

Oral Presentations

[O1] Factors influencing willingness for and uptake of treatment for hepatitis C virus (HCV) infection in illicit drug users in urban care settings in British Columbia, Canada: the Hi-Lo Study

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Background and Aims: The aim of this study was to evaluate treatment willingness and uptake, including relevant factors among those not initiating treatment, in illicit drug users attending primary health care clinics in British Columbia in the context of a non-randomized intervention study.

Methods: HI-Lo is an ongoing prospective, non-randomized interventional study comparing the effect of high and low intensity multidisciplinary HCV treatment programs on virologic response to HCV therapy among inner city drug users. Eligibility criteria included illicit drug use in the previous year and HCV genotypes 1–3. At screening, information collected included socio-demographics, drug use and HCV treatment considerations. In follow-up, factors affecting treatment willingness and uptake were analysed, with an emphasis on those influencing initiation of HCV therapy.

Results: Between 2007 and 2009, 399 HCV antibody-positive participants were enrolled and 370 were viremic (64% male, mean age 44). Injection drug use ever and in the previous 30 days was reported by 98% and 53%, respectively. At screening, 73% indicated being definitely or somewhat willing to receive HCV treatment. Treatment willingness was associated with current enrolment in an opiate pharmacotherapy program (AOR 1.63; 1.04–2.67, $P = 0.034$). To date, 10% ($n = 36$) have initiated HCV treatment. Treatment uptake was associated with male sex (AOR 3.73; 1.37–10.18, $P = 0.010$) and injection (AOR 0.17; 0.06–0.46, $P < 0.001$) and combined drug use (AOR 0.36; 0.15–0.90, $P = 0.029$) in the previous 30 days, but not HIV infection. Among those not having received treatment, the main reasons noted by a practitioner for delaying treatment initiation included lack of patient follow-up (37%), problematic drug/alcohol use (21%) and ineligibility to receive government reimbursement based on mild liver disease ($n = 17\%$), with multiple factors commonly present (median-2, range 1–5). A record of HCV treatment discussed and recommended by a physician was documented in 36% and 25% of individuals, respectively.

Conclusions: Despite a high willingness to receive HCV treatment in this vulnerable population, the majority of the study popu-

lation did not enrol in treatment to date. Multiple factors associated with treatment initiation have been identified which may point to potentially modifiable barriers among patients and care providers towards improving HCV treatment uptake in the target population, requiring further research and evidence-based measures.

[O2] Is multi-disciplinary management sufficient to prompt intravenous drug users on opiate maintenance therapy to treat their chronic hepatitis C?

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Introduction: Few intravenous drug users (IVDU) receive treatment against hepatitis C virus (HCV). This prospective observational study evaluated the possible barriers to the antiviral treatment in patients on opiate maintenance therapy (OMT).

Patients and Methods: Patients on OMT were included by the addiction outpatient unit (AOU) or by the hepatology unit (HU) if they were naïve, RNA HCV positive, HIV and HBV negative. Multidisciplinary team collected informations on hepatic lesions, addictives behaviours and psychiatric tests. If the barriers couldn't be removed after a specific management of one year, it was considered as a failure.

Results: Upon the 30 consecutive DU (21 p of the AOU and 9 of the HU), 21 were fully evaluated. Patients were 42 years old, male (77%) and on methadone (57%). Non-invasive tests showed minimal, moderate and severe hepatic lesions in 67%, 14% and 19% respectively. Alcohol dependence according to the DSM IV was found in 14 (67%). ASI showed moderate disorders in medical, alcohol and psychiatric areas. Nineteen IVDU out of 21 presented at least one barrier (2.1  1.3 barriers per patient). The most frequent barriers were alcohol and psychiatric diseases in 62% (13/21) respectively whereas drug abuse, social difficulties and fear of side effects were found in one fifth each ($p = ns$ between the 2 units). All these 19 IVDU benefited from specific managements (13 alcoholic, 13 psychiatric and three social; $p = ns$). All the barriers were removed in 1/10 (10%) in AOU and 6/9 (67%) in HU ($p = 0.05$). Eight out of 30 included IVDU, 2/21 (10%) in AOU vs 6/9 (67%) in HU ($p = 0,005$) began an antiviral treatment. One IVDU presented a spontaneous viral clearance.

