

REVIEW

Accessing Hepatitis C patients who are difficult to reach: it is time to overcome barriers

P. Bruggmann *Arud Centres of Addiction Medicine, Zurich, Switzerland*

Received August 2012; accepted for publication September 2012

SUMMARY. With the arrival of simple, efficient and safe interferon-free treatment regimens, hepatitis C virus (HCV) therapy will have the potential to be successfully used for the majority of infected patients and prevent the associated morbidity and mortality. With the current treatment uptake rates, only a very small proportion of HCV-infected patients are reached. Paradoxically, treatment rates are lowest in the most affected at-risk group – people who inject drugs (PWID) – which is the major driving force behind the spread of HCV infection. To conquer the

increasing problem of HCV-related liver disease, many existing but modifiable obstacles, which prevent detection, assessment and treatment uptake, have to be overcome in this population. This review article summarizes the existing literature on the most relevant barriers preventing HCV care and describes measures to overcome these obstacles.

Keywords: barriers, drug user, hepatitis C virus, injecting drug use, people who inject drugs, treatment uptake.

INTRODUCTION

During the next decade, tolerability and efficacy of hepatitis C virus (HCV) therapy will improve remarkably [1,2]. With the expected interferon-free regimens, high treatment success rates for all genotypes will become available. Many barriers to treatment imposed by the side effects of interferon will disappear. However, one major barrier will remain, irrespective of increased efficacy and tolerability of future HCV treatment regimens: limited access to tests and therapy.

In the western world, the main driving force behind HCV infections is injecting drug use (IDU). Worldwide, about 10 million people who inject drugs (PWID) are HCV antibody positive. The mid-point HCV antibody prevalence in this at-risk group is 67.5% [3].

People who inject drugs are affected by several comorbidities, such as alcohol dependence, HIV infections and mental diseases with concomitant chronic psychopharmacological medication. All of them compromise liver function and increase liver-related morbidity and mortality [4–6]. HCV, however, can be cured. The burden of advanced HCV-related liver disease among PWID is growing [5,6], when it could in fact be reduced with

higher treatment uptake rates [7,8]. Furthermore, mathematical models predict reduced transmission rates resulting from increased therapy rates [9–11]. Despite this, treatment uptake rates remain low in general [12] and in the drug-using population in particular [13–17]. With the current treatment uptake rates in the United States, antiviral treatments between 2002 and 2030 will prevent only 14% of liver-related deaths caused by HCV [18]. Hence, PWID as the major at-risk group and a virus reservoir are not yet reached well enough with HCV care. Besides developing highly efficient and well-tolerated HCV compounds, the main effort in global HCV care should focus on overcoming barriers to HCV testing, assessment and therapy. As PWID will be responsible for the main future burden of HCV-induced disease, improved access to this population should be the main goal.

To access patients, such as PWID, who are difficult to reach means breaking down barriers at healthcare system level, provider level, but also, indirectly, at individual patient level. Even if a person who uses drugs is ready for therapy, the provider (e.g. general practitioner (GP) or specialist) and/or the healthcare system are often not [19]. This review article gives an overview on modifiable factors preventing HCV care and describes different approaches and patient management settings to overcome these obstacles in the underserved population of PWID.

TESTING: THE FIRST STEP TO THERAPY

Improving access to therapy means first and foremost improving access to testing. Literature on HCV testing

Abbreviations: GP, general practitioner; HCV, hepatitis C virus; IDU, injecting drug use; OST, opioid substitution therapies; PWID, people who inject drugs.

Correspondence: Philip Bruggmann, MD, Head of internal medicine, Arud centres of Addiction Medicine, Konradstrasse 32, CH 8005 Zurich, Switzerland.
E-mail: p.bruggmann@arud.ch

rates in PWID is scarce. Existing literature shows poor testing rates [20–24]. Half of the infected Americans are unaware of their infection [18,20]. In the canton of Zurich, 50% of all patients in opioid substitution therapies (OST) are inadequately tested for hepatitis C [23]. In their qualitative study, Swan *et al.* [25] assessed individual patient barriers to access HCV care. Most often mentioned obstacles were perceptions of HCV as a harmless disease, the fact that patients are not (yet) feeling unwell and a fear of intrusive tests. Due to the lack of symptoms, HCV patients without any other medical problems may not seek medical attention. According to a US investigation from 2009, patients lacking basic medical care (e.g. a GP) were 19 times more likely to be unaware of their diagnosis [18].

Two studies carried out in the United States showed a lack of knowledge about risk factors and testing for hepatitis C among primary care physicians [26,27]. Rein *et al.* [28] presume that difficulties in implementing risk-based screenings are due to the limited time these primary care physicians have with patients and a reluctance to discuss behavioural risks. Another major barrier is the lack of specific medical care in substance abuse treatment programmes [29]. Furthermore, not having health insurance is associated with being unaware of one's HCV status [18], and poorer geographical access to care is also associated with lower HCV detection rates [30,31].

BARRIERS TO HCV ASSESSMENT

Once tested for hepatitis C, only about 50% of patients are further assessed for treatment indication [19,32], even less (about 20%) in PWID [13,33]. Once having tested positive for hepatitis C antibodies, only 77% of GPs performed a viral load determination [34].

Assessment barriers at patient level

At patient level, barriers for assessment were the fear of a liver biopsy and treatment side effects as well as of the stigma associated with HCV [25,35]. Becoming symptomatic, learning that a HCV infection can cause serious liver disease and the desire to rid oneself of a virus associated with drug use were identified as assessment facilitators [25].

Assessment barriers at provider level

One of the main reasons for GPs in Switzerland to withhold referral for therapy is normal liver enzymes [34], despite long-established evidence that such patients can still develop progressive liver disease [36,37].

Having seen a general practitioner specifically about HCV is associated with a higher chance of a specialist assessment [19,33,38].

Assessment barriers at system level

An Australian study showed that the younger the people, the higher the level of formal education on HCV assessments [39]. Being in OST and having low social support were associated with no specialist HCV assessment [19,40].

OBSTACLES TO TREATMENT UPTAKE

Although HCV therapy is proven to be safe and efficient for PWID [41,42], treatment uptake is generally low in this population and lower than in other at-risk groups [13–15,17,33]. In PWID cohorts, treatment uptake levels vary between 1% and 6% [13,15,33]. Volk *et al.* [18] indentified lack of diagnosis as the primary barrier to treatment.

Treatment barriers at patient level

Willingness to start treatment for HCV among PWID lies between 53% and 86% [16,43–45]. Yet, several modifiable barriers at individual patient level remain, such as lack of knowledge, low priority, lack of financial resources and fear of side effects. Most of them correspond with those mentioned as barriers to testing and assessment [25,35,45]. In their recent qualitative study carried out on patients receiving opioid agonist therapy who were offered HCV therapy, Zickmund *et al.* [46] described antiviral therapies, poor relations with health providers and the lack of access to health care as the remaining critical barriers despite intense educational efforts. Patients' negative perceptions of HCV therapy are mainly influenced by their peer networks [25]. Depression amplifies perceived barriers at patient level [35], an important finding for a patient group with high prevalence of mood disorders [47–49].

The knowledge of the potential consequences of HCV, knowing somebody who has died from HCV and being told by a doctor to start treatment are all factors that facilitate treatment uptake [19].

Treatment barriers at provider level

Many physicians are reluctant to treat PWID driven by concerns of adherence, medical comorbidities and the risk of re-infection [34,50–52]. Only 20% of HCV specialists would consider therapy for PWID [53]. Not more than 9% of addiction specialists in an US study provided HCV treatment and only 30% were motivated to do so with the appropriate training and resources [51]. The doctor–patient relationship plays a decisive role for patients whether or not they discuss HCV treatment with their GP [25,39].

Receiving opioid substitution therapy and recent IDU were associated with not getting treated in a cross-sectional study carried out in New South Wales, Australia [19]. Furthermore, PWID face an increased risk of being

stigmatized by healthcare professionals without specific training in addiction medicine [54,55].

Treatment barriers at system level

People who inject drugs are often not able to adhere to the highly structured secondary or tertiary care settings, where HCV assessment and treatment is usually provided. The setting of HCV clinics is normally not adapted to the special, mainly psychosocial needs of the polymorbid population of PWID [56]. PWID face an increased risk of getting lost when transferred from primary to secondary or tertiary care [56]. Limited infrastructure for HCV therapies and long waiting lists for treatment have been identified as further system level barriers [52].

In some countries, health insurance can be a relevant system barrier to HCV treatment for underprivileged patients. In the United States, only one-third of patients with hepatitis C treatment indication had private medical insurance [57]. In this study, HCV infection was independently linked with being uninsured. Limited access to medical care and a lack of health insurance are associated with low treatment uptake rates according to the study of Volk *et al.* [18]. In many regions, HCV treatment is not available at all due to the high cost of the medication.

GENERALLY IMPROVING ACCESS TO CARE

The impact of new hepatitis C compounds will remain negligible as long as access to therapy cannot be expanded worldwide [18,58]. Scaling up access to therapy means improving detection rates, assessment of those tested positive and referral to therapy. From a global point of view, one of the most important measures is to provide HCV medication and testing kits at affordable prices to countries with low-income levels in analogy with the HIV field. At patient level, identification, assessment and treatment should be offered for free for underprivileged populations. The following measures have been studied to access underserved populations like PWID.

IMPROVING ACCESS TO TESTING

Measures at provider level

General practitioners and addiction specialists play a key role in screening PWID and referring them for assessment [19]. GPs often have low caseloads of HCV patients with an average of four patients per practice [34]. Addiction specialists often miss the opportunity to test their patients for hepatitis C and educate them accordingly as they focus their attention on drug-related and mental health issues. Specific training and education about HCV testing and diagnostic criteria should focus on these healthcare professionals [19].

Measures at system level

Hepatitis C virus screening rates could be significantly enhanced with birth cohort testing and a risk-based strategy [59]. Rein *et al.* [60] promote primary care-based birth cohort screenings for those born between 1945 and 1965 as a cost-effective solution. Better access to testing and screening for PWID could be achieved with specific, nurse-led HCV education and counselling for people at risk [25]. According to Volk *et al.* [18], scaling up diagnosis rates requires education of the public and physicians alike, as well as attention to the worsening problem of the uninsured. Patients without health insurance and low literacy may be more likely to seek care in emergency rooms than in clinics or GP practices – a finding with implications for programmes aimed at improving diagnosis among PWID [57].

IMPROVING ACCESS TO ASSESSMENT AND THERAPY

Measures at patient level

Many studies show how important knowledge of and readiness for HCV assessment and treatment is for HCV patients. Training for PWID should focus on the potential health implications of HCV [25]. But the education of patients is only one of several actions to be taken and has its limits [46]. Dealing with pronounced ambivalence – a common phenomenon in addicts – by using motivational interventions (cognitive behavioural therapy, motivational interviewing) can have positive effects on patients' readiness in the long run [61].

As peers who have completed a HCV therapy have the potential to facilitate treatment willingness, peer involvement could be an important measure to enhance positive attitudes towards HCV assessment and therapy among PWID. Patients attending peer support groups showed high rates of HCV care engagement, assessment and treatment uptake [62,63]. Peer involvement can also improve the patients' knowledge [62].

Hepatitis C patients should systematically be screened for depression, as it influences perceived barriers at individual patient level and inhibits pro-active help-seeking behaviour. Feelings of guilt, shame and social stigma are amplified by depression [35]. Untreated HCV patients of a younger age with a history of IDU, a population often not regularly attending healthcare services, should also be within the scope of a continuous education regarding treatment possibilities and the risks of untreated hepatitis C [64].

Measures at provider level

Hepatitis C virus providers' treatment considerations for PWID are often driven by criteria that are lacking in

evidence. Treating PWID has been proven safe with sustained virological response rates comparable to non-drug users [41,65], adherence rates among PWID are similar to non-drug users [66,67], most of the comorbidities of PWID are no contraindication per se for HCV treatment [68], and re-infection has never been proven to be a relevant risk among PWID [69]. Evidence-based guidelines could help overcome the myths and misconceptions about HCV assessment and treatment among PWID.

The training of hepatitis specialists, which focuses on insights into addiction medicine, could address morally based misconceptions and stigmatization towards PWID. Provider education should focus on HCV in undergraduate and postgraduate medical education already [2].

Two studies indicate a high acceptance among PWID of transient elastography to assess liver fibrosis [70,71]. Offering this technology may facilitate assessment and help clear the hurdle of fear of a liver biopsy [25].

Implementing state-of-the-art telehealth technology to provide training and specialist support to general practitioners in rural areas for the management of so far underserved HCV patients has shown to be effective [72]. Patients have been treated by GPs who receive telehealth support with similar rates of treatment success as patients treated at tertiary care level. The authors of this telehealth study discuss several factors that potentially contribute to the success of this model: local community providers are more patient-centred, which improves the provider–patient relationship as well as patient education. Furthermore, they are able to offer more personal contact with the patient, hence enhancing adherence and side effect management [72].

