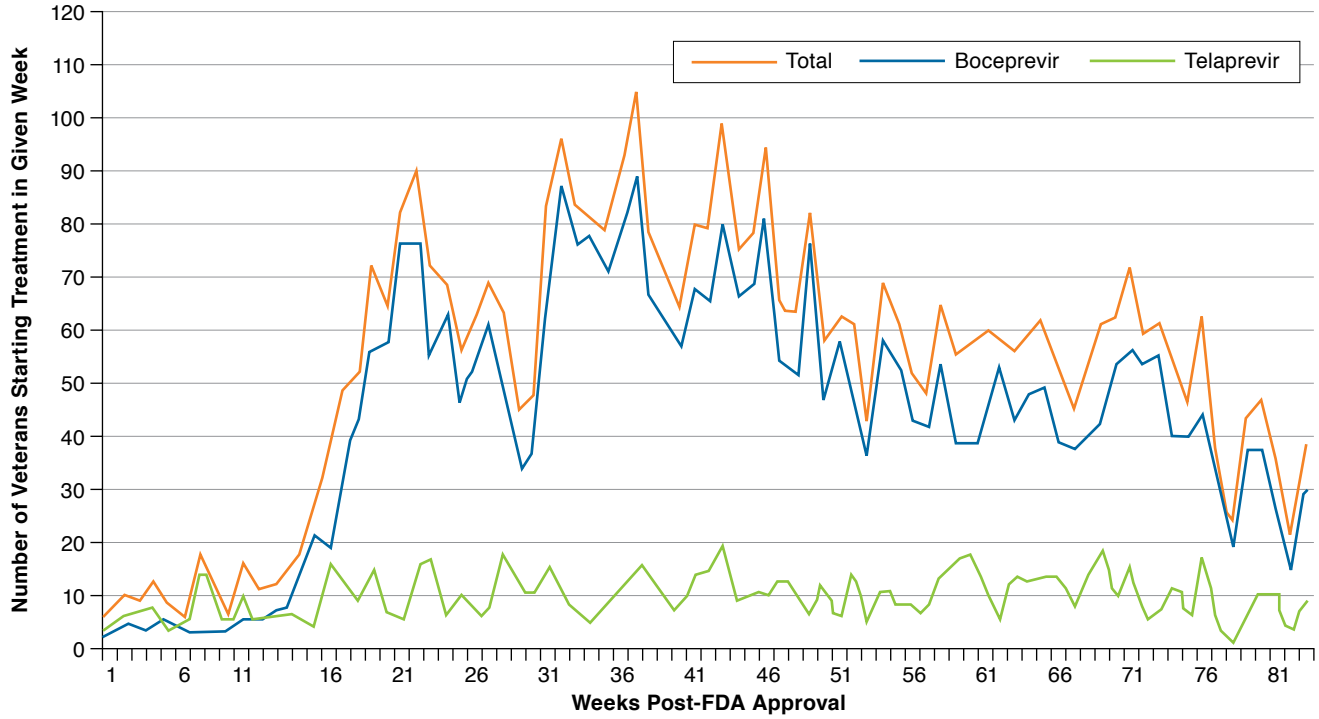
Treatment Eligibility

Using CCR:HCV data, we were able to estimate the number of potentially eligible veterans to receive DAA therapy in the VA to assist leadership and facilities in planning for expenditures. In 2010, the year prior to boceprevir and telaprevir approval, there were 96,435 viremic veterans with HCV genotype 1 infection receiving VA care, approximately 16,000 of whom had prior treatment experience. By region, the number of genotype 1 viremic veterans ranged from 1,840 veterans to 10,451 veterans and from 133 to 2,358 veterans by local facility. Of all HCV-infected veterans in VA care, the prevalence of conditions that may have precluded HCV therapy based on American Association of the Study of Liver Disease guidelines was identified as the following: depression 58%, alcohol use 55%, illicit drug use 40%, chronic obstructive pulmonary disease 20%, schizophrenia 10%, and congestive heart failure 6%.[14]

