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Review

Evidence-based interventions to enhance assessment, treatment, and adherence in the chronic Hepatitis C care continuum

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ABSTRACT

Background: With the explosion of newly available direct acting antiviral (DAA) Hepatitis C virus (HCV) treatments that demonstrate 95% sustained virologic response (SVR) rates, evidence-based strategies are urgently needed to achieve real-world effectiveness in challenging patient populations. While HIV is incurable, lessons from over 30 years of experience overcoming obstacles to the HIV treatment cascade could be applied to the HCV context.

Methods: Using Institute of Medicine guidelines, we conducted a systematic review of published interventions from PubMed, Medline, GoogleScholar, EmBASE, and PsychInfo bibliographic databases and citation indices. Abstracts were first screened by three independent reviewers and studies were included if they involved original research, described a specific intervention, were published in English in a peer-reviewed journal between 2001 and 2014, and had full text available.

Results: Evidence-based interventions to enhance HCV assessment, treatment, and adherence generally fell into one of 4 categories, including those involving: (1) diagnosis or case-finding; (2) linkage to HCV care; (3) pre-therapeutic evaluation or treatment initiation; or (4) treatment adherence. While most available eligible studies described interventions using non-contemporary interferon-based HCV treatments, future research will need to address how these interventions apply to the context of well-tolerated, simple, oral treatment regimens. In some cases, we explored how HIV-specific interventions might be modified to fit the HCV spectrum of care engagement.

Conclusions: Evidence-based interventions should be strategically incorporated into HCV treatment implementation efforts to most effectively deliver treatment and maximize treatment outcomes.

Background

A variety of new therapeutic options have recently emerged to meet the treatment needs of people living with chronic Hepatitis C virus (HCV) infection (Pawlotsky, 2014). The goal of treatment is cure, defined as sustained virologic response (SVR), to avert major complications of HCV, including cirrhosis, hepatocellular carcinoma, and death. Chronic HCV treatment is transformed with new direct acting antivirals (DAAs) that can cure >95% of infections with short-course, simple and well-tolerated regimens. From a public health perspective, HCV prevalence can be reduced if available treatment is not only expanded, but targeted to those most likely to transmit the virus (Martin et al., 2013; Martin, Foster, Vilar, Ryder, & Gordon, 2015; Martin, Vickerman, Goldberg, & Hickman, 2015; Rolls et al., 2013). It is therefore imperative to examine effective strategies to improve treatment outcomes along the entire chronic HCV care continuum from diagnosis through "cure" and have evidence to treat patients deemed by providers as being "challenging."

To translate the promise of clinical trial efficacy into real-world effectiveness, however, well-executed action plans, appropriate resource allocation (Mondelli et al., 2014), and comprehensive

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public health policies (Dalgard & Mauss, 2014) are urgently needed (Department of Health and Human Services, 2014). Evidence-based interventions are critical tools to effectively engage individuals with chronic HCV in care and treatment, since many have underlying comorbid psychiatric and substance use disorders, HIV, and social instabilities (like homelessness and incarceration) that complicate care delivery (Hellard, Sacks-Davis, & Gold, 2009). Among people who inject drugs (PWIDs), the HCV seroprevalence is 60–80% globally, and drug injection is the major driving force behind the HCV pandemic (Nelson et al., 2011). With adequate support, however, PWIDs can overcome social and structural barriers to achieve parity with other people with HCV in terms of treatment success (Robaeys et al., 2006; Soriano & Gallego, 2013; Sylvestre, 2005; Zeremski et al., 2013). A scale-up of antiviral treatment options requires a parallel expansion of evidence-based interventions, like medication-assisted therapies with methadone, buprenorphine (e.g. both better classified as opioid agonist treatments; OAT) and high-coverage needle and syringe exchange programs (NSP), that support effective treatment dissemination and reduce HCV incidence (Martin et al., 2013).

The so-called "continuum of care" (Gardner, McLees, Steiner, Del Rio, & Burman, 2011) provides a useful framework to discuss strategies for intervention. In order to ultimately achieve SVR, individuals must: (1) first be tested for, diagnosed with, and made aware of their HCV infection; (2) then engage with a healthcare provider with treatment knowledge and capacity; (3) then be evaluated for and (4) initiate treatment; (5) adhere to and complete treatment and (6) prevent re-infection. Recent estimates suggest that nearly half of people with HCV remain undiagnosed or unaware of their HCV infection and less than 10% with chronic HCV effectively achieve SVR (Irving et al., 2006; Mondelli et al., 2014; Yehia, Schranz, Umscheid, & Lo Re, 2014). Clinical pathways are frequently neither linear nor continuous, so interventions must often target one or more steps along the care continuum (Robaeys et al., 2013).