Measures at system level

To extend HCV treatment to marginalized groups of PWID, implementation of integrated community-based treatment settings is needed. Reimer describes major principles for successful primary care community-based models such as rapid access to services, high ratio of community-based to office-based appointments, assertive engagement and shared care approach [56]. Because addiction treatment programmes offer an important point of contact, not only testing but the full range of hepatitis care, including counselling, testing, treatment and follow ups, could ideally be offered within this setting [29].

Integrated primary care community-based treatment settings have the potential to overcome several barriers to HCV treatment for PWID, allowing successful HCV therapy in patients who would not be eligible for therapy in secondary or tertiary care-based settings [73,74]. Patients commonly excluded from therapy, such as the homeless or people with ongoing alcohol and/or injecting drug use, can be successfully treated within an integrated community-based setting [73]. Such settings simultaneously address

drug dependence, social support, mental health care and infectious disease assessment and therapy under one roof [17,63,75–77]. Offering everything under one roof overcomes one of the major barriers to hepatitis C care for PWID: patients not attending appointments when referred to a specialist.

Integrating professional counselling and case management by a psychologist into hepatology units can increase eligibility for HCV treatment of PWID who initially would have been deferred from therapy due to mental health and substance abuse-related comorbidities [78].

The involvement of a clinical specialist psychiatric nurse in an integrated mental health and medical care setting can raise the rate of HCV assessments [61]. The duty of the specialist nurse in the setting as described by Knott *et al.* was to administer specific psychotherapies including cognitive behavioural and motivational therapies as well as prescribing psychopharmacological medication in collaboration with a psychiatrist.

Integration of specially trained nurses in rural health clinics in Canada providing counselling and interdisciplinary assessments together with the local physicians and addiction specialists enhanced the efficiency of HCV assessments as well as treatment uptake [79].

A more widespread use of transient elastography would require licensing of this relatively new technology and the reimbursement by health insurances, two preconditions not yet met in many countries.

People who inject drugs have high rates of imprisonment. There are several successful models of HCV therapy for PWID in a prison setting [80–83]. HCV treatment in prisons is another possibility to receive HCV care for PWID.

CONCLUSION

There is not just one way to reach the goal of enhanced HCV detection, assessment and treatment uptake for people who use drugs. Many studies about possible measures to improve HCV management among PWID have been published and are described in this review. Accessing this HCV population that is difficult to reach needs an approach tailored to regional conditions and needs.

The approach of bringing HCV care to the patients instead of sending patients to secondary or tertiary care units is a very promising way of accessing PWID with the potential to overcome many current barriers. Evidence-based guidelines for HCV management for PWID are desperately needed to address myths about assumed contraindications and the supposed inefficiency of HCV treatment in this population. HCV education needs to be aimed at GPs and addiction medicine specialists and patients. The education of HCV specialists should focus on addiction and managing patients who are affected by addiction and its comorbidities.

To coordinate these efforts, they will have to be adapted to the needs of each individual country and applied nationwide. National coordination of action is needed. This action must start today in order to be ready in a few years when simple, well-tolerated and highly efficient HCV therapy regimens will become available.

DISCLOSURE

The author is an advisor of MSD, Abbott and Janssen and has received research/project grants from Roche, MSD, Janssen, Gilead and BMS.