Education and Training

A live 2-day hepatitis C education conference was held in September 2011, in which over 300 VA providers were

FIGURE 1 Number of Veterans Starting Boceprevir- and Telaprevir-Based Therapy, By Week, Post-FDA Approval



FDA = U.S. Food and Drug Administration.

educated on the newest HCV treatments and corresponding VA guidelines. Furthermore, regional pharmacist-specific programs resulted in an additional 380 pharmacists who received 4 continuous hours of live, small group, case-based, concentrated HCV education and training. Postsurvey results from 228 of the 380 pharmacists attending these pharmacist trainings indicated that participants increased their knowledge regarding HCV management (88% of respondents), increased their desire to be involved in management of patients with HCV (90%), and felt more confident in their ability to manage HCV patients (72%). Over a 2-year period between May 2011 and May 2013, when these trainings occurred, the number of pharmacists with a documented scope of practice for HCV increased from 59 to 110 pharmacists—an increase of 86%. This scope of practice authorizes privileges related to drug therapy management, prescribing, and ordering and analyzing laboratory tests relevant to drug therapy.

DAA Uptake

In 2011, 865 veterans received their first DAA, and in 2012, the first full year after FDA approval, 4,062 veterans received their first DAA. The percentage of HCV viremic veterans receiving DAA treatment by region ranged from 3%-7%, and by facility, the percentage ranged from less than 1% to 17%. VA uptake of boceprevir and telaprevir from the time of FDA approval in June 2011 through April 2013 is shown in Figure 1. Within the first 6 months after FDA approval, boceprevir or telaprevir had been prescribed at 94 of 130 VA facilities. One year after FDA approval, DAAs had been prescribed at 120 of 130 VA facilities; 5 of those sites not prescribing DAAs had less than 250 HCV-infected veterans in care and were referring patients to non-VA facilities for HCV care. For the nonprescribing sites, several barriers were subsequently identified, including drug accessibility related to local budget and staffing structure, which were addressed individually with local and national HCV leaders. Providing facility-specific data on utilization trends, including the highest and lowest prescribing sites, allowed national, regional, and local facilities to identify outliers and more closely evaluate treatment and practice patterns.

Appropriate Use

Included in the DAA treatment guidance, careful virologic monitoring was required to assess for treatment futility, so therapy could be promptly discontinued to avoid the emergence of resistance. Upon review of HCV RNA assessments for all veterans receiving boceprevir or telaprevir prior to

TABLE 2 Erythropoietin-Stimulating Agent Use and Ribavirin Dose Reductions in Veterans Receiving Boceprevir- and Telaprevir-Based Regimens

Criteria Evaluated	Patients Receiving Boceprevir n/N (%)	Patients Receiving Telaprevir n/N (%)
Mean hemoglobin value at the time of ESA initiation (± SD)	9.9 ± 1.1	10.0 ± 1.8
Patients with a ribavirin dose reduction while on DAA-based regimen	294/661 (44)	76/198 (38)
Patients who received an ESA while on DAA-based regimen	168/661 (25)	51/198 (26)
Patients with a ribavirin dose reduction and ESA	117/661 (18)	28/198 (14)
Patients who received ESA without ribavirin dose reduction	51/168 (30)	23/51 (45)
Hemoglobin ≥ 10 g/dL at the time of ESA initiation	73/168 (43)	12/51 (24)

DAA = direct-acting antiviral agent; ESA = erythropoietin-stimulating agent; g/dL = grams per deciliter; SD = standard deviation.

January 1, 2012 (n = 859), 15%-17% of those who had received at least 12 weeks of treatment had not had appropriate HCV RNA futility testing as defined by FDA package labeling. The lack of HCV RNA testing at appropriate critical time points for effective treatment management was shared with national and regional leaders. To further aid providers in monitoring patients receiving DAA treatment, a new CCR:HCV report was added to assist local staff in monitoring the population receiving HCV treatment for key laboratory test monitoring. This local report allowed providers to track where patients were in their treatment course and when HCV RNA testing had been done. Within 6 months, HCV RNA futility testing improved such that only 1%-3% of veterans did not have appropriate testing.

