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**Treatment, care and support for people co-infected with HIV and Hepatitis C: A scoping review**

**(Running Title: HIV-HCV co-infection: A scoping review)**

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**Abstract**

**Background:** Important co-morbidities are now emerging among people living with HIV, which has increasing the complexity of their health and healthcare needs. Hepatitis C (HCV) has been identified as one of these diseases and is one of the leading causes of death among people living with HIV.

**Objective:**  To map the sources and types of evidence available and assess the quality of systematic reviews and/or treatment guidelines related to the treatment, epidemiology and care/support/prevention for people co-infected with HIV and hepatitis C (HCV).

**Methods:** We searched 7 databases, hand searched 8 journals and contacted key informants to identify literature from 1996-January 2007. Two reviewers independently applied coding criteria and assessed the quality of the included treatment guidelines and systematic reviews using the AGREE and AMSTAR instruments.

**Results**: Our search strategy yielded 1684 references with 226 meeting the final inclusion criteria. Of the 226 included references, 114 were coded as addressing treatment topics, 49 as epidemiology and 79 as care/support and prevention programming. In addition, we found 9 treatment guidelines with 4 assessed as ‘strongly recommend’ 3 as ‘recommend (with provisos or alterations) and 1 as ‘would not recommend’. 10 systematic reviews were also located with 7 assessed as high, 2 as medium and 1 as low quality.

**Conclusion**: This quality assessed inventory of treatment guidelines and systematic reviews can be used by physicians and service providers to rapidly locate HIV-HCV co-infection research. However, much of the research is based on literature that does not include current injection drug users (IDUs) or people with mental health issues due to the sparse evidence on these populations, which limits its scope and applicability to important populations. This limitation in the literature highlights the need for 1) additional research with these populations for how to deliver treatment and services and 2) integrated HIV and HCV funding for screening, support and prevention.

**Introduction**

The availability and accessibility of highly active antiretroviral therapy (HAART) in Canada has extended the length and improved the quality of life for people living with HIV/AIDS.(1;2) As a result, important co-morbidities are now emerging among people living with HIV, increasing the complexity of their health and healthcare needs(3-5). Hepatitis C (HCV) has been identified as one of these diseases and is one of the leading causes of death among people living with HIV.(1;6)

HCV is a blood-borne virus that primarily affects the liver. Approximately 5%-20% of chronic HCV infections will result in cirrhosis over a period of 20-25 years of which approximately 30% will develop end-stage liver disease (over 10 years) and 1%-2% will develop hepatocellular carcinoma each year.(7) While HCV is firstly a liver disease, it is also occasionally associated with extrahepatic disease including vasculitis and kidney disease.(7) Although HCV is much more infectious than HIV, spreading easily through a minute amount of blood (e.g., through shared syringes, intra-nasal cocaine use, or improperly sterilized tattoo or acupuncture equipment) there is effective treatment available. For people with HCV genotype 1, recommended treatment is peginterferon, plus1000-1200 mg of ribavirin daily, for 48 weeks, which results in sustained virologic response (SVR) in approximately 42%-61% (depending on whether the patient has a high or low viral load at the time of treatment and other key predictors of treatment outcome) of patients.(7;8) For people with HCV genotypes 2 or 3, recommended treatment is peginterferon, plus800 mg of ribavirin daily, for 24 weeks, which results in SVR in approximately 80% of patients(7;9-11). However, when co-infection with HIV occurs, HCV progression is often accelerated(12), HAART may become more difficult to tolerate(13) and HCV treatment is less successful (SVR rate of 16-38% for those with genotype 1 and 43%-60% for those with genotype 2 or 3).(8)

In order to address the continued spread of HCV, the Canadian federal government announced its first commitment to hepatitis C prevention, treatment and care through the Hepatitis C Prevention, Support & Research Program. $50 million over a five-year (1999-2004) period was committed, which has since received single-year funding renewal three times with funding for community-based HCV programs currently suspended. However, this program has not been coordinated with the Canadian Strategy on HIV/AIDS. As a result, HIV care providers and community services are often ill-equipped, under-funded, and often lack sufficient or appropriate information on HCV. HIV clinics and AIDS service organizations (ASOs) across Canada have addressed the increased demand for co-infection treatment, care and support but without official funding or technical supports. There are few HCV experts or healthcare providers that specialize in HIV co-infection issues, and HCV focused community services are almost non-existent(6).

