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Editors' Choice

Recommendations for the management of hepatitis C virus infection among people who inject drugs

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ABSTRACT

In high income countries, the majority of new and existing hepatitis C virus (HCV) infections occur among people who inject drugs (PWID). In many low and middle income countries large HCV epidemics have also emerged among PWID populations. The burden of HCV-related liver disease among PWID is increasing, but treatment uptake remains extremely low. There are a number of barriers to care which should be considered and systematically addressed, but should not exclude PWID from HCV treatment. The rapid development of interferon-free direct-acting antiviral (DAA) therapy for HCV infection has brought considerable optimism to the HCV sector, with the realistic hope that therapeutic intervention will soon provide near optimal efficacy with well-tolerated, short duration, all oral regimens. Further, it has been clearly demonstrated that HCV treatment is safe and effective across a broad range of multidisciplinary healthcare settings. Given the burden of HCV-related disease among PWID, strategies to enhance HCV assessment and treatment in this group are urgently needed. These recommendations demonstrate that treatment among PWID is feasible and provide a framework for HCV assessment and

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care. Further research is needed to evaluate strategies to enhance testing, linkage to care, treatment, adherence, viral cure, and prevent HCV reinfection among PWID, particularly as new interferon-free DAA treatments for HCV infection become available.

Introduction

In high income countries, 50–80% of hepatitis C virus (HCV) infection is among people who inject drugs (PWID), and HCV epidemics have emerged among PWID in many low and middle income countries (Hajarizadeh, Grebely, & Dore, 2013). Within this population are 'current' or 'recent' PWID (Larney et al., 2015), who are at risk of transmitting and acquiring HCV infection (there are varying definitions in the literature, although one month to one year is most common (EMCDDA, 2010; WHO, 2012)). 'Former' PWID (people who have ceased injecting drug use) are also of importance, as a large proportion of existing HCV infections are found in this group (Larney et al., 2015). Given the relapsing nature of drug dependence, determining a cut-off to define permanent vs short-term cessation of injecting drug use (and therefore 'current'/'recent' vs 'former' PWID) is problematic (Larney et al., 2015). These guidelines, however, are predominantly developed for clinical management of HCV in the current PWID population and the term PWID will in general relate to this population. Given a large proportion of PWID have been HCV-infected for two or more decades, many have progressed to advanced fibrosis (Grebely & Dore, 2011; Hajarizadeh et al., 2013). Rates of advanced liver disease complications, associated healthcare costs, and liver-related morbidity and mortality among PWID continue to rise (Grebely & Dore, 2011; Hajarizadeh et al., 2013).

Until recently, HCV treatment guidelines excluded PWID, due to concerns about poor adherence, adverse events and re-infection (NIH, 1997). Successful HCV treatment studies among PWID challenged this paradigm (Alvarez-Uria, Day, Nasir, Russell, & Vilar, 2009; Aspinall et al., 2013; Backmund, Meyer, Von Zielonka, & Eichenlaub, 2001; Bruggmann et al., 2008; Dalgard, 2005; Dimova et al., 2013; Dore et al., 2010; Grebely, Genoway, et al., 2007; Grebely et al., 2010; Grebely, Raffa, et al., 2007; Guadagnino et al., 2007; Hellard, Sacks-Davis, & Gold, 2009; Jack, Willott, Manners, Varnam, & Thomson, 2009; Jafferbhoy et al., 2012; Jeffrey et al., 2007; Lindenburg et al., 2011; Manolakopoulos et al., 2010; Martinez et al., 2010; Matthews, Kronborg, & Dore, 2005; Mauss, Berger, Goelz, Jacob, & Schmutz, 2004; Melin et al., 2010; Neri et al., 2002; Papadopoulos, Gogou, Mylopoulou, & Mimidis, 2010; Robaeys et al., 2006; Sasadeusz et al., 2011; Schaefer et al., 2003, 2007; Sylvestre, 2002; Sylvestre, Litwin, Clements, & Gourevitch, 2005; Van Thiel, Anantharaju, & Creech, 2003; Van Thiel et al., 1995; Waizmann & Ackermann, 2010; Wilkinson et al., 2009). International guidelines from the American Association for the Study of Liver Disease (AASLD)/Infectious Diseases Society of America (IDSA), the European Study for the Association of the Liver (EASL), the International Network for Hepatitis in Substance Users and the World Health Organization now all recommend treatment for HCV infection among PWID (AASLD/IDSA, 2015; European Association for Study of Liver, 2014; Robaeys et al., 2013; WHO, 2014).