Given the importance of medication adherence to HCV treatment success, and concerns by pharmacy leaders of the financial and effectiveness consequences of nonadherence, biannual MPR data were made available by region and facility to allow leaders to examine and address adherence locally. By region, the median and mean proportion of all veterans prescribed boceprevir with an MPR ≥ 0.95 at the first evaluation in July 2012 (n = 2,679) was 78% and 79%, respectively, and at the second evaluation in January 2013 (n = 3,497) was 76% and 76%, respectively. By region, the median and mean proportion of all veterans prescribed telaprevir with an MPR ≥ 0.95 at the first evaluation (n = 567) was 75% and 70%, respectively, and at the second evaluation (n = 653) was 80% and 76%, respectively. By facility, the proportion of veterans prescribed boceprevir with an MPR ≥ 0.95 ranged from 40%-100% (median 80%) and remained consistent at subsequent evaluations. By facility, the proportion of veterans prescribed telaprevir with an MPR ≥ 0.95 ranged from 9%-100% (median 75%) and improved slightly by the second evaluation (range 20%-100%, median 80%).

Clinical Outcomes

Concurrent with an interim 24-week safety analysis of the DAAs in the VA, established criteria for use of ESAs for DAA-related anemia and GCSF for DAA-related neutropenia were evaluated by drug utilization review. Timely feedback from the national utilization review revealed areas where criteria were not being followed. In total, 168 (25%) of the 661 veterans in the cohort who received boceprevir received an ESA; however, 30% (51/168) of those prescribed an ESA received the ESA without first dose-reducing ribavirin as indicated in the criteria for use (Table 2). Of the 198 veterans in the cohort who received telaprevir, 51 (26%) received an ESA, yet 45% (23/51) received an ESA without first dose-reducing ribavirin. Moreover, 43% and 24% of patients receiving boceprevir and telaprevir, respectively, who initiated an ESA had a hemoglobin value greater than the criteria threshold of 10 grams per deciliter (g/dL). Similarly, of the 61 (9%) veterans receiving boceprevir who also received a GCSF, 84% had an absolute neutrophil count above the criteria threshold. Although only 4 telaprevir-treated patients received a GCSF, each had an absolute neutrophil count above the criteria threshold. This review prompted action on the national, regional, and local levels. Subsequent overlapping multidisciplinary educational initiatives occurred in the year following the review to raise awareness of the appropriate use of ESAs and GCSFs for patients receiving HCV treatment with boceprevir and telaprevir. These included written communication describing VA findings, website postings of the data, and 3 live webinars highlighting the most recent data available on this topic. Several regions and local facilities have subsequently undertaken projects to examine and address the appropriate use of these adjunct agents among their local providers.

The ongoing evaluation and preliminary analytic reports of early virologic outcomes, including adverse hematologic effects, and SVR observed with the use of boceprevir and telaprevir within the VA have been consistently communicated with pharmacy benefits management and Office of Public Health leadership and shared with VA field providers. This data sharing led to informed, evidence-based decisions to modify the DAA criteria for use as necessary based on emerging data directly from our veteran HCV population undergoing treatment. Early virologic responses and the final comparative effectiveness evaluation of boceprevir- and telaprevir-based regimens among veterans treated in routine medical practice have been presented and published and can now be used by VA providers for real-world, evidence-based decision making.[15-16]

Discussion

This medication management process demonstrates a collaborative action with a comprehensive multifaceted approach spanning all VA levels, which has provided great insight into HCV treatment patterns and outcomes across this large health care system. Congruent with this process, we were able to affect change in health services, practice, outcomes, and policy in real time.[17]

Concerns regarding complicated regimens, monitoring, adverse effects, system costs, and patient selection needed to be addressed in a timely and efficient manner to ensure access to all veterans in this large health care system. By daily evaluation of uptake, we were able to more closely examine health services, particularly treatment access and patterns among regions and facilities, in order to assess treatment rates. Sharing this information with region leaders and facility HCV providers allowed those leaders to more closely examine variations that may have existed and reasons for such variation. Focused pharmacist training resulted in substantial numbers of new HCV mid-level providers delivering care.