Conclusion: 1) Multidisciplinary management is not sufficient to prompt IVDU on OMT followed at addiction units to treat their chronic hepatitis C, 2) In IVDU with viral hepatitis C, antiviral treatment was started more frequently when the patients were first seen by the hepatologists. To get better access to the antiviral treatment in patients followed at addiction units, several solutions must be investigated: a) longer follow-up by a multidisciplinary team, b) improvement of knowledge of addictologists of chronic hepatitis C.

[O3] Hepatitis C screening and treatment among active drug users in Amsterdam: Promising results of the Dutch-C project (Drug Users Treatment for Chronic Hepatitis C)

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Background and Aims: Although HCV treatment has shown to be effective, uptake of treatment among active drug users (DU) is still low. The DUTCH-C project aims to offer active DU HCV testing and treatment using a multidisciplinary approach. Here, we describe the results of the project.

Methods: The study population comprises DU participating in the Amsterdam Cohort Studies (ACS) since January 2005. End of follow-up was June 2009. DU were offered HCV screening: those chronically infected were offered additional medical and psychiatric screening. Hepatologists, addiction specialists, psychiatrists, and research staff collaborate closely to provide optimal HCV treatment, directly observed and combined with methadone provision. In 2007, the project was extended to chronically HCV-infected DU from all methadone clinics in Amsterdam.

Results: 497 DU of the ACS were offered HCV screening: 83% were Dutch, 8% homeless. The mean age was 44 years. 19% were active IDU, 83% reported non-injecting DU. Screening was accepted by 449/497 (90%), HCV antibodies were found in 267/449 (60%) subjects. 18 were previously treated for HCV in hospitals, 5 (27%) achieved a sustained virologic response (SVR). 183/267 (69%) were HCV viremic at Dutch-C screening: 89 (49%), 19 (10%), 60 (33%) and 9 (5%) with HCV genotype 1, 2, 3 and 4 respectively, 6 (3%) unknown genotype. 59/267 (22.1%) were HIV co-infected.

Combining ACS patients with patients admitted from methadone clinics after 2007 resulted in 58 HIV negative treated DU: 13, 11, 31 and 3 subjects with genotype 1, 2, 3 and 4. 19% were active IDU, 97% non-injecting DU, 84% used methadone, 62% used alcohol. 42% had a (treated) psychiatric disease. 27 of 34 (79%) DU with sufficient follow-up time achieved a SVR, in 11 treatment failed, 3 stopped because of side effects, 7 were HCV RNA negative at the end of treatment, 9 are on treatment, 1 subject died due to a lymphoma.

Conclusion: In a multidisciplinary setting DU with a chronic HCV infection can be treated successfully (overall SVR 79%) for HCV despite active alcohol-, drug use and/or psychiatric diseases. Therefore, access to therapy using an integrated approach should be increased for this group.

[O4] Access to Hepatitis C Testing and Treatment for Substance Users in Rotterdam, The Netherlands; Nurses as Essential Link in the Chain of Care

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Background and Aims: A substantial part of the 2700 substance users (SU) in Rotterdam has injected drugs. Surveillance in 1994 showed that 80% of these injecting SU were infected with hepatitis C. However, only a few SU were in treatment in 2006. The Rotterdam Public Health Service therefore initiated a project to test SU for hepatitis C, educate them on risk behaviour, give them access to treatment, and support them during therapy. The project facilitated extensive multisectoral cooperation between a large addiction treatment centre, institutions for homeless care, and the local university hospital.

Methods: Nurses working in addiction/homeless care were trained to test their patients (counselling and taking blood samples) and support them during therapy. They had at least weekly appointments and accompanied the patients to medical appointments. The hospital physician came to the collaborating institutions to supervise the treatment.

The process of the two-year project was evaluated by qualitative interviews with participants and professionals, while efficacy was evaluated by combining the standardised patient registration with the laboratory results.