In response to community demand for an official response to HIV-HCV co-infection, the Ontario HIV Treatment Network (OHTN) convened a working group in September 2006 comprised of representatives from the Hepatitis C Secretariat, The HIV/AIDS Bureau of the Ontario Ministry of Health and Long-Term Care, the Canadian Treatment Action Council, the Ontario Aboriginal AIDS Strategy, medical experts in the field, provincial community health organizations and advocacy organizations. The working group organized a multi-stakeholder Think Tank (held on April 16th, 2007) to address issues related to treatment, care and support for people co-infected with HIV and HCV. This scoping review was commissioned in order to provide an evidence-base that could be used to inform the Think Tank and be disseminated to additional medical, community, policy and scholarly stakeholders. Therefore, our objectives were to:

1. identify and assess the quality of systematic reviews and/or treatment guidelines about treatment, care and support as well as about the epidemiological profile for people co-infected with HIV and HCV; and
2. map the sources and types of evidence that are available, identify areas where systematic reviews could be completed and highlight where additional primary research is needed.

**Methods**

In general, the aim of a scoping review is to “map *rapidly* the key concepts underpinning a research area and the main sources and types of evidence available” (14, emphasis in original). Scoping reviews are often conducted to examine previous research activity, determine the value of conducting a full systematic review, disseminate findings and/or to identify gaps in the research(15). We addressed these objectives in the areas of treatment, care and support for people co-infected with HIV and HCV using an iterative methodology that allowed for reflexivity at each stage in order to ensure that our final search terms and inclusion criteria were appropriate.

**Literature Search**

Our literature search consisted of three strategies – database search, journal hand search and key contacts - to identify both published and unpublished literature from 1996-January 2007 (i.e., the post HAART era). Our search strategies were designed to provide a balance between achieving a rapid assessment of the literature and obtaining a comprehensive survey of the literature about HIV-HCV co-infection. First, we searched 7 databases (MEDLINE, PubMed, Cochrane Library, Psyclinfo, AIDSearch, Canadian HIV/AIDS Policy and Law Review and Google Scholar) using pre-specified search terms (HIV OR AIDS combined with Hepatitis C OR HCV) that we developed through consultation with a librarian at the University of Toronto. We then hand searched 8 journals (CMAJ, AIDSCare, AIDS Policy and Law, Annals of Internal Medicine, Canadian Journal of Gastroenterology, HIV Medicine, JAIDS, and NEJM) and kept any systematic reviews and primary research that addressed treatment, care and support issues for people co-infected with HIV and HCV (inclusion and coding criteria were applied later in the review process). Lastly, we contacted relevant national and local organizations within Canada working in the field of HIV and HCV and asked them to identify published and/or unpublished works.

**Inclusion and Coding Criteria Development**

We undertook an iterative and reflexive three stage approach to developing inclusion and coding criteria. First, we coded 200 titles and abstracts that we located from the electronic database search based on whether the reference addressed a question about HIV-HCV co-infection, whether it studied or discussed a Canadian study population or an international population, the methods used and the subject area addressed. We then met as a team, collectively revised our framework to include additional codes for specific study populations and subject areas of interest and applied the revised framework to all of the search results.