REFERENCES

- Chung RT. A watershed moment in the treatment of hepatitis C. *N Engl J Med* 2012; 366(3): 273–275.
- Clark PJ, Muir AJ. Overcoming barriers to care for hepatitis C. *N Engl J Med* 2012; 366(26): 2436–2438.
- Nelson PK, Mathers BM, Cowie B *et al*. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. *Lancet* 2011; 378(9791): 571–583.
- Weber R, Sabin CA, Friis-Moller N *et al*. Liver-related deaths in persons infected with the human immunodeficiency virus: the D:A:D study. *Arch Intern Med* 2006; 166(15): 1632–1641.
- Grebel J, Dore GJ. What is killing people with hepatitis C virus infection? *Semin Liver Dis* 2011; 31(4): 331–339.
- Grebel J, Raffa JD, Lai C *et al*. Impact of hepatitis C virus infection on all-cause and liver-related mortality in a large community-based cohort of inner city residents. *J Viral Hepat* 2011; 18(1): 32–41.
- Matser A, Urbanus A, Geskus R *et al*. The effect of hepatitis C treatment and human immunodeficiency virus (HIV) co-infection on the disease burden of hepatitis C among injecting drug users in Amsterdam. *Addiction* 2012; 107(3): 614–623.
- Hutchinson SJ, Bird SM, Goldberg DJ. Modeling the current and future disease burden of hepatitis C among injection drug users in Scotland. *Hepatology* 2005; 42(3): 711–723.
- Zeiler I, Langlands T, Murray JM, Ritter A. Optimal targeting of Hepatitis C virus treatment among injecting drug users to those not enrolled in methadone maintenance programs. *Drug Alcohol Depend* 2010; 110(3): 228–233.
- Vickerman P, Martin N, Hickman M. Can Hepatitis C virus treatment be used as a prevention strategy? Additional model projections for Australia and elsewhere *Drug Alcohol Depend* 2011; 113(2–3): 83–85.
- Martin NK, Vickerman P, Foster GR, Hutchinson SJ, Goldberg DJ, Hickman M. Can antiviral therapy for hepatitis C reduce the prevalence of HCV among injecting drug user populations? A modeling analysis of its prevention utility *J Hepatol* 2011; 54(6): 1137–1144.
- Letmeier B, Muhlberger N, Schwarzer R *et al*. Market uptake of new antiviral drugs for the treatment of hepatitis C. *J Hepatol* 2008; 49(4): 528–536.
- Mehta SH, Genberg BL, Astemborski J *et al*. Limited uptake of hepatitis C treatment among injection drug users. *J Community Health* 2008; 33(3): 126–133.
- Grebel J, Petoumenos K, Matthews GV *et al*. Factors associated with uptake of treatment for recent hepatitis C virus infection in a predominantly injecting drug user cohort: The ATAHc Study. *Drug Alcohol Depend* 2010; 107(2–3): 244–249.
- Grebel J, Raffa JD, Lai C *et al*. Low uptake of treatment for hepatitis C virus infection in a large community-based study of inner city residents. *J Viral Hepat* 2009; 16(5): 352–358.
- Strathdee SA, Latka M, Campbell J *et al*. Factors associated with interest in initiating treatment for hepatitis C Virus (HCV) infection among young HCV-infected injection drug users. *Clin Infect Dis* 2005; 40(Suppl. 5): S304–S312.
- Lindenburg CE, Lambers FA, Urbanus AT *et al*. Hepatitis C testing and treatment among active drug users in Amsterdam: results from the DUTCH-C project. *Eur J Gastroenterol Hepatol* 2011; 23(1): 23–31.
- Volk ML, Tocco R, Saini S, Lok AS. Public health impact of antiviral therapy for hepatitis C in the United States. *Hepatology* 2009; 50(6): 1750–1755.
- Grebel J, Bryant J, Hull P *et al*. Factors associated with specialist assessment and treatment for hepatitis C virus infection in New South Wales, Australia. *J Viral Hepat* 2011; 18(4): e104–e116.
- 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(10): 705–714.
- Hagan H, Campbell J, Thiede H *et al*. Self-reported hepatitis C virus antibody status and risk behavior in young injectors. *Public Health Rep* 2006; 121(6): 710–719.
- Kwiatkowski CF, Fortuin CK, Booth RE. The association between knowledge of hepatitis C virus status and risk behaviors in injection drug users. *Addiction* 2002; 97(10): 1289–1294.
- Schulthess K. Versorgungsqualität von opioidsubstituierten Patienten mit chronischer Hepatitis C – Eine Querschnitt-Studie im Kanton Zürich University of Zurich, Switzerland; 2011.
- Strehlow AJ, Robertson MJ, Zerger S *et al*. Hepatitis C among clients of health care for the homeless primary care clinics. *J Health Care Poor Underserved* 2012; 23(2): 811–833.
- Swan D, Long J, Carr O *et al*. Barriers to and facilitators of hepatitis C testing, management, and treatment among current and former injecting drug users: a qualitative exploration. *AIDS Patient Care STDS* 2010; 24(12): 753–762.
- Shehab TM, Sonnad SS, Lok AS. Management of hepatitis C patients by primary care physicians in the USA: results of a national survey. *J Viral Hepat* 2001; 8(5): 377–383.