Results: Process evaluation: It was feasible to train nurses working in addiction care for their new tasks, which they experienced as enriching. The project failed in a few homeless institutes, where the profession of nurses and a basic health care policy were not properly instituted. Additional financial coverage of the extra nursing time was essential to get the commitment of managers; this took much effort.

The participants themselves were enthusiastic about the project, especially about the extensive support.

Efficacy evaluation: In January 2009 for 293 participants the pre-test counselling registration had been filled in, and for 255 of them laboratory results were available. From the 73 HCV (RNA) positives (HCV prevalence 27%), 64 persons (88%) were registered by the hospital physician (June 2009). More detailed prevalence outcomes and treatment results will be presented separately.

Conclusions: This project is a big step forward for the integration of hepatitis C treatment within the broader addiction care in Rotterdam. In a context of multisectoral cooperation, nurses in addiction/homeless care form an essential link, giving SU access to testing and treatment for hepatitis C.

[O5] Continuation of Treatment of Inmates with Hepatitis C Infection on Discharge to the Community: The Inmate Community Health Reintegration Services Project (INCoHRs) experience: Vancouver, British Columbia

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Background: An estimated 24 to 35% of inmates of Canadian federal correctional institutions have hepatitis C (Canadian Legal Network; 2001). We started treating inmates in their respective institutions for HCV in 1999. A barrier for initiating treatment has been the capability for continuing the treatment and follow on discharge to the community. To address this, we started the INCoHRS (Inmate Community Health Reintegration Services) project in 2004, the first in Western Canada.

Objectives: To evaluate the utility of the INCoHRS project.

Methods: Retrospective chart reviews of inmates diagnosed with HCV, discharged between January 2004 and May 2009, and were referred to, or received services through INCoHRS.

Results: Of 536 inmates assessed for treatment and with relevant data, 393 (73.3%) initiated treatment in various correctional institutions. Of these, 96 (24.4%) were lost to follow up. Of the 297 (all genotypes), 59 (15%) had treatment discontinued early per protocol because of inadequate response, and 11 (2.7%) because of adverse reactions; 152 (38.6%) achieved successful end of treatment responses (EOT); and 134 (34%) experienced sustained virologic responses (SVR (HCV not detected 6 months post EOT)). Ten were re-infected (after SVR). At least 200 of these inmates received services through INCoHRS from January 2004–May 2009. Services included: Liaising with the correctional institution; initiation as well as continuation of treatment; applying for Provincial coverage for treatment; referral to Social Services for income assistance, housing, primary care, mental health assessments and addiction and counseling services. Of 712 scheduled post-release appointments, 426 (60%) were kept. Individuals who used INCoHRS had rates of adherence to the treatment regimen of 86%, and better treatment outcomes.

Conclusion: A program such as INCoHRS has been demonstrated to be very useful to facilitate continuity of care and a necessary link between inmates in correctional institutions and the community. Concerns to address include difficulties in finding of family physicians, housing, stability, work, social services, and health care insurance coverage. These all affect the likelihood of continuing treatment when discharged. Once addressed would encourage continuing health seeking behaviour started in the institutions.

[O6] Treatment of recent hepatitis C virus infection in a predominantly injection drug user cohort: the ATAHc Study

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Background and Aims: Treatment of acute hepatitis C virus (HCV) infection produces high sustained virological response (SVR) rates, but few studies have examined outcomes among injecting drug users (IDUs). We evaluated the efficacy of treatment of recent HCV infection (acute and early chronic HCV), within a predominantly IDU-acquired HCV population.

Methods: The Australian Trial in Acute Hepatitis C (ATAHC) was a prospective study of the natural history and treatment of recent HCV infection. Participants were eligible if they were within 6 months of their first anti-HCV antibody positive result *and* had a documented anti-HCV seroconversion within 24 months, *or* acute clinical HCV within the past 12 months. HCV participants received PEG-IFN α -2a (180 μ g/week, n = 74) and HCV/HIV co-infected participants received PEG-IFN α -2a (180 μ g/week) with ribavirin (n = 35) for 24 weeks.