Upon completion of the full review of the search results we collectively developed inclusion criteria across three domains – 1) treatment, 2) epidemiology and 3) care/support/programming and prevention - and applied the criteria to all titles and abstracts that were marked as applicable to HIV-HCV co-infection in the previous coding stage. Inclusion criteria for treatment required that studies were primary research (including systematic reviews/meta-analyses) or treatment guidelines, assessed either Pegylated-Interferon and Ribavirin for HCV (these are now determined to be the standard of care) treatment or HAART for HIV treatment (or both). Treatment studies that only assessed populations of haemophiliacs and those conducted in the developing world were excluded as we deemed these groups to be distinct with different contexts that require separate analysis. For epidemiological studies we included primary research and excluded studies that only assessed populations of hemophiliacs and those from the developing world. For care/support/programming and prevention, we included all studies/reports with a focus on co-infection as the literature in these areas is quite sparse.

**Reviewing**

Title and abstract, full-text and quality assessment reviews were conducted in a systematic and rigorous manner. All titles and abstracts were coded and assessed for inclusion by two pairs of independent reviewers with one pair conducting half the reviews and another pair conducting the other half.

We then retrieved the full-text articles of included systematic reviews and treatment guidelines and conducted a quality assessment using two independent raters. For systematic reviews, two raters applied (disagreements were resolved by consensus) the AMSTAR (A MeaSurement Tool to Assess Reviews) instrument, which has been shown to be the strongest quality assessment tool for systematic reviews and demonstrates strong face and content validity(16;17). AMSTAR produces a quality score between 0-11 with score ranges of low, medium and high(18). For treatment guidelines, we used the AGREE (Appraisal of Guidelines Research and Evaluation) as it is the only internationally tested instrument, is designed to be used by a wide range of professionals and demonstrates strong reliability(19). AGREE consists of 23 items (four-point Likert scales) across six domains, which are used to produce three possible conclusions: ‘strongly recommend’, ‘recommend (with provisos or alterations)’ or ‘would not recommend’(20).

**Review Funding**

This scoping review was funded by the Ontario HIV Treatment Network by providing the staff support and the office resources needed to conduct the review and prepare the manuscript.

**Results**

Our search strategy yielded 1684 references (2598 before duplicate removal) with 226 meeting the final inclusion criteria. Figure 1 outlines the progression of the reviewing process. Table 1 contains a listing of quality assessment scores from AMSTAR and AGREE as well as study characteristics of all the systematic reviews and treatment guidelines contained within the 226 included references. Furthermore, in Tables 2-4, key findings (with a focus on Canadian findings) from each of the 3 primary domains are presented along with a breakdown of the included studies based on methods used, population(s) (a study was coded for a specific population only if it was the focus of the study), country of study (Australia, Canada, Europe, United States and ‘other’) and study scope (local, multi-city/national and multi-country studies). These key findings are not meant to be an exhaustive analysis of outcomes that would normally be found in a systematic review but rather an outline of the primary themes that emerged from the systematic reviews, treatment guidelines, longitudinal studies and key care, support and programming references that were included in the review. This outline of key themes was conducted in order to provide a broad evidence-base for the multi-stakeholder Think Tank that this scoping review was originally commissioned for.

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As can be seen in Table 1, we located 9 treatment guidelines and 10 systematic reviews that have information relevant to HIV-HCV co-infection. From our quality assessments of the treatment guidelines, 4 are ‘strongly recommended’(7;8;21;22), 3 are ‘recommended (with provisos or alterations)’(23-25) and 1 was classified as ‘we would not recommend’(26) and one was not assessed for quality because it could not be located. Of the 10 systematic reviews that we included, 3 addressed topics related to treatment, 3 were focused on epidemiological questions, 4 were focused on care/support questions and 4 focused on prevention questions (some reviews addressed more than one domain). Our quality assessments of the included systematic reviews indicated that most are high quality(27-33) with only two rated as medium quality (34;35) and one as low quality(36).