- 27 Shehab TM, Orrego M, Chunduri R, Lok AS. Identification and management of hepatitis C patients in primary care clinics. *Am J Gastroenterol* 2003; 98(3): 639–644.
- 28 Rein DB, Smith BD, Wittenborn JS *et al.* The cost-effectiveness of birth-cohort screening for hepatitis C antibody in U.S. primary care settings. *Ann Intern Med* 2012; 156(4): 263–270.
- 29 Bini EJ, Kritz S, Brown LS Jr, Robinson J, Alderson D, Rotrosen J. Barriers to providing health services for HIV/AIDS, hepatitis C virus infection and sexually transmitted infections in substance abuse treatment programs in the United States. *J Addict Dis* 2011; 30(2): 98–109.
- 30 Monnet E, Collin-Naudet E, Bresson-Hadni S *et al.* Place of residence and distance to medical care influence the diagnosis of hepatitis C: a population-based study. *J Hepatol* 2006; 44(3): 499–506.
- 31 Shiffman ML, Mihas AA, Millwala F *et al.* Treatment of chronic hepatitis C virus in African Americans with genotypes 2 and 3. *Am J Gastroenterol* 2007; 102(4): 761–766.
- 32 Rocca LG, Yawn BP, Wollan P, Kim WR. Management of patients with hepatitis C in a community population: diagnosis, discussions, and decisions to treat. *Ann Fam Med* 2004; 2(2): 116–124.
- 33 Stooze MA, Gifford SM, Dore GJ. The impact of injecting drug use status on hepatitis C-related referral and treatment. *Drug Alcohol Depend* 2005; 77(1): 81–86.
- 34 Overbeck K, Bruggmann P, Helbling B. Chronic Hepatitis C virus infection in Swiss primary care practices: low case loads-high barriers to treatment? *Eur J Gen Pract* 2011; 17(2): 103–108.
- 35 Evon DM, Simpson KM, Esserman D, Verma A, Smith S, Fried MW. Barriers to accessing care in patients with chronic hepatitis C: the impact of depression. *Aliment Pharmacol Ther* 2010; 32(9): 1163–1173.
- 36 Shiffman ML, Stewart CA, Hofmann CM *et al.* Chronic infection with hepatitis C virus in patients with elevated or persistently normal serum alanine aminotransferase levels: comparison of hepatic histology and response to interferon therapy. *J Infect Dis* 2000; 182(6): 1595–1601.
- 37 Zeuzem S, Alberti A, Rosenberg W *et al.* Review article: management of patients with chronic hepatitis C virus infection and “normal” alanine aminotransferase activity. *Aliment Pharmacol Ther* 2006; 24(8): 1133–1149.
- 38 Kanwal F, Hoang T, Spiegel BM *et al.* Predictors of treatment in patients with chronic hepatitis C infection – role of patient versus nonpatient factors. *Hepatology* 2007; 46(6): 1741–1749.
- 39 Treloar C, Newland J, Rance J, Hopwood M. Uptake and delivery of hepatitis C treatment in opiate substitution treatment: perceptions of clients and health professionals. *J Viral Hepat* 2010; 17(12): 839–844.
- 40 Dore GJ, Hellard M, Matthews GV *et al.* Effective treatment of injecting drug users with recently acquired hepatitis C virus infection. *Gastroenterology* 2010; 138(1): 123–135.
