**SEX DISCREPANCIES IN THE PROTECTIVE EFFECT OF OPIOID AGONIST THERAPY ON INCIDENT HEPATITIS C INFECTION**


1. The Kirby Institute for Infection and Immunity in Society, UNSW Sydney, Sydney, NSW, Australia
2. Clinical Research Education, Icahn School of Medicine at Mount Sinai, New York, NY, USA
3. University of Washington School of Medicine, Seattle, WA, USA
4. CRCHUM, Université de Montréal, Montreal, QC, CA
5. Burnet Institute, Melbourne, VIC, Australia
6. Cluster Infectious Diseases, GGD Public Health Service of Amsterdam, Amsterdam, The Netherlands
7. University of California San Francisco, San Francisco, CA, USA
8. Harvard Medical School, Boston, MA, USA
9. Department of Medicine, Johns Hopkins University, Baltimore, MD, USA
10. University of New Mexico Health Sciences Center, Albuquerque, NM, USA

The InC3 Collaborative Steering Committee includes: Andrea Cox, Georg Lauer, