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Abstract

Depression has long been acknowledged as a significant predictor of negative clinical outcomes in HIV and hepatitis C infections. Patients with both viruses may be however at increased risk. The aim of this study was to carry out a systematic review and meta-analysis of the differences in the prevalence of depression and presence of depressive symptoms between HIV/HCV co-infection, HIV mono-infection, and HCV mono-infection. A systematic electronic search of bibliographic databases was performed to locate articles published from the earliest available online until December 2014. Prospective and retrospective studies were included. Outcomes of depression were based on clinical interviews and validated self-reported measures of depression/depressive symptoms. Of the 188 records initially screened, 29 articles were included in the descriptive systematic review and six were included in the meta-analysis. Consistent with the individual conclusions of the studies included in the descriptive review, the meta-analytic results indicated that, as measured by self-reported measures of depression, HIV/HCV co-infected patients were significantly more likely to report depressive symptoms than either HIV (SMD = 0.24, 95% CI: 0.03-0.46, p = .02) or HCV mono-infected (SMD = 0.55, 95% CI: 0.17-0.94, p = .005) patients. The variability of the results of the reviewed studies, largely dependent on the samples' characteristics and the methods of assessment of depression, suggests that a clear interpretation of how depression outcomes are affected by the presence of HIV/HCV co-infection is still needed. Failing to diagnose depression or to early screen depressive symptoms may have a significant impact on patients' overall functioning and compromise treatments' outcomes.

Keywords: depression, HIV/HCV, meta-analysis, systematic review.

Introduction

Depression is the most common neuropsychiatric manifestation in HIV infection (Nanni, Caruso, Mitchell, Meggiolaro, & Grassi, 2015). A meta-analysis examining the risk for depression in HIV found that HIV-infected patients were more likely to have had an episode of major depressive disorder (MDD) than HIV-negative patients (Ciesla & Roberts, 2001). Regarding hepatitis C virus (HCV) infection, there is also evidence of an increased prevalence of neuropsychiatric disorders, with depression being one of the most significant disorders during hepatitis C treatment as well as in untreated HCV-infected patients (Schaefer et al., 2012). The high prevalence of psychiatric comorbidities in HCV-infected patients has been associated with direct effects of the virus on the central nervous system (CNS) (Raison et al., 2009) or adverse effects of hepatitis C treatment (Udina et al., 2012). Because the diagnosis of MDD during interferon treatment if often missed (Leutscher et al., 2010) and depression is a well-known risk factor for treatment failure (Schaefer et al., 2012), a timely screening and treatment of depression is of major relevance.

This may be more complex in the presence of HIV/HCV co-infection. This is particularly important because dual-diagnosed patients may face numerous emotional and psychosocial stressors (e.g., adjustment to and management of two chronic medical conditions, coping with stigma and discrimination, and coping with changes in relationships and social networks), which pose unique challenges for mental health providers (Silberbogen, Ulloa, Janke, & Mori, 2009). However, the prevalence of depression and depressive symptoms in HIV/HCV has been less studied, and the comparison with mono-infected populations yielded heterogeneous findings. Summarizing the results of studies comparing the prevalence of depression among co-infected patients with HIV and HCV mono-infected patients is needed to improve current understanding of the consequences of depression/depressive symptoms for dual-infected patients, particularly because of the evidence suggesting that depressive symptoms may compromise antiretroviral treatment compliance (Roux et al., 2013) and add complexity to treatment planning (Baillargeon et al., 2008). This knowledge is also of major importance, as it may allow for a closer monitoring of co-infected patients, who may be at increased risk of poorer mental health and thus may benefit from additional psychosocial support or antidepressant treatment.

Accordingly, the aim of this study was to carry out a systematic review and meta-analysis of the differences in the prevalence of depression and of depressive symptoms between HIV/HCV co-infected, HIV mono-infected, and HCV mono-infected patients.

Methods

Search strategy

The Cochrane Central Registered of Control Trials Library, SCOPUS, Medline and PsycINFO were systematically searched for records from the earliest data available online to December 2014. Each database was searched separately. The key terms "*depress**" AND *"HIV - HCV co-infection"* were used, combining search strategies using Boolean operator (AND) and (*) related terms. The search was supplemented with additional information from reference lists and contact with the authors in the field of depression and HIV/HCV co-infection. The selection was limited to English publications only. The study was designed according to the PRISMA statement (Figure 1; Moher, Liberati, Tetzlaff, & Altman, 2009).

Eligibility criteria

Study inclusion criteria were: (1) Type of studies: prospective and retrospective studies assessing depression or presence of depressive symptoms in HIV/HCV co-infection; (2) Participants: individuals diagnosed with HIV/HCV and control subjects from these studies with either HIV or HCV mono-infection; (3) Interventions: with and without HCV treatment; and (4) Primary outcome: incidence of depression/depressive symptoms in co-infected patients, including during HCV treatment, as assessed by clinical interview or any validated depression measure. Secondary outcome: any other reported assessment measure of depressive symptoms. The following exclusion criteria were applied: (1) studies with participants under 18 years; (2) post-mortem studies; (3) articles with overlapping samples (samples duplicated in different research reports); and (4) articles not written in English.

Data extraction

Two authors (RF and MP) independently reviewed all references from electronic and non-electronic sources, selected the relevant studies for the review and extracted relevant data. Disagreements were resolved by discussion. The following information was extracted from each

study: year of publication, country, design, sample size, population characteristics (e.g., age, gender, past and/or current intravenous drug use (IDU) or IDU as risk factor for infection acquisition), measures to assess depression/depressive symptoms and prevalence of MDD and/or symptoms of depression. To assess the risk of bias, a checklist was developed based on a quality assessment instrument, and included the following parameters: objectives explicitly stated, selection and representativeness of the study samples, inclusion/exclusion criteria, clear identification of measures, data adequately reported, and discussion addressing the primary outcome and validity of depression measures (Higgins & Green, 2011).

Data analysis

All studies meeting eligibility criteria were included in the systematic review. Of these, a sub-set of six studies with available data to perform statistical synthesis and appropriate control groups were entered into the meta-analysis. Meta-analysis quantifying the differences in depression outcomes between HIV/HCV, HIV and HCV mono-infected groups was performed with the Review Manager, version 5.3. Because studies whose results were combinable used different measures to assess depressive symptoms, the standardised mean difference (SMD) between HIV/HCV and control groups and its associated 95% confidence interval (CI) were computed as the summary statistic for the estimate of effects. The heterogeneity between-studies was assessed by computing the χ^2 and I^2 statistics. An I^2 of 0% indicates no heterogeneity and a value above 50% is considered as substantial heterogeneity (Higgins, Thompson, Deeks, & Altman, 2003). Though moderate to substantial heterogeneity was identified, as suggested by Higgins and Green (2011), both fixed and random-effects models were used for testing differences in the summary effects.