As can be seen in Tables 2-4 we found 114, 49 and 79 publications/reports in the treatment, epidemiology and care/support/programming/prevention domains respectively. Across all three domains, most studies were either local or multi-city/national studies with most treatment studies coming from Europe (n=64) and the United States (n=33). For the treatment domain we found 21 studies that included information related to both HAART for HIV and peginterferon and ribavirin treatment for HCV, 53 studies that investigated topics only related to HAART in co-infected people and 40 studies that investigated topics only related to peginterferon and ribavirin treatment in co-infected people. In the care/support/programming/prevention domain, 43 addressed topics only related to care/support/programming, 5 addressed topics only related to prevention and 31 addressed both with just under half of the publications/reports in this domain addressing issues related to IDUs (a full list of the references found for each of the three domains is available upon request).

**Discussion**

**Principal Findings**

Overall, we found that the literature on co-infection is fairly well-defined with nine treatment guidelines and 10 systematic reviews that address one or more of the three topic domains, which provide a reliable evidence-base for those delivering treatment, care and support to draw upon. The quality assessed inventory of treatment guidelines and systematic reviews that we have created can be used by physicians and service providers to rapidly determine 1) if there are guidelines or reviews available that are specific to their jurisdiction to help with decision-making about treatment or other service delivery issues and 2) if the guideline or review is of sufficient quality to use in their decision-making.

**Implications**

Despite the fact that we found a number of treatment guidelines and systematic reviews, they are often based on literature that does not include current IDUs or people with mental health issues due to the sparse evidence on these populations (especially in the treatment literature). As a result, they often indicate that treatment in these populations should proceed on a ‘case by case basis’. This finding is particularly salient given the fact that the epidemiological literature indicates that co-infection is mostly found among IDUs and that those with serious mental illness are at high-risk of co-infection. Therefore, much of the evidence (particularly in the treatment literature) is either limited in its scope and applicability to important co-infected and at-risk populations or lacks detail for how to deliver treatment to these populations, while ensuring the appropriate supportive care during treatment.

Given the epidemiological profile in Canada, with high levels of HIV-HCV co-infection among vulnerable populations such as IDUs, people with mental health illness and prisoner populations there is an increasing need to integrate screening, care/support/programming and prevention efforts and the funding streams for existing programs. An integrated programming and funding strategy will allow for populations to not only receive care, support and prevention services for co-infection but also for other co-morbidities such as substance use and mental health illnesses.

**Strengths and Weaknesses**

The primary strengths of this scoping review are that it provides 1) a rigorous systematic assessment of the literature on HIV-HCV co-infection across three domains, 2) an inventory of high-level evidence (i.e., treatment guidelines and systematic reviews) that has been assessed for quality, 3) a clear sense of the populations that have been focused on (and those have not been focused on) in the co-infection literature, and 4) a direction for future research initiatives (see below).

The primary weaknesses of this scoping review are that it 1) lacks the depth of a traditional systematic review, 2) focuses only on developed countries, and 3) excludes studies that focus exclusively on haemophiliacs.

**Future Research**

Given the limited scope of some of the literature we located, there is a need to expand co-infection research initiatives (particularly in the treatment and support domains) to IDU and mental health populations and ensure that existing systematic reviews and treatment guidelines are updated with new data that emerges from these initiatives. In addition, beyond topics of methadone treatment and needle exchange for IDUs, the care/support/programming and prevention literature appears to lack enough depth for a full systematic review. Therefore, future research should attempt to evaluate or highlight integrated efforts for the treatment, care or support for people who are co-infected with HIV and HCV. Lastly, continued tracking of the epidemiological profile of HIV-HCV co-infection needs to be continued with rigorous longitudinal models.