Results: Between June 2004 and February 2008, 167 participants with recent HCV infection were enrolled (79% had injected in the previous 6 months). Among treated participants (n = 109), those with HCV/HIV co-infection (n = 35) were older, more likely to be male (100% vs. 62%), and more likely to have acquired HCV through sexual contact (63% vs. 5%), and had better social functioning. Among 74 HCV participants receiving PEG-IFN α -2a, the SVR was 55% overall and 72% among adherent participants (n = 50). In multivariate analyses, baseline factors associated with reduced SVR included decreased social functioning and current opiate pharmacotherapy. The SVR rates were higher among adherent participants (63% vs. 29%, $P = 0.025$). Among those reporting ever having injected drugs (n = 63), the SVR rate was similar for those with and without injecting during treatment (59% vs. 53%, $P = 0.76$) and was not related to frequency of injecting. Among 35 HCV/HIV participants receiving PEG-IFN α -2a/ribavirin, the SVR was 74% overall and 75% among adherent participants (n = 32). Among all adherent participants (n = 82), there were 11 non-responders, 1 viral breakthrough and 8 viral relapses.

Conclusions: Treatment of recent HCV among adherent IDUs including those with HIV co-infection is effective. Strategies to enhance adherence among IDUs with recent HCV infection should improve treatment outcomes.

[O7] The Incidence of Hepatitis C Virus (HCV) Infection and Relapse/Re-Infection in Illicit Drug Users (IDUs)

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Background and Aims: The possibility of recurrent viremia is often cited as a reason for not initiating HCV treatment in IDUs, although observational data suggest this risk may have been overestimated. These data are most often limited and retrospective. With this in mind, we have undertaken a prospective study of the incidence of viremic HCV infection in previously infected and uninfected IDUs with ongoing risk behaviors for the acquisition of infection.

Methods: Potential subjects were identified as either never having been infected with HCV (non-infected arm), having spontaneously cleared the virus (spontaneous arm), or having achieved a sustained virologic response on antiviral treatment (SVR arm). At baseline and every 6 months, a questionnaire was administered to collect socio-demographic information, data regarding health status (emphasizing symptomatic hepatitis), drug use or other risk factors for HCV infection. Blood tests to determine the presence of viremic HCV infection were done at each visit, more frequently if clinically indicated.

Results: A total of 518 subjects were screened (12/07–02/09), with 245 (47%) being viremic and 69 (13%) meeting criteria for inclusion in the study: 18 in the non-infected, 29 in the spontaneous and 22 in the SVR arms. There were no significant differences among the 3 groups with respect to age, ethnicity, source of income, unstable housing, and being on opiate maintenance program. Over 5–18 months follow-up, 20% of the non-infected group became viremic, as compared to 0% of the other two groups ($p = 0.04$). Injecting drugs in past 30 days ($p = 0.004$), sharing non injection equipment ($p = 0.015$), heroin, amphetamines, and combined drugs use was significantly higher in the non-infected arm compared to SVR arm ($p = 0.02$, 0.04 and 0.02 respectively). There were no significant differences in drug use and risk behavior between non-infected and spontaneous arms.

Conclusion: In a prospective cohort, viremic HCV infection is more likely to occur in those who have never been previously infected, and that this susceptibility to infection cannot be completely explained by an increase in risk behavior. The decreased rate of viremia in the SVR group may relate to host or behavioral factors, and is currently under study in our centre.

[O8] Comprehensive care approach in HCV treatment: high response and low reinfection

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Background and Aims: Czech Republic (CR) is HCV low prevalence country. Even among IDUs it is on the lower side of European prevalence interval with approximately 30%. Infected IDU population in CR is usually young, with short time from acquisition and thus with limited fibrosis. The main challenge remains, to keep IDUs adherent to treatment. To address this issue we have established a clinic where comprehensive services are available in one place, with psychiatric, psychosocial and medical interventions. Patient's suitability for treatment is evaluated strictly individually without any general limits. The decision to treat is made in multidisciplinary setting involving all experts who worked with the patient during the pretreatment phase of stabilization.