Results

Study selection and quality of studies

The study selection process is described in Figure 1. Briefly, the electronic search identified 188 records. After removal of duplicated articles (n=18), 170 were subjected to abstract review. One hundred and thirty-one were excluded, leaving 39 articles for full-text review and further assessment of eligibility. Twenty-nine papers fulfilled the inclusion criteria and were included in the systematic

review. Six of those studies were included in the quantitative analysis. Selected studies were published between 2001 and 2014.

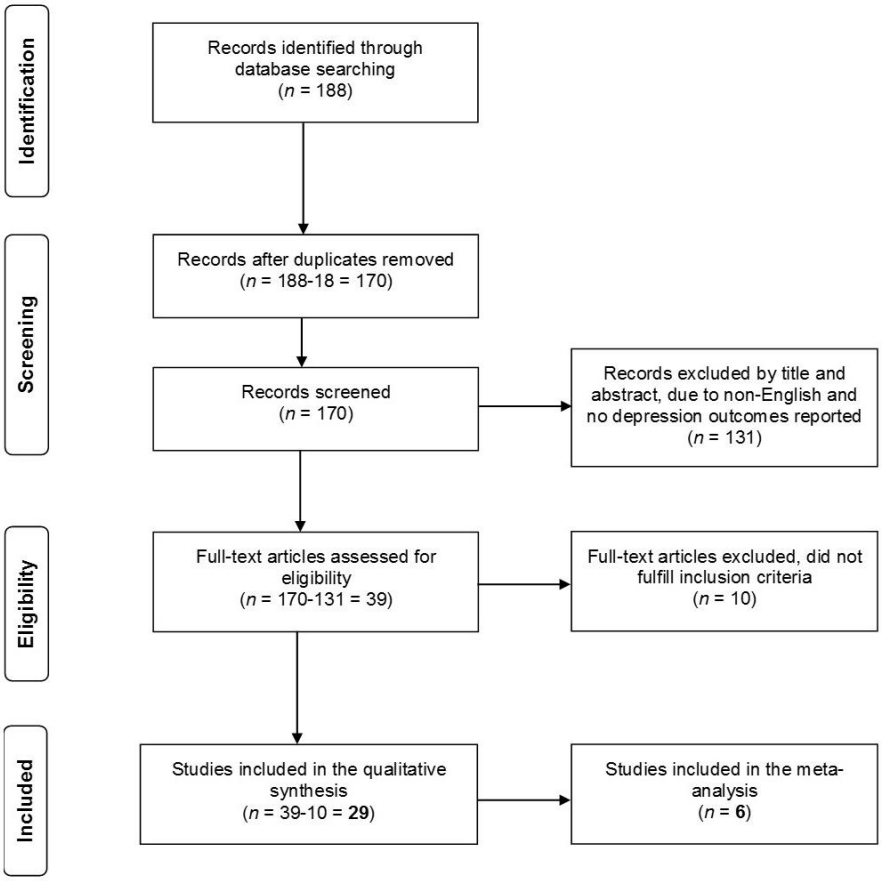

Figure 1. Flow diagram outlining the study selection process

For all studies included in the review, a low risk of bias was observed when considering the identification of the studies' aims, definition of inclusion and exclusion criteria, reporting of results, and discussion of the main outcomes. However, low-moderate to high bias was found regarding the selection of participants (e.g., a systematic difference between the characteristics of groups that were compared was identified), which limited their representativeness, as well as in identification of the procedures associated with how outcomes were determined (e.g., in six studies it was not clear how depression was assessed). Regarding the six studies included in the meta-analysis, with the exception of two studies (Richardson et al., 2005; von Giesen et al., 2004), in which systematic differences between the comparison groups were identified, a low risk of bias was observed.

Study characteristics

This systematic review covers 29 studies from eight countries (one study from Italy and Portugal, two studies from Australia, France and Germany, three studies from Canada and Spain, and 15 studies from the USA). The number of co-infected participants ranged between 15 and 6,782. Study designs were mostly cross-sectional (*n* = 16, 55.2%) and included only a HIV/HCV group (*n* = 10, 34.5%) or a comparison between co-infected and HIV mono-infected groups (*n* = 10, 34.5%). Most studies included both male and female participants and one study included only females (Richardson et al., 2005). The proportion of co-infected males ranged between 65.1% (von Giesen et al., 2004) and 100% (Pantalone, Hessler, Bankoff, & Shah, 2012; Sun et al., 2013; Thein et al., 2007). Among co-infected patients, the proportion of participants reporting IDU (past and/or current) ranged between 31.5% (Pantalone et al., 2012) and 94% (Landau et al., 2001). In 18 studies, the proportion of IDU was above 60%. General characteristics and comparison groups in each study are described in Table 1.

[Insert_Table_1]

Descriptive analysis

A summary of the relevant findings of the 29 studies included in the descriptive analysis is presented in Table 2 and briefly described above.

[Insert_Table_2]

Depression in HIV/HCV patients without HCV treatment

A total of 18 studies assessed depression among co-infected patients outside HCV treatment. The three retrospective studies used the International Classification of Diseases (ICD-9) codes to assess depression. Of these, two studies reported that co-infected patients had a higher prevalence of depression than HIV mono-infected patients (Backus, Boothroyd, & Deyton, 2005; Goulet, Fultz, Mcginnis, & Justice, 2005) and one study found that the co-infected group had a higher prevalence of depression than the HCV mono-infected group (Butt, Justice, Skanderson, Good, & Kwoh, 2006).

Cross-sectional and prospective studies similarly indicated that co-infected patients were more likely to report depressive symptoms than HIV mono-infected patients (Baillargeon et al., 2008; Baum, Jayaweera, Duan, & Ms, 2008; Braitstein et al., 2005; Butt et al., 2009; Clifford, Evans, Yang,

& Gulick, 2005; Pantalone et al., 2012; Pereira, Fialho, & Canavarro, 2014; Sun et al., 2013; Yoon et al., 2011) and HCV mono-infected patients (Sun et al., 2013). In three studies no significant differences were found between the co-infected group and the HIV and HCV mono-infected groups (Ciccarelli et al., 2013; Richardson et al., 2005; Thein et al., 2007), and one study did not find differences between co-infected and HIV mono-infected patients (Ryan et al., 2004). Additionally, one study indicated that depression was associated with HIV illness progression in co-infection (Michel et al., 2010). Tavakkoli and colleagues (2013) found that a diagnosis of major depression was significantly less common among HIV/HCV patients than among HCV mono-infected patients.

Depression in HIV/HCV patients during HCV treatment

Ten studies assessed depression during hepatitis C treatment. Alavi and colleagues (2012) described similar proportions of new-onset depression during treatment between HCV mono-infected (33%) and co-infected patients (38%). Fumaz and colleagues (2007) indicated that 59% of co-infected patients as having treatment-emergent mild or moderate depression. One study showed that depression did not influence treatment outcomes (Alavi et al., 2012) and another indicated that increased depressive symptoms was significantly associated with reduced role, social and cognitive functioning (Kemmer et al., 2012). Six studies reported occurrence of depression during HCV treatment (Laguno et al., 2004; Landau et al., 2001; Moreno et al., 2004; Myers et al., 2004; Rockstroh et al., 2002; Sulkowski et al., 2004) and five indicated depression as cause of treatment discontinuation (Laguno et al., 2004; Landau et al., 2001; Moreno et al., 2004; Myers et al., 2004; Rockstroh et al., 2002). Klein and colleagues (2014) found that prophylactic citalopram compared to treatment of depression was not associated with reduce depression symptoms among co-infected patients.