**Table 1: Systematic reviews and treatment guidelines – Quality and local applicability**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Domain** | **Study type** | **Quality** | **Study Characteristics** | | |
| **Timeframe** | **Population** | **Interventions/topic** |
| Sherman et al.(8) | treatment | Treatment guideline | Recommend (with provisos or alterations) | 2007 | Canada | Managing chronic HCV |
| Sherman et al.(25) | treatment | Treatment guideline | Strongly recommend | 2004 | Canada | Managing chronic HCV |
| Antonucci et al.(37) | treatment | Treatment guideline | No assessment completed\* | 2004 | Italy | Managing HCV-HIV co-infection |
| Strader et al.(7) | treatment | Treatment guideline | Strongly recommend | 2004 | United States | Diagnosis, management and treatment of HCV |
| Soriano et al.(22) | treatment | Treatment guideline | Strongly recommend | 2004 | Spain | Care for co-infected patients |
| The National Institutes of Health(21) | treatment | Treatment guideline | Strongly recommend | 2004 | United States | Treatment of opportunistic infections in HIV-infected adults |
| Nelson et al.(26) | treatment | Treatment guideline | Would not recommend | 2005 | United Kingdom | Treatment for HIV and chronic HCV |
| Alberti et al.(23) | treatment | Treatment guideline | Recommend (with provisos or alterations) | 2005 | International | Treatment of chronic hepatitis B & C in HIV-infected patients |
| Boucher and Gruslin(24) | treatment  care/support | Treatment guideline | Recommend (with provisos or alterations) | 1966-2000 | Canada | Reproductive care for women living with HCV |
| Shepherd et al.(33) | treatment | Systematic review (part of an HTA) | High (8/11) | All literature up to 2003 | HCV-infected patients from clinical trials | Peg-interferon-2a and -2b with Ribavirin |
| Kim et al.(30) | Treatment | Systematic review | High (8/11) | All literature up to 2005 | Co-infected patients in RCTs | Peg-interferon and Ribavirin |
| Mohsen et al.(36) | treatment  epidemiology | Systematic review | Low (2/11) | 1993-2000 | Outpatients, IDU, prisoners, MSM | Epidemiology and clinical implications of co-infection |
| Graham et al.(35) | epidemiology | Systematic review | Medium (4/11) | 1966-1999 | Co-infected patients with liver disease | Impact of HIV on the course of HCV |
| Gebo et al.(34) | epidemiology  care/support | Systematic review | Medium (6/11) | 1996-2002 | Patients with chronic HCV | Treatment and screening strategies for HCV |
| O’Connor et al.(32) | care/support | Systematic review | High (9/11) | All literature up to 2002 | People facing healthcare decisions | Decision-aids for treatment or screening decisions |
| Faggiano et al.(28) | prevention  care/support | Systematic review | High (10/11) | All literature up to 2001 | IDU | Methadone maintenance programs |
| Leonard et al.(31) | prevention  care/support | Systematic review | High (8/11) | 1997-1999 | IDU, Prisoners and  Women | Needle exchange programs |
| Amato et al.(27) | prevention | Systematic review | High (9/11) | All literature up to 2004 | IDU | Tapered methadone doses |
| Gowing et al.(29) | prevention | Systematic review | High (8/11) | All literature up to 2003 | IDU | Oral substitution treatment for opioid dependence |

\*We did not complete a quality assessment of Antonnuci et al. because we were unable to locate a copy of the full paper.