- 41 Hellard M, Sacks-Davis R, Gold J. Hepatitis C treatment for injection drug users: a review of the available evidence. *Clin Infect Dis* 2009; 49(4): 561–573.
- 42 Zanini B, Lanzini A. Antiviral treatment for chronic hepatitis C in illicit drug users: a systematic review. *Antivir Ther* 2009; 14(4): 467–479.
- 43 Doab A, Treloar C, Dore GJ. Knowledge and attitudes about treatment for hepatitis C virus infection and barriers to treatment among current injection drug users in Australia. *Clin Infect Dis* 2005; 40(Suppl. 5): S313–S320.
- 44 Walley AY, White MC, Kushel MB, Song YS, Tulsy JP. Knowledge of and interest in hepatitis C treatment at a methadone clinic. *J Subst Abuse Treat* 2005; 28(2): 181–187.
- 45 Grebely J, Genoway KA, Raffa JD *et al.* Barriers associated with the treatment of hepatitis C virus infection among illicit drug users. *Drug Alcohol Depend* 2008; 93(1–2): 141–147.
- 46 Zickmund SL, Campbell SA, Tirado CF, Zook CL, Weinrieb RM. Perceived barriers to hepatitis C therapy for patients receiving opioid agonist treatment. *J Addict Med* 2012; 6(3): 233–239.
- 47 Savant JD, Barry DT, Cutter CJ *et al.* Prevalence of mood and substance use disorders among patients seeking primary care office-based buprenorphine/naloxone treatment. *Drug Alcohol Depend* 2012; <http://www.sciencedirect.com/science/article/pii/S0376871612002529>.
- 48 Hilsabeck RC, Hassanein TI, Carlson MD, Ziegler EA, Perry W. Cognitive functioning and psychiatric symptomatology in patients with chronic hepatitis C. *J Int Neuropsychol Soc* 2003; 9(6): 847–854.
- 49 Golden J, O’Dwyer AM, Conroy RM. Depression and anxiety in patients with hepatitis C: prevalence, detection rates and risk factors. *Gen Hosp Psychiatry* 2005; 27(6): 431–438.
- 50 Thompson VV, Ragland KE, Hall CS, Morgan M, Bangsberg DR. Provider assessment of eligibility for hepatitis C treatment in HIV-infected homeless and marginally housed persons. *AIDS* 2005; 19(Suppl. 3): S208–S214.
- 51 Litwin AH, Kunins HV, Berg KM *et al.* Hepatitis C management by addiction medicine physicians: results from a national survey. *J Subst Abuse Treat* 2007; 33(1): 99–105.
- 52 Grebely J, Tyndall MW. Management of HCV and HIV infections among people who inject drugs. *Curr Opin HIV AIDS* 2011; 6(6): 501–507.
- 53 Myles A, Mugford GJ, Zhao J, Krahn M, Wang PP. Physicians’ attitudes and practice toward treating injection drug users with hepatitis C: results from a national specialist survey in Canada. *Can J Gastroenterol* 2011; 25(3): 135–139.
- 54 Paterson BL, Backmund M, Hirsch G, Yim C. The depiction of stigmatization in research about hepatitis C. *Int J Drug Policy* 2007; 18(5): 364–373.
- 55 Moore GA, Hawley DA, Bradley P. Hepatitis C: studying stigma. *Gastroenterol Nurs* 2008; 31(5): 346–352.
- 56 Reimer J, Haasen C. Need-adapted HCV-treatment setting for injection drug users. *Lancet* 2009; 373(9681): 2090–2091.
- 57 Stepanova M, Kanwal F, el-Serag HB, Younossi ZM. Insurance status and