Making data available and accessible helped inform population policy, oversight, and field stakeholders fostering appropriate HCV disease management. Comprehensive data and outcome sharing improved clinical practice as measured by improved HCV RNA monitoring and attention to adherence and further contributed to more appropriate management of DAA-related anemia with ESAs and boceprevir-related neutropenia with GCSF use. The timely evaluation and sharing of observed key safety and effectiveness outcomes validated earlier policy decisions relating to formulary status yet highlights the need for re-assessment given the unpredictability of outcomes in a real-world population. In addition to national and regional stakeholders, apprising HCV field providers with interim summaries, updated local data, presentations from national meetings, and publications provided evidence they could rely upon to support their current practice.

This approach offers insight for other health care systems or managed care organizations on population management strategies for high-impact therapies with the use of clinical data, real-time oversight and feedback, outcome sharing, and education. As demonstrated, such a strategy can be specifically used to address patient management, adherence, comparative effectiveness and safety, and appropriate utilization. This clinically focused comprehensive approach can form a template that can be utilized in a proactive manner to address other high cost, intensively managed medications or disease states. This may be particularly relevant given the simultaneous approval of 2 more new HCV medications, simeprevir and sofosbuvir, in 2013 and other HCV agents on the horizon. Although the process has been demonstrated here in the context of HCV treatment, these principles and this framework extends beyond HCV and is applicable to any population receiving treatment for any disease.

Limitations

There are several limitations to the processes we describe. The VA is a large integrated national health care system, and resources for this type of population-based medication surveillance may not be available for other settings. However, components of this approach could be adopted, modified, and implemented for most health care environments. We also recognize that other factors beyond what we evaluated may have impacted uptake, appropriate use, and management of the HCV medications.

Conclusions

By utilizing the population-based framework described herein, we were able to operationally examine the adoption of 2 novel HCV therapies in a large national health care system. Identifying potentially eligible patients to receive boceprevir- or telaprevir-based regimens allowed facilities to plan for utilization and expenditures. In this large health care system, drug uptake was rapid with nearly all sites prescribing DAAs within 1 year after approval. Focused trainings resulted in an increase in the number of pharmacists acquiring a scope of practice for hepatitis C care. Furthermore, this clinically focused, comprehensive, population-based medication management approach affected real-time change in health services, practice, and outcomes. This is evidenced by widespread and rapid DAA uptake, and improved HCV RNA monitoring, attention to adherence, and more appropriate management of DAA-related anemia with timely outcome sharing—which also provided decision makers and clinicians evidence to support current HCV practices.

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DISCLOSURES

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APPENDIX ICD-9-CM Diagnosis Codes Used to Identify Cirrhosis and Advanced Liver Disease

456.0	Espohageal varices with bleed
456.1	Esophageal varices without bleed
456.20	Esophageal varices in diseases classified elsewhere, with bleeding
456.21	Esophageal varices in diseases classified elsewhere, without mention of bleeding
567.23	Spontaneous bacterial peritonitis
571.2	Alcoholic cirrhosis of liver
571.5	Cirrhosis of liver, not otherwise specified
571.6	Biliary cirrhosis
572.2	Hepatic coma
572.3	Portal hypertension
572.4	Hepatorenal syndrome
572.8	Other sequelae of chronic liver disease
789.5	Ascites

ICD-9-CM = International Clinical Diseases, Ninth Revision, Clinical Modification.