A Window of Opportunity: Maximizing the Effectiveness of New HCV Regimens in the United States With the Expansion of the Affordable Care Act

Patients with chronic HCV have predictable overlapping comorbidities that reduce access to care. The Affordable Care Act (ACA) presents an opportunity to focus on the benefits of the medical home model for integrated chronic disease management.

New, highly effective HCV treatment regimens in combination with the medical home model could reduce disease prevalence. We sought to address challenges posed by comorbidities in patients with chronic HCV infection and limitations within our health care system, and recommend solutions to maximize the public benefit from ACA and the new drug regimen. (*Am J Public Health.* 2015; 105:457–463. doi:10.2105/AJPH.2014.302327)

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OVER 180 MILLION PEOPLE worldwide have HCV-related chronic liver disease, with an estimated yearly incidence of 17 000 and prevalence of 3.2 million people in the United States alone.[1,2] Years of undetected infection and untreated disease might culminate in hepatic fibrosis, cirrhosis, hepatocellular carcinoma, and liver transplantation, accompanied by increased morbidity and mortality. Approximately 20% of chronically infected adults develop cirrhosis within 20 years.[3,4]

Each stage of disease incurs increasing human and economic costs, with medical treatment of infected patients in the United States estimated as high as $9 billion in 2012.[5–7] Curing HCV infection, measured by a sustained virological response (negative HCV-RNA PCR) 24 weeks after the end of therapy (SVR 24), reduces mortality and the risk of hepatocellular carcinoma.[8,9] Regrettably, the reach of curative therapy has been limited by the efficacy and tolerability of past regimens.

A radical shift in standard therapy for HCV infection is occurring in which new regimens exceed 90% cure rates, eliminate injectable interferon and its attendant adverse effects, reduce dosing frequency and pill burden potentially to 1 pill daily, and reduce treatment duration to as short as 3 months. Currently, an interferon-free regimen exists for the treatment of genotype 1. It combines sofosbuvir with simeprevir. Because the efficacy trial combined drugs from separate manufacturers, the regimen is not explicitly supported by either drug label.[10] There are multiple regimens with high efficacy in genotype 1 without interferon that are expected to be approved by fall 2014.[11]

For the past decade, treatment has consisted of peginterferon (pegINF) α-2a/2b plus ribavirin, administered up to 12 months, which has clinical trial efficacy rates among genotype 1 treatment-naive patients that range from 41% to 55%.[12–14] In 2012, the efficacy of regimens for genotype 1, estimated to comprise more than 70% of HCV-infected patients in the United States, modestly improved when 2 new protease inhibitors, boceprevir[15] and telaprevir[15] were approved. However, both of these medications must be administered in addition to the standard regimen of interferon and ribavirin, add significant toxicity, and are unlikely to continue to play a significant role in future treatment regimens.

In 2013, the US Food and Drug Administration approved 2 novel HCV drugs: simeprevir,[16] an NS3/4A protease inhibitor, and sofosbuvir,[17] an oral nucleotide inhibitor of HCV polymerase. Sofosbuvir enables the first all-oral, interferon-free regimen approved for the cure of chronic HCV infection, though an indication for an interferon-free regimen for genotype 1 is not yet available. Treatment with sofosbuvir plus pegylated interferon plus ribavirin yields cure in an unprecedented 89% of genotype 1 patients in only 3 months.[17] In the near-term, other novel antiviral agents are expected to become available that will enable interferon-free regimens for genotype 1. Already, phase 2 trials have shown that sofosbuvir in combination with ledipasvir and ribavirin, without interferon, achieves 100% cure rates in genotype 1 patients without cirrhosis, with an excellent safety profile.[18]

This dramatic improvement in HCV treatment has the potential to substantially reduce the public health burden of chronic liver disease as earlier therapy yielded low efficacy, was long in duration, and had burdensome side effects that deterred both physicians and patients. Better treatment regimens could lead to more screening, more diagnoses, stronger adherence, more cures, and ultimately reduce HCV-associated cirrhosis and liver cancer, liver transplantation, mortality, and lower health care system costs associated with chronic HCV infection.

Maximizing the public health benefit from this therapeutic innovation will require addressing the barriers that US patients with chronic HCV face when attempting to access treatment. Most people in the United States with chronic HCV live in areas of high poverty, lack health insurance or rely on public insurance[19] and have

a history of injection drug use.[20] With multiple medical and behavioral health co-morbidities, patients with HCV face a fragmented health care delivery system.