Despite revised guidelines, few PWID have received HCV treatment (Alavi et al., 2014; Grebely et al., 2009; Iversen et al., 2014; Mehta et al., 2008; NCHECR, 2009; Strathdee et al., 2005). Enhanced HCV assessment and treatment in PWID will be required to reduce future HCV-related morbidity and mortality (Hutchinson, Bird, & Goldberg, 2005b). The availability of effective, tolerable and simpler interferon-free direct acting antiviral (DAA) regimens should improve the feasibility of this approach (Dore & Feld, 2015). The International Network for Hepatitis in Substance Users (INHSU) established an expert panel to develop recommendations to enhance HCV assessment, management and treatment among PWID, with the first recommendations published in 2013 (Robaeys et al., 2013). These recommendations have been updated to reflect the rapidly changing landscape of HCV therapy and have been updated to be in line with the methodologies used by international guidelines from AASLD and IDSA (AASLD/IDSA, 2015).

Methods

The guidance is presented in the form of RECOMMENDATIONS. Each RECOMMENDATION is rated in terms of the level of the evidence and strength of the recommendation, using a scale developed by AASLD/IDSA (AASLD/IDSA, 2015). Recommendations are based on scientific evidence and expert opinion (Table 1). Each recommended statement includes a Roman numeral (I, II, or III) that represents the level of the evidence that supports the recommendation, and a letter (A, B, or C) that represents the strength of the recommendation.

Epidemiology and prevention of HCV

HCV prevalence among PWID populations ranges from <20% to >80% (mid-point HCV estimate: 67% antibody positive; 50% RNA positive), with a global estimate of 10 million HCV antibody positive PWID (7.5 million with chronic HCV infection) (Hagan, Pouget, Des Jarlais, & Lelutiu-Weinberger, 2008; Nelson et al., 2011). HCV genotypes 1a, 1b, and 3a are common among PWID (Pybus, Cochrane, Holmes, & Simmonds, 2005), 4d is common among PWID in Europe (van Asten et al., 2004), and 6 in Southeast Asia (Sievert et al., 2011). HCV incidence among PWID also varies considerably from 2% to 66% per annum (Hagan et al., 2008; Page, Morris, Hahn, Maher, & Prins, 2013; Wiessing et al., 2014). Studies on time to HCV infection have demonstrated highest incidence in the initial years of injecting (Hagan et al., 2008; Roy, Boudreau, & Boivin, 2009).

High coverage of combined harm reduction programs (opioid substitution treatment [OST] and needle and syringe programs [NSP]) can reduce HCV incidence (Degenhardt et al., 2010; Hagan, Pouget, & Des Jarlais, 2011; MacArthur et al., 2014; Turner et al., 2011; van den Berg et al., 2007). Further, recent evidence has corroborated the impact of OST alone, reporting HCV transmission reductions by 50–80% (Aspinall et al., 2014; Nolan et al., 2014; Tsui, Evans, Lum, Hahn, & Page, 2014; White, Dore, Lloyd, Rawlinson, & Maher, 2014). Additional beneficial effects of OST dose–response (Nolan et al., 2014) and adjunct therapy during OST (Wang et al., 2014) have been observed.

Several modeling studies suggest that HCV treatment for PWID can lead to substantial reductions in HCV prevalence and reduce transmission (de Vos, Prins, & Kretzschmar, 2015; Hellard et al., 2014; Martin, Hickman, Hutchinson, Goldberg, & Vickerman, 2013; Martin et al., 2011; Martin, Vickerman, et al., 2013), particularly when combined with other "harm reduction' interventions such as NSP and OST (Martin, Hickman, et al., 2013). Therefore, a combination prevention strategy including HCV treatment as prevention is critical for achieving reductions in HCV prevalence/