Meta-analysis: Depression in HIV/HCV vs. HIV and HCV mono-infection

Six out of the 29 studies included data enabling meta-analysis. Because in these studies, depressive symptoms were assessed with different measures (see Table 2), SMD were computed as the summary statistic for the estimate of effects.

The meta-analysis (random-effects model) comparing HIV/HCV and HIV mono-infected patients indicated a significant difference between groups, showing that the HIV mono-infected

groups were less likely to report symptoms of clinical depression than the HIV/HCV co-infected groups (SMD = 0.24, 95%CI: 0.03-0.46, p = .02). Similarly, the meta-analysis comparing HIV/HCV and HCV mono-infected groups indicated that the latter groups were less likely to exhibit depressive symptoms than the co-infected groups (SMD = 0.55, 95%CI: 0.17-0.94, p = .005) (see Figure 2). In both comparisons, moderate to substantial heterogeneity was found (I^2 range = 39%-62%). Data analysis using fixed-effects models yielded similar results in the comparison with HIV mono-infected (SMD = 0.24, 95%CI: 0.08-0.40, p = .004) and HCV mono-infected groups (SMD = 0.53, 95%CI: 0.30-0.76, p <.00001).

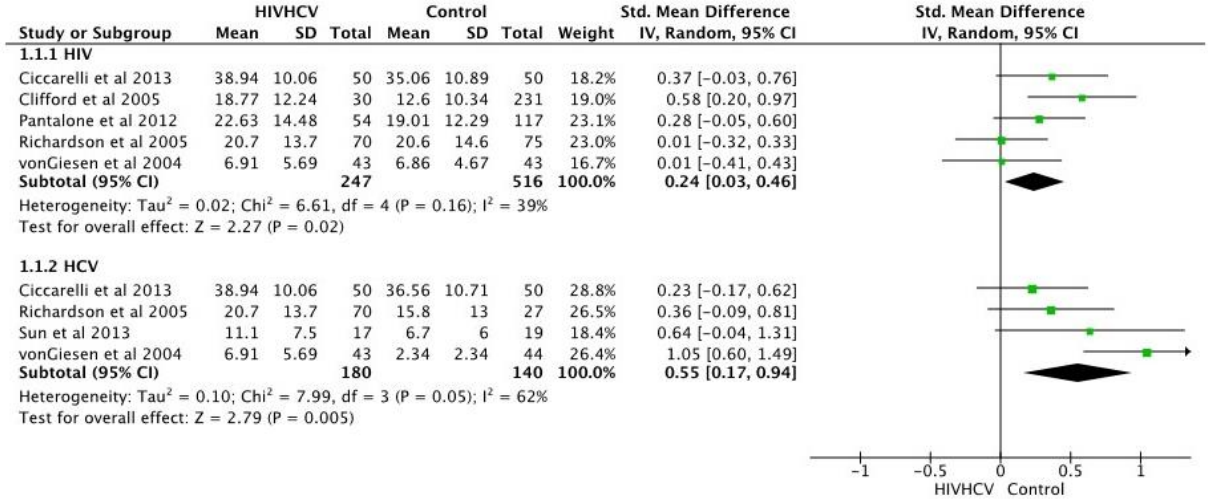

Figure 2. Forest plots of meta-analyses of differences in depression outcomes between study groups. Abbreviations: SD, standard deviation; CI, confidence interval

Discussion

In this first systematic review and meta-analysis examining the prevalence of depression and depressive symptoms among patients co-infected with HIV and hepatitis C, in comparison to HIV and HCV mono-infected patients, the main findings indicate a significant difference in depression outcomes between the comparison groups, and suggest that patients co-infected with HIV and HCV are more likely to report depressive symptoms than those with mono-infections.

Our results indicate a relevant prevalence of depression/depressive symptoms among co-infected patients, and suggest that the stigmatisation and strain of living with HIV is likely to be greater when coexisting with other medical conditions. Potential explanations for this result may be

related to well-known psychosocial factors that are common among co-infected patients, such as the higher prevalence of past history of IDU, ongoing alcohol and drug abuse (Backus et al., 2005; Clifford et al., 2005) and greater psychiatric comorbidity (Backus et al., 2005; Pereira et al., 2014). These factors, cumulatively with antiviral treatments and its side-effects are likely to increase the vulnerability of developing mental health disorders of co-infected patients, particularly in comparison with mono-infected patients. Interestingly, our findings indicated that the SMD was greater in the comparison between HIV/HCV and HCV mono-infected patients. This may be associated with the findings of one study (von Giesen et al., 2004), in which the mean score on depression was significantly lower among HCV mono-infected patients (2.34 vs. 6.86), probably because of the lower proportion of mono-infected patients reporting IDU as risk factor (18.2% vs. 62.8%).

It is also likely that depression may represent a behavioural side effect of these viruses. For instance, research demonstrated that depression associated with HIV is in part driven by immune dysregulation, characterized by an increased production of pro inflammatory cytokines and proliferation of immune cells (Nasi, Pinti, Mussini, & Cossarizza, 2014). Recent evidence also suggested that in a healthy brain, inflammation is an acute and controlled process; but when inflammation is chronic, it may contribute to the development of depression (Jones & Thomsen, 2013). HCV chronic infection also represents a chronic inflamed state that is maladaptive and that has been associated witg an elevated choline/creatine ratio in basal ganglia and white matter, depression and cognitive dysfunction (Forton et al., 2008; Weissenborn et al., 2004). Since these same changes would be anticipated in both HIV and HCV, the fact that co-infected patients were more depressed than HIV and HCV mono-infected groups also seems to suggest that these inflammation-related changes may represent a determinant factor of depression emergence.

Retrospective studies consistently shown a significant prevalence of depression among co-infected patients, and significantly higher than the comparison groups (Backus et al., 2005; Butt et al., 2006; Goulet et al., 2005). The sample sizes of these studies were large suggesting the relevance of the findings. However, retrospective studies may be vulnerable to information bias that can negatively impact the reported outcomes, such as non-standardized observations, use of different measures for assessing depression, and multiple information sources from clinical notes. It is notable that all

retrospective studies included veterans with overlapping mental illness comorbidities, which reduces the generalizability of the findings to other populations.

Regarding the descriptive narrative of prospective studies, mixed findings were reported. Some studies found that co-infected groups reported higher depression levels (or symptoms of depression) than mono-infected groups (e.g., Baillargeon et al., 2008; Pereira et al., 2014; Sun et al., 2013) but others did not find such differences (e.g., Ciccarelli et al., 2013; Thein et al., 2007). These differing findings may be related to several factors, including studies' differences in methodological approaches (e.g., study design, variations in the diagnostic/screening tools for assessing depression) and samples' characteristics. It is noteworthy that most studies included significant proportions of participants reporting IDU as a risk factor. However, there is also evidence suggesting changes in the epidemiological patterns of co-infection, particularly a higher incidence of HCV among HIV-infected men who have sex with men (MSM; Pantalone et al., 2012; van de Laar, Matthews, Prins, & Danta, 2010). Thus, future studies considering this emerging sexually transmitted infection are warranted, particularly because of recent evidence suggesting an association between depressive symptoms and higher engagement in sexual risk-behaviours among HIV-infected MSM (O'Cleirigh et al., 2013).