Historically, the chasm between clinical trial HCV cure rates (efficacy) and cure rates in the community (effectiveness) has been considerable.[21,22] The specific efficacy-effectiveness gap in curative HCV therapy has been modeled to suggest that even a substantial improvement in the efficacy of a curative regimen alone is unlikely to move the effectiveness bar very far.[23] One model suggests that if the new antiviral treatments consistently resulted in an 80% response rate and half of all HCV-infected patients were treated, then incidence of cirrhosis would decline by 15%.[24] Consequently, to move beyond treatment efficacy to improved cure rate, greater attention must be given to the social determinants of health, consistent access to care, as well as patient and provider acceptance of treatment therapy.[25,26]

A key component of the efficacy-effectiveness gap is the readiness of the health care system to identify patients, address comorbidities, safely and effectively administer a curative regimen, reduce the risk of reinfection, and measure population-level progress. Fortunately, the Affordable Care Act (ACA)[27] represents a timely opportunity to engage HCV infected patients in care and achieve a higher community-level cure rate.

POTENTIAL BARRIERS TO NEW HCV THERAPY

New HCV regimens resolve several of the medical barriers that have prevented patients with chronic HCV from achieving cures. Moreover, with a substantial reduction of treatment duration, elimination of side effects associated with interferon-based regimens, and reduction in pill burden, it is likely that more patients will seek testing and treatment. However, as demand increases, other historical system challenges, such as workforce capacity and training, the cost of new regimens, and the costs associated with effective delivery of care will mount. These challenges cannot be underestimated.

The treatment of patients with chronic HCV in the United States will continue to be complicated by significant medical comorbidities, including substance use disorders,[28] mental illness,[29] hepatitis B, and HIV.[30] One study of intravenous drug users found the HCV/HIV coinfection rate to be 26%,[31] an ominous finding since HIV might accelerate progression of HCV liver disease.[32] Still, perhaps no other comorbidity is as consequential as substance use disorders. Intravenous drug use is the most common risk factor for acquiring HCV infection,[20] but noninjection drug use is a risk factor as well, suggesting the importance of behavioral disinhibition in the ongoing transmission of HCV.[33] In turn, untreated substance use disorders compromise treatment adherence (even to 3-month regimens), predispose patients to reinfection, and might exacerbate the potential development of antiviral resistance.[30,34]

Though guidelines encourage HCV treatment in drug users,[25,35] several studies have indicated that only 1% to 6% of drug users receive antiviral therapy.[36,37] Despite evidence that HCV treatment efficacy among patients engaged in opioid treatment is similar to those without a history of substance abuse, physicians appear reluctant to prescribe therapy to intravenous drug users due to anticipated poor adherence, comorbid mental illness and concern for deterioration with interferon therapy.[38,39] In turn, population treatment rates might not improve uniformly even as highly effective and tolerable short-course regimens become available.[40,41]

Even as improved HCV treatment regimens might stimulate physicians to offer and patients to seek HCV treatment, the long-term success of that interaction will depend on a sustained campaign to align the medical care and substance use disorders treatment systems.[42] Despite policy advances,[43] earlier concerns about publicly funded patients' limited access to specialty behavioral health care[44,45] have reemerged.[46,47] Historically, the substance abuse specialty care treatment system has been segregated from its medical counterpart.[48] Not surprisingly, intervention rates for substance use disorders in primary care have been lower than for other behavioral health issues, including physician recommendations for patients to exercise (35%),[49] lose weight (42%),[50] and quit smoking (37%).[51] In fact, fewer than 11% of all patients diagnosed with alcohol dependence (*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV]*)[52] or alcohol use disorder (*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [DSM-V]*)[53] in primary care received an indicated treatment referral.[54] Historically, weak counselor retention, inadequate professional development, limited Medicaid billing[55] and a dearth of electronic health record systems,[56] constrained integration with primary care.[57]

Successful and sustained disease identification and intervention is predicated on robust, integrated systems.[58] Treatment integration can occur in any number of ways including external referrals, colocation, and service integration.[59] Under the latter, one potential strategy is to increase the integration of HCV therapy with primary care pharmacotherapy for opiate dependence (*DSM-IV*),[52] or opiate use disorders (*DSM-V*[53]; e.g., buprenorphine/naloxone or methadone maintenance therapy), since treating individuals with opiate use disorders for HCV reduces the risks of rapid reinfection, constrains costs related to repeated treatment, and diminishes the risk of HCV drug resistance.[60,61]