**Table 2: Key Findings – Treatment for HIV-HCV co-infection**

|  |  |
| --- | --- |
| **Types of Literature Available** | **Key Findings** |
| **Total Treatment Studies Included** = 114  **Methods Used**  Treatment Guidelines: 10  Systematic Reviews: 3  RCTs: 17  Health Technology Assessment: 1  Longitudinal (prospective): 48  Longitudinal (retrospective): 13  Cross-sectional/case study/case-control: 19  Qualitative: 1  Grey literature studies: 2  **Populations Studied**  Other (clinic or hospital/institution based): 75  Other: 22  IDUs: 5  Women: 3  MSM: 2  Aboriginals: 1  Youth: 1  **Countries Studied**  Europe: 64  United States: 33  Canada: 14  Australia: 7  Other: 6  **Scope of Studies**  Local: 53  Multi-city/national: 46  Multi-country: 9 | **Canada Specific Findings:**   * Canada has treatment guidelines for HIV and Hepatitis C co-infection (published in 2004 and updated in 2007) (8;25) with the most recent being consistent with international guidelines (7;21-23;26;37). * Canadian guidelines encourage clinicians to assess people with mental illness or substance use issues for HCV treatment on a case-by-case basis(8;25).   **General Findings:**   * The current standard for treating HCV is co-administration of pegylated interferon alpha (peg-IFN) and ribavirin (RBV), which takes 12-48 months depending on factors such as HCV genotype(8). * Treating both HIV and HCV simultaneously is not advised due to combined side effects(25). The decision about which disease to treat first is based on the stage of HIV disease (as measured by CD4 count)(8): * for individuals with CD4+ cell counts > than 350 x 109 cells/L and relatively low plasma HIV RNA levels and no history of alcohol abuse, hepatitis C should be treated before initiating antiretroviral therapy for HIV(7;21-23;25;26;37); * for individuals with CD4+ cell counts < 200 x 109 cells/L, hepatitis C should be treated only after antiretroviral therapy has been initiated, plasma HIV RNA levels are suppressed, and CD4+ cell counts have risen(7;21-23;25;26;37); * for individuals with CD4+ cell counts between 200 and 350 x 109 cells/L and already on antiretroviral therapy for HIV, treatment for hepatitis C may be considered after assessing factors, such as the severity of liver disease, HCV genotype, and the extent of suppression of HIV replication(7;21-23;25;26;37); * HCV treatment is not recommended for individuals with current or previous liver decompensation and contraindicated for pregnant women(7;21-23;25;26;37).   **Side Effects:**   * People being treated for hepatitis C experience significant side-effects such as loss of appetite, nausea, anaemia, depressive symptoms, and mood changes(38) and need close monitoring(8). Strategies to manage side effects include therapies, such as growth factors and/or antidepressants(38) as well as individual or group counselling, harm-reduction and peer-support groups(39).   **Treatment Eligibility:**   * Co-infected individuals who have mental illness or substance use problems have traditionally been excluded from clinical trials/treatment because of poor adherence and/or psychiatric side effects of HCV treatment, so little is known about the efficacy of HCV treatment in these populations(7;21-23;25;26;37;40). |

**Table 3: Key findings – Epidemiology for HIV-HCV co-infection**

|  |  |
| --- | --- |
| **Types of Literature Available** | **Key Findings** |
| **Total Treatment Studies Included** = 49  **Methods Used**  Systematic Reviews: 3  RCTs: 1  Longitudinal (prospective): 16  Longitudinal (retrospective): 2  Model: 3  Policy/position paper: 2  Cross-sectional/case study/case-control: 23  Qualitative: 2  Grey literature studies: 5  **Populations Studied**  Other (clinic or hospital/institution based): 14  Other: 7  IDUs: 21  Women: 2  MSM: 2  Aboriginals: 3  Youth: 6  Mental Health: 4  Prisoners: 8  **Countries Studied**  Europe: 13  United States: 24  Canada: 15  Australia: 2  Other: 4  **Scope of Studies**  Local: 20  Multi-city/national: 24  Multi-country: 3 | **Canada Specific Findings:**   * In 1999, approximately 11,194 people in Canada were estimated to be co-infected with hepatitis C; 87% of co-infected Canadians lived in three provinces: 34% in Quebec, 29% in British Columbia and 25% in Ontario)(41). * Among those infected with HIV, prevalence of co-infection is estimated at 18%(42). * Injection drug users and men who have sex with men *and* use injection drugs (MSM-IDU) made up 71% and 15% respectively of co-infections in Canada in 1999; in British Columbia, 16% of youth injection drug users are estimated to be co-infected(41;43). * The risk of co-infection is higher for Aboriginal people (First Nations, Inuit, Métis) and injection drug users who are incarcerated than for other people(44;45). In 1999, about 1,477 Aboriginal people and 611 people in federal and provincial prisons were co-infected(41). * Among inmates (based on a study with youth and adult inmates across 12 facilities in Ontario)(46): * Adult women have significantly higher rates of HCV infection compared to men * prevalence of co-infection was significantly higher among those with a self-reported history of IDU * Of the 25 adults who were infected with HIV, 17 were HCV positive for a prevalence rate of 68.0% (95% C.I. 49.7-86.3).  Of the 282 adults who had Hepatitis C, 17 were HIV positive * The current HIV prevalence rate among adult inmates (1.6%) is 9X higher than the HIV prevalence estimated in the general population. * The current HCV prevalence rate among adult inmates (19.1%) is 24X higher than in the general population (0.8%).   **General Findings:**   * Between 16% and 37% of people living with HIV are co-infected with hepatitis C (42;47-49) * The strongest predictor or risk factor for co-infection is injection drug use; co-infection rates are estimated to be as high as 92% in some groups of injection drug users(41-45;47;48;50-53). * Rates of co-infection are also high in people who received transfusions of blood products and in men who have sex with men and who are also injection drug users(42). * Co-infection rates are higher among prisoners who have HIV. They range from 11% to 70%(54) * People who are co-infected with HIV and hepatitis C are more likely to have a history of mental illness, depression, alcohol abuse, substance use and hard drug use(47) |