Studies in the context of HCV treatment indicated that depression was common (Alavi et al., 2012; Fumaz et al., 2007) and considered depression to be a risk factor for discontinuation of HCV treatment among co-infected patients (e.g., Laguno et al., 2004; Myers et al., 2004; Rockstroh et al., 2002). However, these results should be carefully interpreted, particularly because of how depression was measured in these studies. Indeed, different measures have been used to assess depression, and in four studies the measures were not clearly reported, thus leading to likely bias, as well as to under or over-representation of depression and its potential impact on treatment.

Regarding hepatitis C treatment, the interferon-induced depression paradigm has been robustly studied, and it has been reported that 1 out of 4 HCV patients receiving interferon-alpha and ribavirin therapy may develop MDD (Udina et al., 2012). Despite the notable advances of antiviral treatments for hepatitis C, particularly the emergence of direct acting-antivirals (DAAs), interferon-based therapy is still actively prescribed in a sub-set of patients. This means that the risk of depression may remain. Additionally, HCV treatment in co-infection is not as straightforward as in HCV mono-

infection due to potential drug-drug interactions (Chen & Jain, 2015). Accordingly, a routine screening of depression in co-infected patients would still be critical to a prompt diagnosis and adequate planning of antidepressant treatment during HCV therapy, which has been however considered safe (Martin-Subero, & Diez-Quevedo, 2016).

This systematic review is not without limitations. First, the literature search was restricted to articles written in English. Second, methodological differences between the studies should be considered in the interpretation of the results, including the heterogeneity of the participants' characteristics, the relatively small sample sizes, the preponderance of cross-sectional studies and the variability of approaches for assessing depression/depressive symptoms (only a limited number of studies performed a clinical diagnosis of depression). Third, the studies' methodological heterogeneity, particularly the lack of information regarding depression measures and quantitative outcomes did not allow us to perform a meta-analysis on depression during HCV treatment. Also, our meta-analysis' results were pooled from a small sample of studies that used different depression measures, which may lead to biased results and explain the substantial heterogeneity. Despite this limitation, restrict the selection of studies to those that used the same instrument would lead to a significant loss of information. Accordingly, the interpretation of these findings should be performed with caution. Finally, because of the emerging epidemiological patterns in HIV/HCV, this review is largely dependent of studies involving participants with history of IDU. Further studies are warranted, particularly those involving MSM as well as women, which are still under-represented in the HIV/HCV literature.

This comparative analysis on the prevalence of depression in HIV, HCV mono-infected and co-infected samples, indicates that depression appears to be more common among co-infected patients. This finding has important clinical implications, as it provides an opportunity for targeted and timely screening of depression in populations at higher risk, and before the exacerbation of symptoms. In this context, the use of reliable measures of depression is essential. Despite the wide-ranging number of well-established tools for the assessment of depressive symptoms, their scope and scores are often different (Uher et al., 2012) and are not directly comparable (Wahl et al., 2014). A standardized metric for the assessment of depression severity, as the proposed by Wahl and

colleagues (2014) may be valuable. For a more complete and accurate assessment, the combination of clinician-rated scales and self-reported measures would also be useful, as it provide unique information that may be important to predict treatment outcomes (Uher et al., 2012).

Finally, there is evidence that the prevalence of depression in HIV and HCV mono-infection as well as in HIV/HCV co-infection vary. Accordingly, a differential diagnosis will be critical, because both host factors (e.g., interferon exposure in HCV treatment) and virus factors (e.g., CNS-related infections) responsible for mood symptoms can be manageable. Moreover, factors such as lack of social support, stress and maladaptive coping strategies are also associated with an increased risk of depression (Slot et al., 2015). Because these factors are amenable to change, addressing these factors may also reduce depressive symptoms and contribute for improved well-being of patients. As recommended by Schaefer et al. (2012), increased education of both patients and health professionals on mental health issues is central to allow early detection of psychological symptoms, particularly those that are likely to contribute to treatments' failure. A close monitoring and comprehensive management of psychological symptoms is also highly recommended, as it may contribute to maximize the likelihood of successful treatments.

References

Alavi, M., Grebely, J., Matthews, G. V, Petoumenos, K., Yeung, B., Day, C., … Haber, P. S. (2012). Effect of pegylated interferon-α-2a treatment on mental health during recent hepatitis C virus infection. *Journal of Gastroenterology and Hepatology, 27*, 957-965. doi:10.1111/j.1440-1746.2011.07035.x

Backus, L. I., Boothroyd, D., & Deyton, L. R. (2005). HIV, hepatitis C and HIV/Hepatitis C virus co-infection in vulnerable populations. *AIDS, 19*(Suppl. 3), S13-S19. doi:10.1097/01.aids.0000192065.09281.01

Baillargeon, J. G., Paar, D. P., Wu, H., Giordano, T. P., Murray, O., Raimer, B. G., ... Pulvino, J. S. (2008). Psychiatric disorders, HIV infection and HIV/hepatitis co-infection in the correctional setting. *AIDS Care*, *20*, 124-129. doi:10.1080/09540120701426532

Baum, M. K., Jayaweera, D. T., Duan, R., Sales, S., Lai., S., Rafie, C., … Campa, A. (2008). Quality of life, symptomatology and healthcare utilization in HIV/HCV co-infected drug users in Miami. *Journal of Addictive Diseases, 27*(2), 37-48. doi:10.1300/J069v27n02_05

Braitstein, P., Montessori, V., Chan, K., Montaner, J. S., Schechter, M. T., O'Shaughnessy, M. V., & Hogg, R. S. (2005). Quality of life, depression and fatigue among persons co infected with HIV and hepatitis C: Outcomes from a population based cohort. *AIDS Care, 17,* 505-515. doi:10.1080/09540120412331291733

Butt, A. A., Justice, A. C., Skanderson, M., Good, C., & Kwoh, C. K. (2006). Rates and predictors of hepatitis C virus treatment in HCV–HIV-coinfected subjects. *Alimentary Pharmacology &Therapeutics, 24,* 585-591. doi:10.1111/j.1365-2036.2006.03020.x

Butt, A. A., Khan, U. A., Shaikh, O. S., McMahon, D., Dorey-Stein, Z., Tsevat, J., & Lo Re III, V. (2009). Rates of HCV treatment eligibility among HCV-monoinfected and HCV/HIV-coinfected patients in tertiary care referral centers. *HIV Clinical Trials, 10,* 25-32. doi:10.1310/hct1001-025