Both buprenorphine/naloxone and methadone medical maintenance can be successfully administered by physicians in office-based settings.[62,63] However, office-based buprenorphine/naloxone and methadone maintenance treatment in primary care remains limited.[64,65] In addition, despite earlier evidence,[66] a recent study suggests that brief behavioral intervention strategies delivered in primary care without pharmacotherapy are not effective in reducing drug use.[67] As such, until primary care buprenorphine/naloxone or methadone maintenance treatment becomes more widely available,[68] in light of current barriers to integration,[69] models that rely on colocation and enhanced referrals will be critical for treating drug-related substance use disorders among patients infected with HCV.[69,70]

Moreover, because methadone maintenance is offered under strict governmental and medical oversight,[71] primary health care centers might want to coordinate HCV treatment with opioid treatment programs.[72] Including HCV treatment within opioid treatment programs and prisoner release programs might prove an effective strategy for reducing disease

prevalence.[73] In addition, coordinated treatment of addiction and HCV might prove synergistic to medically stabilize the patient and facilitate substance use disorders treatment engagement.[74]

Beyond the clinical complexities of managing comorbidities lies the challenge of improving the capacity of the US health care system to deliver curative HCV regimens and measure success. Most states do not submit reports of HCV seroprevalence to the Centers for Disease Control and Prevention (CDC).[75] Indicative of these limits, in 2010 the CDC estimated that the total number of newly acquired (i.e., acute) infections in the United States to be 17 000,[2] while during the same year the city of New York, New York, where the health code mandates laboratory reporting of HCV infections, logged 9992 newly identified cases.[76] Without accurate surveillance, the success of a population-based treatment approach will be difficult to measure. According to the Institute of Medicine,

> surveillance data do not provide accurate estimates of the current burden of disease, are insufficient for program planning and evaluation, and do not provide the information that would allow policy-makers to allocate sufficient resources to viral hepatitis prevention and control programs.[77(p3)]

To effectively reduce disease prevalence, a comprehensive disease surveillance system for HCV is needed. HCV screening, which was once time consuming and expensive, has advanced so that screening tests for HCV infection can be conducted with a new sensitive and specific point of care test which delivers results in 20 minutes. Improved detection and surveillance are achievable.

Amid advances in HCV screening and treatment, there is ongoing concern regarding primary care workforce shortages and a lack of provider education.[78,79] Even as gastroenterologists, infectious disease specialists, primary care physicians, and non-physician clinicians are all potential providers, programs to train a definable workforce with consistent quality standards, including attention to comorbidities, will be critical to successfully bridge the efficacy-effectiveness gap. Innovative health care delivery models, such as specialty consultation via telemedicine, should be considered to extend treatment opportunities to high need, medically underserved areas.[80] Moreover, targeted telemedicine could reduce disease prevalence by promoting treatment integration and access to improve historically low treatment rates for racial and ethnic minorities.[81,82] Furthermore, new HCV treatment regimens underscore the need for a coordinated public health response that should include prevention of new infections, screening, social support and medical management for those infected.[77]

Although there has been strong evidence supporting the cost effectiveness of both HCV screening[83] and treatment,[84,85] many states are not expanding health coverage under the ACA, making a coordinated effort to reduce HCV among high-risk populations particularly challenging. As of September 30, 2013, for example, 21 states limited Medicaid eligibility to less than 100% of the federal poverty level while just 24 states expanded coverage to meet ACA standards.[86] In addition, medication approval processes vary by state and some Medicaid payment policies preclude same-day billing and tightly restrict reimbursement.[87] Although the Centers for Medicare and Medicaid Services (CMS) will almost certainly negotiate a discount for new HCV medications, both simeprevir and sofosbuvir might face availability restrictions[88,89] as governments weigh the costs of curative pharmaceutical regimens against the costs of chronic liver disease, cirrhosis, liver cancer, and liver transplant.[84,85]

OPPORTUNITIES AFFORDED BY THE AFFORDABLE CARE ACT

One specific aim of the ACA is to integrate medical and behavioral health care.[90] In turn, the ACA expands Medicaid eligibility, offers health care consumers premium subsidies through state health insurance exchanges, defines substance abuse treatment as an essential benefit, and confers parity between substance abuse disorders and medical care treatment.[91] The law will extend medical and behavioral health care[92] coverage for up to an additional 14 million people.[93]

The ACA also includes a prohibition against copayments for US Preventive Services Task Force (USPSTF) grade A and B recommendations,[90] effectively lowering patients' out of pocket costs and potentially improving providers' adoption of the USPSTF grade B recommendation to screen patients at highest risk for chronic HCV and those born between 1945 and 1965.[94] Given that at least half of all infected HCV patients do not know that they are infected,[95] expanded insurance coverage under the ACA in combination with new pharmacotherapy innovations could increase screening and treatment rates to reduce disease prevalence.