**Table 4: Key Findings – Care/support/ and Prevention programming for HIV-HCV co-infection**

|  |  |
| --- | --- |
| **Types of Literature Available** | **Key Findings** |
| **Total Studies Included**: 79  Care/support/programming only: 43  Prevention only: 5  care/support/programming and prevention: 31  **Methods Used**  Treatment Guidelines: 1  Systematic Reviews: 6  RCTs: 3  Longitudinal (prospective): 13  Longitudinal (retrospective): 1  Cross-sectional/case study/case-control: 19  Qualitative: 8  Grey literature studies: 11  Model: 11  Policy/position paper: 23  Program evaluation: 5  **Populations Studied**  Other (clinic or hospital/institution based): 10  Other: 7  IDUs: 49  Women: 7  Aboriginals: 3  Youth: 1  Mental Health: 11  Prisoners: 17  **Countries Studied**  Europe: 17  United States: 36  Canada: 21  Australia: 6  Other: 2  **Scope of Studies**  Local: 22  Multi-city/national: 47  Multi-country: 5 | **Canada Specific Findings:**   * There is presently no consensus on, or strategy direction, at the provincial and federal levels as to whether HIV-HCV co-infection should be part of a broader HIV strategy or a broader HCV strategy. As such, funding streams for HIV and HCV have not been integrated and coordinated interventions for co-infection are limited(6;55). * This lack of strategic direction and coordination has resulted in a lack of available information and educational opportunities for physicians, heath care providers and patients alike regarding HCV testing, treatment and care, and support required for the unique challenges faced in the context of co-infection(6;55). * Despite Canada’s treatment guidelines, many co-infected individuals who also have a mental illness and/or substance use problems are faced with various barriers to accessing HCV testing, treatment, care and support services. Many services that are available require abstinence from illicit drug use as a pre-condition to receive mental health and medical health services(52). Anticipated poor adherence, psychiatric side-effects of HCV treatment, and hesitation to take on patients with substance use issues or with mental illness are common barriers to accessing HCV treatment(52). * There are few HIV or HCV programs and services designed specifically for Aboriginal peoples, incarcerated women and/or incarcerated Aboriginal peoples(56;57). * Although all national prisons fall under the same HIV/HCV policy direction as set out by the Correctional Services Canada (CSC), there is significant variability in pre- and post-test counselling, and barriers to optimal HIV combination therapy in most jurisdictions(56;58).   **General Findings:**   * Internationally, harm reduction programs have demonstrated to provide the framework for effective HIV and HCV prevention among venerable and high-risk populations including prisoners and IDUs(59). |