Ciesla, J. A., & Roberts, J. E. (2001). Meta-analysis of the relationship between HIV infection and risk for depressive disorders. *American Journal of Psychiatry*, *158*, 725-730. doi:10.1176/appi.ajp.158.5.725

Ciccarelli, N., Fabbiani, M., Grima, P., Falasca, K., Tana, M., Baldonero, E., … Di Giambenedetto, S. (2013). Comparison of cognitive performance in HIV or HCV mono-infected and HIV-HCV co-infected patients. *Infection, 41*, 1103-1109. doi:10.1007/s15010-013-0503-2

Clifford, D. B., Evans, S. R., Yang, Y., & Gulick, R. M. (2005). The neuropsychological and neurological impact of hepatitis C virus co-infection in HIV-infected subjects. *AIDS, 19*(Suppl. 3), S64-S71. doi:10.1097/01.aids.0000192072.80572.43

Forton, D. M., Hamilton, G., Allsop, J. M., Grover, V. P., Wesnes, K., O'Sullivan, C., … Taylor-Robinson, S. D. (2008). Cerebral immune activation in chronic hepatitis C infection: A magnetic resonance spectroscopy study. *Journal of Hepatology, 49*, 316-322. doi:10.1016/j.jhep.2008.03.022

Fumaz, C. R., Muñoz-Moreno, J. A., Ballesteros, A. L., Paredes, R., Ferrer, M. J., Salas, A., … Clotet, B. (2007). Influence of the type of pegylated interferon on the onset of depressive and neuropsychiatric symptoms in HIV-HCV coinfected patients. *AIDS Care, 19*, 138-145. doi:10.1080/09540120600645539

Goulet, J. L., Fultz, S. L., Mcginnis, K. A., & Justice, A. C. (2005). Relative prevalence of comorbidities and treatment contraindications in HIV-mono-infected and HIV / HCV-co-infected veterans. *AIDS, 19*(Suppl. 3), S99-S105. doi:10.1097/01.aids.0000192077.11067.e5

Higgins, J. P. T., & Green, S. (2011). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0*. The Cochrane Collaboration. Retrieved from www.cochrane-handbook.org

Higgins, J. P. T., Thompson, S. G., Deeks, J. J., & Altman, D. G. (2003). Measuring inconsistency in meta-analyses. *British Medical Journal 327*, 557-560. doi:10.1136/bmj.327.7414.557

Hilsabeck, R. C., Hassanein, T. I., Carlson, M. D., Ziegler, E. A., & Perry, W. (2003). Cognitive functioning and psychiatric symptomatology in patients with chronic hepatitis C. *Journal of the International Neuropsychological Society, 9*, 847-854. doi:10.1017/S1355617703960048

Jones, K. A., & Thomsen, C. (2013). The role of the innate immune system in psychiatric disorders. *Molecular and Cellular Neurosciences, 53*, 52-62. doi:10.1016/j.mcn.2012.10.002

Kemmer, N., Hua, L., Andersen, J. W., Chung, R. T., Butt, A. A., & Sherman, K. E. (2012). Health-related quality of life in subjects with HCV/HIV coinfection: Results from ACTG 5178 study. *Journal of Viral Hepatitis, 19*, 792-800. doi:10.1111/j.1365-2893.2012.01609.x

Klein, M. B., Lee, T., Brouillette, M. J., Sheehan, N. L., Walmsley, S., Wong, D. K., ... Singer, J. (2014). Citalopram for the prevention of depression and its consequences in HIV-hepatitis C coinfected individuals initiating pegylated interferon/Ribavirin therapy: A multicenter randomized double-blind placebo-controlled trial. *HIV Clinical Trials, 15*, 161-175. doi:10.1310/hct1504-161

Laguno, M., Murillas, J., Blanco, J. L., Martínez, E., Miquel, R., Sánchez-Tapias, J. M., ... & Mallolas, J. (2004). Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for treatment of HIV/HCV co-infected patients. *AIDS, 18*, F27-F36. doi:10.1097/00002030-200409030-00003

Landau, A., Batisse, D., Piketty, C., Paul, J., Huyen, D. Van, Bloch, F., … Kazatchkine, M. D. (2001). Long-term efficacy of combination therapy with interferon-α2b and ribavirin for severe chronic hepatitis C in HIV-infected patients. *AIDS, 15*, 2149-2155.

Leutscher, P. D. C., Lagging, M., Buhl, M. R., Pedersen, C., Norkrans, G., Langeland, N., ... & Bech, P. (2010). Evaluation of depression as a risk factor for treatment failure in chronic hepatitis C. *Hepatology*, *52*, 430-435. doi:10.1002/hep.23699

Martin-Subero, M., & Diez-Quevedo, C. (2016). Mental disorders in HIV/HCV coinfected patients under antiviral treatment for hepatitis C. *Psychiatry Research, 246*, 173-181. doi:10.1016/j.psychres.2016.09.041

Michel, L., Villes, V., Dabis, F., Spire, B., Winnock, M., Loko, M. A., ... & Carrieri, M. P. (2010). Role of treatment for depressive symptoms in relieving the impact of fatigue in HIV-HCV co-infected patients: ANRS Co13 Hepavih, France, 2006–2008. *Journal of Viral Hepatitis, 17*, 650-660. doi:10.1111/j.1365-2893.2009.01223.x

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine, 6*(6), e1000097. doi:10.1371/journal.pmed1000097

Moreno, L., Quereda, C., Moreno, A., Perez-Elías, M. J., Antela, A., Casado, J. L., … Moreno, S. (2004). Pegylated interferon alpha2b plus ribavirin for the treatment of chronic hepatitis C in HIV-infected patients. *AIDS, 18*, 67-73. doi:10.1097/00002030-200401020-00008

Myers, R. P., Benhamou, Y., Bochet, M., Thibault, V., Mehri, D., & Poynard, T. (2004). Pegylated interferon alpha 2b and ribavirin in HIV/hepatitis C virus-co-infected non-responders and relapsers to IFN-based therapy. *AIDS, 18*, 75-79. doi:10.1097/00002030-200401020-00009

Nanni, M. G., Caruso, R., Mitchell, A. J., Meggiolaro, E., & Grassi, L. (2015). Depression in HIV infected patients: A review. *Current Psychiatry Reports, 17*(1), 530. doi:10.1007/s11920-014-0530-4

Nasi, M., Pinti, M., Mussini, C., & Cossarizza, A. (2014). Persistent inflammation in HIV infection: Established concepts, new perspectives. *Immunology letters*, *161*, 184-188. doi:10.1016/j.imlet.2014.01.008

O'Cleirigh, C., Newcomb, M. E., Mayer, K. H., Skeer, M., Traeger, L., & Safren, S. A. (2013). Moderate levels of depression predict sexual transmission risk in HIV-infected MSM: A longitudinal analysis of data from six sites involved in a "prevention for positives" study. *AIDS and Behavior, 17*, 1764-1769. doi:10.1007/s10461-013-0462-8

Pantalone, D. W., Hessler, D. M., Barkoff, S. M., & Shah, B. J. (2012). Psychosocial correlates of HIV-monoinfection and HIV/HCV-coinfection among men who have sex with men. *Journal of Behavioral Medicine, 35*, 520-528. doi:10.1007/s10865-011-9381-1

Pereira, M., Fialho, R., & Canavarro, M. C. (2014). Prevalence and correlates of emotional distress in HIV/HCV co-infection. *AIDS Care*, *26*(Suppl.1), S56-S64. doi:10.1080/09540121.2014.906549

Raison, C. L., Borisov, A. S., Majer, M., Drake, D. F., Pagnoni, G., Woolwine, B. J., … Miller, A. H. (2009). Activation of central nervous system inflammatory pathways by interferon-alpha: Relationship to monoamines and depression. *Biological Psychiatry, 65*, 296-303. doi:10.1016/j.biopsych.2008.08.010

Richardson, J. L., Nowicki, M., Danley, K., Martin, E. M., Cohen, M. H., Gonzalez, R., … Levine, A. M. (2005). Neuropsychological functioning in a cohort of HIV- and hepatitis C virus-infected women. *AIDS, 19*, 1659-1667. doi:10.1097/01.aids.0000186824.53359.62

Ryan, E. L., Morgello, S., Isaacs, K., Naseer, M. G., Gerits, P., & Manhattan HIV Brain Bank. (2004). The neuropsychiatric impact of hepatitis C on advanced HIV. *Neurology, 62*, 957-962. doi:10.1212/01.WNL.0000115177.74976.6C

Rockstroh, J. K., Mudar, M., Lichterfeld, M., Nischalke, H. D., Klausen, G., Gölz, J., ... Mauss, S. (2002). Pilot study of interferon alpha high-dose induction therapy in combination with ribavirin for chronic hepatitis C in HIV-co-infected patients. *AIDS, 16*, 2083-2085. doi:10.1097/00002030-200210180-00016

Roux, P., Lions, C., Cohen, J., Winnock, M., Salmon-Céron, D., Bani-Sadr, F., … Carrieri, M. P. (2013). Impact of HCV treatment and depressive symptoms on adherence to HAART among coinfected HIV-HCV patients: Results from the ANRS-CO13-HEPAVIH cohort. Antiviral Therapy. Advance online publication. doi:10.3851/IMP2699

Schaefer, M., Capuron, L., Friebe, A., Diez-Quevedo, C., Robaeys, G., Neri, S., … Pariante, C. M. (2012). Hepatitis C infection, antiviral treatment and mental health: A European expert consensus statement. *Journal of Hepatology, 57*, 1379-1390. doi:10.1016/j.jhep.2012.07.037

Silberbogen, A. K., Ulloa, E. W., Janke, E. A., & Mori, D. L. (2009). Psychosocial issues and mental health treatment recommendations for patients with hepatitis C. *Psychosomatics, 50*, 114-122. doi:10.1176/appi.psy.50.2.114

Slot, M., Sodemann, M., Gabel, C., Holmskov, J., Laursen, T., & Rodkjaer, L. (2015). Factors associated with risk of depression and relevant predictors of screening for depression in clinical practice: A cross-sectional study among HIV-infected individuals in Denmark. *HIV Medicine, 16*, 393-402. doi:10.1111/hiv.12223

Sulkowski, M. S., Felizarta, F., Smith, C., Slim, J., Berggren, R., Goodman, R., ... & Hepatitis Resource Network Clinical Trials Group. (2004). Daily versus thrice-weekly interferon alfa-2b plus ribavirin for the treatment of chronic hepatitis C in HIV-infected persons: A

multicenter randomized controlled trial. *JAIDS Journal of Acquired Immune Deficiency Syndromes, 35*, 464-472. doi:10.1097/00126334-200404150-00004

Sun, B., Abadjian, L., Rempel, H., Monto, A., & Pulliam, L. (2013). Differential cognitive impairment in HCV coinfected men with controlled HIV compared to HCV monoinfection. *Journal of Acquired Immune Deficiency Syndromes, 62*, 190-196. doi:10.1097/QAI.0b013e31827b61f1

Tavakkoli, M., Ferrando, S. J., Rabkin, J., Marks, K., & Talal, A. H. (2013). Depression and fatigue in chronic hepatitis C patients with and without HIV co-infection. *Psychosomatics, 54*, 466-471. doi:10.1016/j.psym.2013.02.009

The Cochrane Collaboration (2014). *Review Manager (RevMan) [Computer program], Version 5.3*. Copenhagen: The Nordic Cochrane Centre.

Thein, H., Maruff, P., Krahn, M., Kaldor, J., Koorey, D., Brew, B., & Dore, G. (2007). Cognitive function, mood and health-related quality of life in hepatitis C virus (HCV)-monoinfected and HIV/HCV-coinfected individuals commencing HCV treatment. *HIV Medicine, 8*, 192-202. doi:10.1111/j.1468-1293.2007.00452.x

Udina, M., Castellví, P., Moreno-España, J., Navinés, R., Valdés, M., Forns, X., … Martín-Santos, R. (2012). Interferon-induced depression in chronic hepatitis C: A systematic review and meta-analysis. *Journal of Clinical Psychiatry, 73*, 1128-1138. doi:10.4088/JCP.12r07694

Uher, R., Perlis, R. H., Placentino, A., Dernovšek, M. Z., Henigsberg, N., Mors, O., … Farmer, A. (2012). Self-report and clinician-rated measures of depression severity: Can one replace the other? *Depression and Anxiety, 29*, 1043-1049. doi:10.1002/da.21993

van de Laar, T. J., Matthews, G. V., Prins, M., & Danta, M. (2010). Acute hepatitis C in HIV-infected men who have sex with men: An emerging sexually transmitted infection. *AIDS, 24*, 1799-1812. doi:10.1097/QAD.0b013e32833c11a5

von Giesen, H.-J., Heintges, T., Abbasi-Boroudjeni, N., Kücükköylü, S., Köller, H., Haslinger, B. A., … Arendt, G. (2004). Psychomotor slowing in hepatitis C and HIV infection. *Journal of Acquired Immune Deficiency Syndromes, 35*, 131-137. doi:10.1097/00126334-200402010-00005

Weissenborn, K., Krause, J., Bokemeyer, M., Hecker, H., Schüler, A., Ennen, J. C., … Böker, K. W. (2004). Hepatitis C virus infection affects the brain - Evidence from psychometric studies and magnetic resonance spectroscopy. *Journal of Hepatology, 41,* 845-851. doi:10.1016/j.jhep.2004.07.022

Wahl, I., Löwe, B., Bjorner, J. B., Fischer, F., Langs, G., Voderholzer, U., … Rose, M. (2014). Standardization of depression measurement: A common metric was developed for 11 self-report depression measures. *Journal of Clinical Epidemiology, 67,* 73-86. doi:10.1016/j.jclinepi.2013.04.019

Yoon, J. C., Crane, P. K., Ciechanowski, P. S., Harrington, R. D. Kitahata, M. M., & Crane, H. M. (2011). Somatic symptoms and the association between hepatitis C infection and depression in HIV-infected patients. *AIDS Care, 23*, 1208-1218. doi:10.1080/09540121.2011.555739