HCV infection tends to concentrate among the poor and disadvantaged. Thirty percent of those infected have no insurance and 43% rely on government insurance.[19] By law, Federally Qualified Health Centers (FQHCs) must treat the uninsured. Not surprisingly, 72% of current FQHC patients live in poverty, 39% are served by Medicaid and 8% by Medicare, and 36% are uninsured.[96] In 2012, FQHCs reported screening 225 775 patients for HCV infection, identified a HCV diagnosis among 132 078 patients and 254 348 patients with a primary substance use disorder diagnosis, excluding alcohol and tobacco.[97] These patient numbers are nearly certain to increase as ACA implementation continues.

Under the ACA expansion, two thirds of newly insured patients will be served by FQHCs and look alikes,[98] which will effectively double the number of FQHC patients.[99] In anticipation of increased patient demand, both the American Recovery and Reinvest Act[100] and the ACA supported workforce development for health shortage areas; the latter established the Community Health Center Fund, which provides $11 billion over 5 years for the expansion, construction, and operation of health centers.[101]

The expansion has direct bearing on HCV rates as health center growth will target areas of high poverty. Furthermore, patients with a regular source of care are more likely to receive and initiate recommended screenings[102] and are less likely to delay treatment.[103] Moreover, under the ACA, formerly uninsured patients with behavioral health needs might have less difficulty accessing specialty care.[104] As such, the ACA has the potential to substantially improve HCV screening and treatment rates among the poor.

Beyond insurance coverage and capital expansions, the ACA provides numerous incentives to improve quality, improve care

coordination, and reduce costs, especially for patients with one or more chronic condition. Robust medical evidence supports the ability of chronic disease management, including integrated behavioral health management,[105,106] to improve health and to reduce medical sequelae, including hospitalizations.[107–110] The ACA also directly supports the creation of Patient Centered Medical Homes (PCMH), providing comprehensive, coordinated, and continuous patient-centered care led by a primary care provider.[111]

Under the legislation, health homes, the Medicaid equivalent of PCMH, are to be comprised of a team of health professionals capable of providing comprehensive services. Six chronic conditions are explicitly named: mental health condition, substance use disorders, asthma, diabetes, heart disease and having body mass index (BMI; weight in kg divided by height in m^2) over 25. States might opt to cover additional conditions.[90] To be eligible for a Medicaid health home, patients must have 2 or more conditions, or 1 chronic condition and be at risk for a second, or a serious and persistent mental health condition.[86] Importantly, to qualify for health home reimbursement rates, FQHCs must receive PCMH certification by the National Committee for Quality Assurance. At the end of 2010, National Committee for Quality Assurance had certified more than 1500 FQHC practices as PCMHs.[112]

Although adding HCV as a qualifying condition to the Executive Office of Health and Human Services' original list of 6 is preferred, most HCV-infected patients have a qualifying comorbidity.[20,28,113] As such, new HCV pharmacotherapy regimens with improved efficacy and reduced duration could be nested within a chronic care model[108] that integrates behavioral health,[105] combats undertreatment,[74] and avoids reinfection and the potential development of antiviral resistance.

A WAY FORWARD

We believe that the ACA rollout can be harnessed to realize a tremendous public health impact from these new curative HCV regimens. Translating unprecedented efficacy and tolerability into broad effectiveness will require implementation through a more integrated health care system that has the capacity to intervene and track progress across medical and behavioral health. To support this, the following recommendations are offered:

(1) *Develop and maintain a national surveillance system.* As recommended by the Institute of Medicine, a national surveillance system is needed, including a thorough surveillance evaluation by the CDC and the development of collaborative agreements by CDC with states and territories to support core HCV surveillance.[77] A successful system will include full implementation of HCV screening in primary care for patients at risk as per CDC[2] and USPSTF[94] recommendations. Our capacity to meet the population health goals set forth in the ACA and to reduce health disparities will be severely limited unless we can accurately measure disease prevalence.

(2) *Enhance primary care providers' capacity to screen and treat HCV.* As recommended by the Institute of Medicine, CMS should adopt guidelines for HCV screening and assure that infected patients receive appropriate medical management. Similarly, the US Congress should provide resources to the Health Resources and Services Administration (HRSA) for FQHCs in high prevalence areas for comprehensive viral-hepatitis services.[77] In addition, the CDC should continue to work with state and local governments and other partners to develop HCV educational programs for health-care providers.[77]

(3) *Develop and test best practices for integrated behavioral and medical care HCV treatment.* Federal funding should be made available to adapt the collaborative care model,[105,106] chronic care model[114] and other paradigms. Innovative models to train and support primary care providers using telemedicine have been tested in rural areas,[80] and urban replications are happening.[76] The models should be further assessed and scaled for adoption.