While we are just beginning to understand and shape the chronic HCV care continuum, the HIV treatment community has been grappling for decades with care engagement issues (Lazarus et al., 2014). Although HIV, unlike HCV, is currently incurable and requires lifelong commitment to daily medications, the two chronic viral infections are similar in terms of epidemiology, routes of transmission, and associated stigma, and many people live with both HIV and HCV. Moreover, both HIV and HCV disparately affect individuals marginalized from systems of care, by virtue of their race/ethnicity, socioeconomic status, health illiteracy, substance use, and interactions with the criminal justice system. As such, where there is a paucity of data on HCV-related interventions, we extrapolate from the HIV literature (Kamarulzaman & Altice, 2015; Meyer, Althoff, & Altice, 2013). In doing so, we address the call to apply lessons learned from the HIV epidemic to identify specific interventions that have high likelihood to facilitate the chronic HCV care continuum (Lazarus et al., 2014). Whereas models of care have previously been reviewed (Bruggmann & Litwin, 2013), we focus instead on specific evidence-based intervention strategies. The purpose of this systematic review was to identify and synthesize data on evidence-based interventions that strategically target one or more steps along a chronic HCV care continuum (Fig. 1).

Methods

We systematically reviewed published scientific literature using Institute of Medicine guidelines (Institute of Medicine, 2011). We first searched PubMed, Medline, Google Scholar, EmBASE, and PsychInfo using key words "Hepatitis C," "surveillance," "testing," "adherence," "treatment," and "intervention"; additional references were extracted from citation indices. Titles and abstracts were then screened by three independent authors (JPM, YM, and RM) for the following inclusion criteria: in English, full text available, original research, described an intervention with measurable outcomes, and published between 2001 and 2014 (2001 was chosen because this was the year that pegylated interferon first became available). Full texts of included abstracts were then further reviewed and critical data were extracted for analysis, using a standardized tracking sheet. Final studies were selected through an iterative process involving three authors (JPM, YM, and RM), in which the inclusion criteria described above were applied to each manuscript and selected manuscripts were categorized by topic area. Where disagreement about classification occurred, the third reviewer broke the tie. Because the chronic HCV treatment cascade of care is rapidly evolving, there is no single definition of "linkage to care." Some studies describe "linkage" in terms of completing a referral for specialty care, whereas others equate "linkage" with undergoing fibrosis staging or initiating treatment. To include all possible studies, we defined "linkage to care" interventions as those with the common purpose of shifting HCV-diagnosed individuals towards HCV-specific care for further evaluation and treatment. With the simplicity of treatment with newer DAAs, however, treatment may move towards primary care venues (Westergaard et al., 2014). Specific details about quantity of and reasons for exclusions are described in Section "Results" that follows. Beyond the HCV-specific systematic review, for each

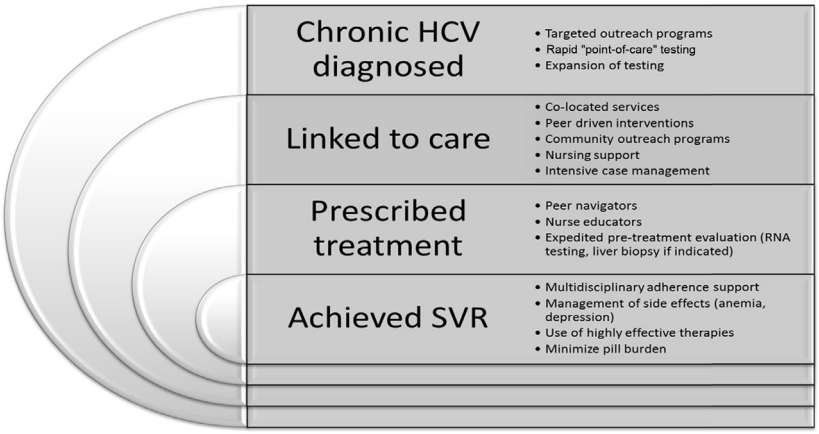

Fig. 1. Overview of the continuum of care for chronic Hepatitis C virus with targeted interventions. HCV, Hepatitis C virus; SVR, sustained virologic response.