Table 1. General characteristics of the 29 studies included in the systematic review

Authors, Year	Country	Design	Sample (*N*)	Gender (% male)	Age[a]	IDU
Alavi et al., 2012	Australia	Prospective cohort	Total = 163	71%	34.3 ± 9.9	76% history IDU
			HIV/HCV = 50			
Backus et al., 2005	USA	Retrospective cohort	HIV = 11,567	97.4%	47.9 ± 10.3	20.6% hard drug abuse
			HIV/HCV = 6,782	98.3%	49.8 ± 6.3	62.9% hard drug abuse
Baillargeon et al., 2008	USA	Prospective cohort	HIV = 3,783	83.2%	NR	NR
			HIV/HCV = 2,275	87%	NR	NR
Baum et al., 2008	USA	Cross-sectional	HIV = 135	75.6%	41.0 ± 7.3	10.3% history IDU
			HIV/HCV = 57	71.9%	45.4 ± 6.5	40.3% history IDU
Braitstein et al., 2005	Canada	Cross-sectional	HIV = 379	97%	43 (mean)	5% history IDU
			HIV/HCV = 105	82%	42 (mean)	79% history IDU
Butt et al., 2006	USA	Retrospective cohort	HCV = 114,005	96.9%	50	38.9%
			HIV/HCV = 6,502	98.2%	48	56.2%
Butt et al., 2009	USA	Prospective cohort	HCV = 241	58.5%	49.7 ± 10.9	50.6% recent IDU
			HIV/HCV = 158	81.6%	48.4 ± 7.4	60.2% recent IDU
Ciccarelli et al., 2013	Italy	Cross-sectional	HIV = 50	64%	48 (45-53)[b]	4% history IDU
			HCV = 50	72%	48 (42-52)[b]	38% history IDU
			HIV/HCV = 50	78%	48 (42-55)[b]	78% history IDU
Clifford et al., 2005	USA	Cross-sectional	HIV = 234	80%	38.05 ± 8.63	4% history IDU
			HIV/HCV = 30	77%	40.27 ± 7.75	47% history IDU
Fumaz et al., 2007	Spain	Prospective longitudinal	Peg-IFN a-2a = 32	71.8%	40.7 ± 4.08	78.1% IDU risk factor

			Peg-IFN a-2b = 31	67.7%	39.2 ± 5.03	90.3% IDU risk factor
Goulet et al., 2005	USA	Retrospective cohort	HIV = 20,627	94%	47.1 (median)	22%[c]
			HIV/HCV = 4,489	98%	46.9 (median)	58%[c]
Kemmer et al., 2012	USA	Prospective longitudinal	HIV/HCV = 329	83.3%	48 (median)	NR
Klein et al., 2014	Canada	Randomized, double-blind placebo-controlled trial	Citalopram = 36	72.2%	45.6 (38.7–50.9)[b]	52.8% IDU risk factor
			Placebo = 40	100%	46.7 (42.6–52.9)[b]	47.5% IDU risk factor
Laguno et al., 2004	Spain	Randomized open-label	Peg-IFN a-2b + RBV = 52	63%	40 (mean)	75% IDU risk factor
			IFN a-2b + RBV = 43	74%	40 (mean)	91% IDU risk factor
Landau et al., 2001	France	Prospective longitudinal	HIV/HCV = 51	76.5%	39 ± 5 (30-59)	94%
Michel et al., 2010	France	Cross-sectional	HIV/HCV = 328	69.8%	42 (40-46)[b]	63.6% IDU risk factor
Moreno et al., 2004	Spain	Prospective longitudinal	HIV/HCV = 35	69%	38 (35-39)[b]	83% IDU risk factor
Myers et al., 2004	Canada	Open-label study	HIV/HCV = 32	78%	40 ± 6 (26-55)	78% history IDU
Pantalone et al., 2012	USA	Cross-sectional	HIV = 117	100%	43.75 ± 8.80	6.1% IDU risk factor
			HIV/HCV = 54	100%	44.80 ± 7.66	31.5% IDU risk factor
Pereira et al., 2014	Portugal	Cross-sectional	HIV = 462		41.19 ± 10.01	19.5% IDU risk factor
			HIV/HCV = 248		38.75 ± 6.54	68.8% IDU risk factor
Richardson et al., 2005	USA	Cross-sectional	HIV = 75	100% female	33.8 ± 7.2	NR
			HCV = 27	100% female	37.3 ± 9.2	NR
			HIV/HCV = 70	100% female	39.6 ± 6.5	NR
Rockstroh et al., 2002	Germany	Prospective longitudinal	HIV/HCV = 23	78.3%	42 (median)	NR
Ryan et al., 2004	USA	Cross-sectional	HIV = 49	77.6%	41.9 ± 7.2	NR
			HIV/HCV = 67	73.1%	45.1 ± 7.2	NR

Sulkowski et al., 2004	USA	Randomized open-label	Daily IFN + RBV = 90	77.8%	43.7 ± 5.7	57.8% history IDU
			TIW IFN + RBV = 90	74.4%	43.7 ± 8.6	65.6% history IDU
Sun et al., 2013	USA	Cross-sectional	HIV = 14	100%	51.6 ± 7.2	NR
			HCV = 19	100%	56.6 ± 4.5	63% history IDU
			HIV/HCV = 17	100%	54.5 ± 5.2	71% history IDU
Tavakkoli et al., 2013	USA	Cross-sectional	HCV = 65	56.9%	47.5 ± 7.1	50.8%
			HIV/HCV = 102	75.5%	49.7 ± 9.6	54.9%
Thein et al., 2007	Australia	Cross-sectional	HIV = 30	100%	34.7 ±7.4	NR
			HCV = 19	63.2%	42.6 ±6.5	89.5% history IDU
			HIV/HCV = 15	100%	35.5± 7.0	86.7% history IDU
von Giesen et al., 2004	Germany	Cross-sectional	HIV = 43	65.1%	38.0 ± 8.1	62.8% IDU risk factor
			HCV = 44	35.6%	43.2 ± 13.7	18.2% IDU risk factor
			HIV/HCV = 43	65.1%	37.4 ± 7.8	62.8% IDU risk factor
Yoon et al., 2011	USA	Cross-sectional	HIV = 604	88%	45 (median)	15% IDU risk factor
			HIV/HCV = 160	83%		63% IDU risk factor

NR: Not reported; RBV: Ribavirin; Peg-INF: pegylated interferon; INF: interferon; TIW: thrice-weekly.