(4) *Improve primary care and substance abuse treatment integration.* Greater buprenorphine/naloxone or methadone maintenance treatment availability in primary care,[63] colocation of substance abuse treatment, and stronger referral practices[69] are needed to curb new HCV infections. Given the evidence,[38,39] a substance use disorder diagnosis, including injection drug use, should not preclude HCV treatment. Lastly, the Substance Abuse Mental Health Services Administration and other federal agencies might want to further assess the feasibility of Opioid Treatment Programs' capacity to actively treat HCV infections.[73,115,116]

(5) *Expand local and national primary and secondary HCV prevention efforts.* Increase primary and secondary prevention efforts at opioid treatment programs, correctional facilities and community based organizations, including needle exchange programs as recommended by the IOM.[77]

(6) *Assess costs.* Given the rapidly changing patient population,[117] drug regimen, and insurance response,[118] an assessment of the costs related to HCV is beyond the scope of our analysis. Still, at nearly $1000[118] per pill, the costs of the new treatment regimen must be reconciled with population health needs.

The FQHC system, in combination with the ACA and US Food and Drug Administration approval of improved, all-oral, short-course, curative therapy for chronic HCV infection, presents a dramatic public health opportunity to reduce the prevalence of HCV. With sufficient infrastructure support, HCV regimens could be delivered across integrated care settings in combination with substance use disorders therapies to drastically reduce underdiagnosis and under-treatment and to avoid the too-predictable outcomes of reinfection and subsequent antiviral resistance. Consequently, a concentrated effort might dramatically reduce chronic HCV prevalence. ■

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This article was accepted September 13, 2014.

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S. J. Haley conceptualized the essay and led the writing. M. J. Kreek provided critical technical expertise and assisted with revisions.

Acknowledgments

We wish to thank Marshall Fordyce, MD, Director of Clinical Research at Gilead Sciences, Inc. for helpful discussions regarding the concept for this article, organizational and editorial help, and review of data supporting new HCV regimens. The authors thank Michal Blum, MPH, for her administrative support and the four anonymous reviewers for their terrific comments. In addition, M. J. K. gratefully acknowledges support from the Adelson Medical Research Foundation.

Human Participant Protection

No institutional review board approval was necessary because the research did not involve human participants.

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A Comprehensive Approach to Address the Prescription Opioid Epidemic in Washington State: Milestones and Lessons Learned

An epidemic of morbidity and mortality has swept across the United States related to the use of prescription opioids for chronic noncancer pain. More than 100 000 people have died from unintentional overdose, making this one of the worst manmade epidemics in history.

Much of health care delivery in the United States is regulated at the state level; therefore, both the cause and much of the cure for the opioid epidemic will come from state action.

We detail the strong collaborations across executive health care agencies, and between those public agencies and practicing leaders in the pain field that have led to a substantial reversal of the epidemic in Washington State. (*Am J Public Health.* 2015; 105:463–469. doi:10.2105/AJPH.2014.302367)

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PRESCRIPTION OPIOID–related morbidity and mortality constitute a national public health crisis, requiring an urgent need for more effective policy responses.[1,2] States play a central role in protecting public health and public safety; regulate health care and practice of health professions; are primary payers of health care through Medicaid, state employee benefits, corrections, and workers' compensation; and manage prescription drug monitoring programs. Therefore, state-level action is critical to reversing the prescription drug overdose epidemic.[3]

In recent years, a number of states have engaged in efforts to address prescription drug overdose. Documentation of state experience in implementing interventions and their impacts is greatly needed. This information can inform other states' efforts and prevent them from pursuing policies that have minimal impact. Washington State has been an innovative leader in efforts to reduce prescription drug overdose. In this article, we detail Washington's experience to comprehensively address this serious public health threat.

THE ORIGINS OF THE EPIDEMIC IN WASHINGTON STATE

Use of chronic opioid therapy was historically reserved for patients with cancer or end-of-life pain. The shift toward more liberal use of opioids for chronic, noncancer pain (CNCP) began in the mid- to late 1980s when an early case series suggested that patients with CNCP, if well chosen, could take opioids long term safely and with few severe problems (e.g., abuse or addiction).[4] On the basis of this study and similar studies, pain advocacy groups and specialists sought state-based regulatory changes to reverse perceived undertreatment of chronic pain.[5] These organizations successfully lobbied state medical boards and legislatures to change statutes and regulations to ensure more permissive use of opioids in the CNCP population, and to reduce the risk of sanction for prescribers. By January 2003, only 5 states and the District of Columbia had not changed their statutes or regulations.[6]