- treatment candidacy of hepatitis C patients: analysis of population-based data from the United States. *Hepatology* 2011; 53(3): 737–745.
- 58 Thomas DL, Leoutsakas D, Zabransky T, Kumar MS. Hepatitis C in HIV-infected individuals: cure and control, right now. *J Int AIDS Soc* 2011; 14: 22.
- 59 Litwin AH, Smith BD, Drainoni ML *et al.* Primary care-based interventions are associated with increases in hepatitis C virus testing for patients at risk. *Dig Liver Dis* 2012; 44(6): 497–503.
- 60 Rein DB, Wittenborn JS, Weinbaum CM, Sabin M, Smith BD, Lesesne SB. Forecasting the morbidity and mortality associated with prevalent cases of pre-cirrhotic chronic hepatitis C in the United States. *Dig Liver Dis* 2011; 43(1): 66–72.
- 61 Knott A, Dieperink E, Willenbring ML *et al.* Integrated psychiatric/medical care in a chronic hepatitis C clinic: effect on antiviral treatment evaluation and outcomes. *Am J Gastroenterol* 2006; 101(10): 2254–2262.
- 62 Sylvestre DL, Clements BJ. Adherence to hepatitis C treatment in recovering heroin users maintained on methadone. *Eur J Gastroenterol Hepatol* 2007; 19(9): 741–747.
- 63 Grebely J, Knight E, Genoway KA *et al.* Optimizing assessment and treatment for hepatitis C virus infection in illicit drug users: a novel model incorporating multidisciplinary care and peer support. *Eur J Gastroenterol Hepatol* 2010; 22(3): 270–277.
- 64 Treloar C, Hull P, Dore GJ, Grebely J. Knowledge and barriers associated with assessment and treatment for hepatitis C virus infection among people who inject drugs. *Drug Alcohol Rev* 2012; doi: 10.1111/j.1465-3362.2012.00468.x.
- 65 Bruggmann P, Falcato L, Dober S *et al.* Active intravenous drug use during chronic hepatitis C therapy does not reduce sustained virological response rates in adherent patients. *J Viral Hepat* 2008; 15(10): 747–752.
- 66 Mauss S, Berger F, Goelz J, Jacob B, Schmutz G. A prospective controlled study of interferon-based therapy of chronic hepatitis C in patients on methadone maintenance. *Hepatology* 2004; 40(1): 120–124.
- 67 Robaey G, Van VH, Mathei C, Van RM, Bruckers L, Buntinx F. Similar compliance and effect of treatment in chronic hepatitis C resulting from intravenous drug use in comparison with other infection causes. *Eur J Gastroenterol Hepatol* 2006; 18(2): 159–166.
- 68 Schaefer M, Capuron L, Friebe A *et al.* Hepatitis C infection, antiviral treatment and Mental Health: A European Expert Consensus Statement. *J Hepatol* 2012; doi:10.1016/j.jhep.2012.07.037.
- 69 Corson S, Greenhalgh D, Palmateer N, Weir A, Hutchinson S. Risk of Hepatitis C virus re-infection following spontaneous viral clearance in injecting drug users: a systematic review. *Int J Drug Policy* 2011; 22(2): 102–108.
- 70 Foucher J, Reiller B, Jullien V *et al.* FibroScan used in street-based outreach for drug users is useful for hepatitis C virus screening and management: a prospective study. *J Viral Hepat* 2009; 16(2): 121–131.
- 71 Moessner BK, Jorgensen TR, Skamling M *et al.* Outreach screening of drug users for cirrhosis with transient elastography. *Addiction* 2011; 106(5): 970–976.
- 72 Arora S, Thornton K, Murata G *et al.* Outcomes of treatment for hepatitis C virus infection by primary care providers. *N Engl J Med* 2011; 364(23): 2199–2207.
- 73 Wilkinson M, Crawford V, Tippet A *et al.* Community-based treatment for chronic hepatitis C in drug users: high rates of compliance with therapy despite ongoing drug use. *Aliment Pharmacol Ther* 2009; 29(1): 29–37.
- 74 Jack K, Willott S, Manners J, Varnam MA, Thomson BJ. Clinical trial: a primary-care-based model for the delivery of anti-viral treatment to injecting drug users infected with hepatitis C. *Aliment Pharmacol Ther* 2009; 29(1): 38–45.
- 75 Litwin AH, Harris KA Jr, Nahvi S *et al.* Successful treatment of chronic hepatitis C with pegylated interferon in combination with ribavirin in a methadone maintenance treatment program. *J Subst Abuse Treat* 2009; 37(1): 32–40.
- 76 Bellfiori B, Ciliegi P, Chiodera A *et al.* Peginterferon plus Ribavirin for chronic hepatitis C in opiate addicts on methadone/buprenorphine maintenance therapy. *Dig Liver Dis* 2009; 41(4): 303–307.
- 77 Harris KA Jr, Arnsten JH, Litwin AH. Successful integration of hepatitis C evaluation and treatment services with methadone maintenance. *J Addict Med* 2010; 4(1): 20–26.
- 78 Evon DM, Simpson K, Kixmiller S *et al.* A randomized controlled trial of an integrated care intervention to increase eligibility for chronic hepatitis C treatment. *Am J Gastroenterol* 2011; 106(10): 1777–1786.
- 79 Hill WD, Butt G, Alvarez M, Krajden M. Capacity enhancement of hepatitis C virus treatment through integrated, community-based care. *Can J Gastroenterol* 2008; 22(1): 27–32.
- 80 Boonwaat L, Haber PS, Levy MH, Lloyd AR. Establishment of a successful assessment and treatment service for Australian prison inmates with chronic hepatitis C. *Med J Aust* 2010; 192(9): 496–500.
- 81 Farley JD, Wong VK, Chung HV *et al.* Treatment of chronic hepatitis C in Canadian prison inmates. *Can J Gastroenterol* 2005; 19(3): 153–156.
- 82 Allen SA, Spaulding AC, Osei AM, Taylor LE, Cabral AM, Rich JD. Treatment of chronic hepatitis C in a state correctional facility. *Ann Intern Med* 2003; 138(3): 187–190.
- 83 Skipper C, Guy JM, Parkes J, Roderick P, Rosenberg WM. Evaluation of a prison outreach clinic for the diagnosis and prevention of hepatitis C: implications for the national strategy. *Gut* 2003; 52(10): 1500–1504.