[a] Unless indicated, data are presented as mean ± SD (or range); [b] Data is presented as Median (Interquartile range); [c] Comorbid drug disorder

Table 2. Synthesis of findings on depression/depressive symptoms of the 29 studies included in the systematic review

Authors, Year	Depression measures	Main Findings
Alavi et al., 2012	Mini International Psychiatric Interview (MINI). Depression, Anxiety and Stress Scale (DASS-21)	Before HCV treatment, at baseline, the co-infected group was significantly less depressed than the HCV mono-infected group. During treatment, the prevalence of new-onset depression was higher among the co-infected group when compared with the HCV mono-infected group (38% vs. 33%), but the difference was not significant.
Backus et al., 2005	Clinical notes based on the International Classification of Diseases, 9th Revision (ICD9)	Both co-infected and HIV mono-infected patients presented high prevalence of mental illness, particularly depression. However, the HIV/HCV co-infected group was more likely to present a diagnosis of depression, alcohol abuse and substance abuse compared with the HIV mono-infected group.
Baillargeon et al., 2008	Clinical appointments using the International Classification of Diseases (ICD-10)	In comparison to HIV mono-infected inmates, those with HIV/HCV co-infection had an elevated prevalence of any psychiatric disorder (20.6% vs. 16.7%). No increased odds were observed in relation to Major Depression (8.4% vs. 7%).
Baum et al., 2008	NR	In comparison to HIV mono-infected patients, the HIV/HCV co-infected patients reported depression (36.8% vs. 8.1%), fatigue, headache, diarrhoea and apathy as the most prevalent physical and mental health symptoms.
Braitstein et al., 2005	Centre for Epidemiologic Studies Depression Scale (CESD)	The co-infected group showed higher scores on symptoms consistent with depression, increased fatigue and poorer quality of life. The impact of HCV on quality of life, depression and fatigue was better explained by socio-demographic factors related to poverty and IDU than by HCV itself.
Butt et al., 2006	Clinical notes using the ICD9 codes	The HIV/HCV co-infected group were more frequently diagnosed with major depression (23% vs. 18.4%) and mild depression (35.4% vs. 32.4%) than the HCV mono-infected group. Additionally, depression was associated with a lower likelihood of hepatitis treatment prescription.
Butt et al., 2009	Structured questionnaires	HIV/HCV co-infected patients were more likely to be depressed (67.4% vs. 39.9%) and tended to

		present higher prevalence of ongoing alcohol abuse than HCV mono-infected patients.
Ciccarelli et al., 2013*	Zung Depression Scale	No significant differences were found in the depression scores between HIV/HCV co-infected groups and the HIV and HCV mono-infected groups.
Clifford et al., 2005*	Centre for Epidemiologic Studies Depression Scale (CESD)	The HIV/HCV co-infected group presented significantly more depressive symptomatology than the HIV mono-infected group (57% vs. 32%).
Fumaz et al., 2007	Beck Depression Inventory (BDI)	Among HIV/HCV co-infected patients, there were no significant differences in depression scores between types of hepatitis C treatment; however, the rates of depressive symptoms were high in both groups during treatment (overall, 58.7% of patients presented mild to moderate depressive symptoms).
Goulet et al., 2005	Clinical notes using the ICD9 codes	The HIV/HCV co-infected patients were significantly more likely to have psychiatric disorders, including depression (43% vs. 28%), than HIV mono-infected patients.
Kemmer et al., 2012	Centre for Epidemiologic Studies Depression Scale (CESD)	Depression was significantly associated with a decline in role, social and cognitive function in HIV/HCV co-infection.
Klein et al., 2014	Beck Depression Inventory-II (BDI-II) Montgomery–Åsberg Depression Rating Scale (MADRS) Structure Clinical Interview for DSM-IV Axis I Disorders (SCID-I)	Prophylactic citalopram compared to treatment of emergent depression was not associated with a reduction in treatment-limiting depression, nor did significantly reduce depressive symptoms among HIV/HCV co-infected patients during hepatitis C treatment.
Laguno et al., 2004	World Health Organization Scale	A high incidence of depressive symptoms was reported among HIV/HCV co-infected patients (43%); however, most of them were not severe and improved with antidepressant therapy, without reduction or cessation of hepatitis C treatment.
Landau et al., 2001	NR	Depressive symptoms were reported in 8% of HIV/HCV co-infected patients under hepatitis C treatment.

Michel et al., 2010	Centre for Epidemiologic Studies Depression Scale (CESD)	Depressive symptoms and treatment for depressive symptoms was significantly associated with the cognitive, social and physical dimensions of fatigue impact.
Moreno et al., 2004	World Health Organization Scale	A prevalence of 9% of depression was reported as an adverse event during hepatitis C treatment.
Myers et al., 2004	NR	Psychiatric manifestations were the main reason for discontinuation of hepatitis C treatment (19%); depression was the most common reason for discontinuation, followed by agitation and delirium and anxiety.
Pantalone et al., 2012*	Centre for Epidemiologic Studies Depression Scale (CESD)	Depression scores were elevated in HIV mono-infected and HIV/HCV co-infected groups; HIV/HCV co-infected MSM were significantly more depressed than HIV mono-infected MSM.
Pereira et al., 2014	Brief Symptom Inventory (BSI)	HIV/HCV co-infected patients reported significantly higher scores on the subscale Depression of the BSI than HIV mono-infected patients. As well, compared to HIV mono-infected patients, a greater proportion of HIV/HCV co-infected patients met caseness for depression (17.7% vs. 12%).
Richardson et al., 2005*	Centre for Epidemiologic Studies Depression Scale (CESD)	The depression scores were not significantly different between HIV/HCV, HIV and HCV mono-infected groups.
Rockstroh et al., 2002	NR	During hepatitis C treatment, 3 out of 9 patients developed depression, which resulted in treatment discontinuation.
Ryan et al., 2004	Psychiatric Research Interview for Substance and Mental Disorders (PRISM)	There were no significant differences on the prevalence of primary mental disorders between HIV/HCV co-infected and HIV mono-infected patients. However, past and current depression was the most common diagnosis in both groups.
Sulkowski et al., 2004	NR	Depression was observed in patients during hepatitis C treatment among HIV/HCV co-infected patients.
Sun et al., 2013*	Beck Depression Inventory (BDI-II)	The HIV/HCV co-infected group was found to have significantly more depressive symptoms than the HCV mono-infected group and the healthy controls, after adjusting for education and general intellect (IQ).

Tavakkoli et al., 2013	Patient Health Questionnaire -9 (PHQ-9)	A diagnosis of major depression was significantly less common among HIV/HCV co-infected patients, in comparison to HCV mono-infected patients (24.7% vs. 41.4%).
Thein et al., 2007	Depression Anxiety Stress Scales (DAAS)	The mean DAAS scores were similar between HIV/HCV co-infected, HIV and HCV mono-infected patients and uninfected controls prior to hepatitis C treatment.
von Giesen et al., 2004*	Hamilton Depression Rating Scale (HAMD)	HCV mono-infected patients presented significantly lower scores of depression than HIV mono-infected and HIV/HCV co-infected patients.
Yoon et al., 2011	Patient Health Questionnaire -9 (PHQ-9)	A high prevalence and severity of depression was found among HIV/HCV co-infected patients, even adjusting for differences in substance use. The mean depression severity scores for HIV/HCV patients were 3.4 points higher than for HIV mono-infected patients; the association between HCV and greater depression severity remained significant even adjusting for antidepressant medication and current illicit drug use.

* Studies included in the meta-analyses

NR: Not reported; MSM: Men who have sex with men