The primary objective of this study was to assess the sustained virological response (SVR) in this setting.

Methods: 173 treatment-naïve adult patients with HCV infection, former or current IDUs were prospectively recruited in 2003–2008. All patients were treated with standard regimen of peginterferon- α -2a (180 μ g/week) and weight-based ribavirin 800–1,200 mg/day for 24/48 weeks.

95 (55%) were males, mean age 27.9 (18–53) years. Pretreatment ALT normal in 45 (26%) cases; 28% viremia $> 800,000$ IU/ml; 125 (72%) genotype-1, 2 genotype-2 and 42 genotype-3, 2 genotype 1b/4a, 1 genotype 4, 1 was untypeable. Fibrosis stage (Ishak) was 0 in 57 (36%) cases, 1 in 69 (43%), 2 in 13 (8%), 3 in 1 and 6 in 2; in 31 unavailable.

Modified intention-to-treat-analysis (ITT) was performed, included were all patients who have taken at least first dose of medication.

Results: Overall SVR regardless of genotype was achieved in 143 (83%), for genotype-1 and non-1 in 108 (84.4%); 95% CI:76.5–93.3, and 34 (77.3%); 95% CI:59.7–87.6 respectively.

15 (8.7%) patients were lost to follow-up while the documented treatment failure was rare – only 15 (8.7%) of cases, of them 2 (1.2%) were true non-responders and 13 (7.5%) relapsed in follow-up. SVR in patients on opiate substitution wasn't statistically different.

Over 76% of those achieving SVR were further followed with only 2 reinfections documented, frequency of 0.6% per person/year was calculated.

Conclusions: our data show that HCV in the described population and setting is nearly fully curable disease even with current standard of care. Treatment can be important preventative measure.

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[O9] Hepatitis C virus superinfection and reinfection in injection drug users

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Background and Aims: Little is known about superinfection and reinfection. The aim was to evaluate the incidence and natural history of HCV superinfection and reinfection among individuals with recent HCV infection.

Methods: The Australian Trial in Acute Hepatitis C (ATAHC) was a prospective study of the natural history and treatment of recent HCV. Treated participants received pegylated interferon alfa-2a for 24 weeks (with ribavirin if HCV/HIV). Confirmed superinfection and reinfection were defined by detection of infection with an HCV strain distinct from the primary infecting strain in the setting of persistence (defined by HCV RNA > 10 IU/mL from presentation to week 12 with no HCV RNA < 10 IU/mL) and viral suppression (one RNA < 10 IU/ml), respectively. Possible reinfection was defined by recurrence that could not be

sequenced (low-level viremia). Reinfection and superinfection were detected by RT-PCR amplification and sequencing of the region encoding E1 and the hypervariable region 1 of E2. Viruses with > 4.5% E1/HVR1 sequence divergence were identified as distinct from the primary strain. Mixed-genotype infections were also detected by the genotype (G) specific RT-PCR assay of the HCV core region.

Results: Overall, 163 participants were enrolled (109 treated, mean age 34.3 ± 9.9). Among patients with viral persistence (n = 36), confirmed HCV superinfection was observed in six participants [17%, 40.9 per 100 person-yrs (95% CI, 18.4–91.0)]; three of whom had received treatment. Three subjects (two treated) eventually cleared their infections. Following superinfection, five of six demonstrated a peak HCV RNA greater than that at clinical presentation (mean log₁₀ HCVRNA = 1.31 ± 0.42). The one patient without an increase was receiving HCV treatment when superinfection occurred. Among participants with viral suppression (n = 115), HCV reinfection was observed in eight [5.7 per 100 person-yrs (95% CI, 2.9–11.4)], with five confirmed [3.6 per 100 person-yrs (95% CI, 1.5–8.6)] and three possible. Clearance of reinfection was observed in five of eight (treated: three of six, untreated: two of two).

Conclusions: HCV superinfection is frequent during early HCV infection and may compromise treatment responsiveness in high-risk individuals. Although reinfection following spontaneous and treatment-induced HCV clearance can occur, the rate of persistent HCV reinfection is low, particularly following spontaneous clearance.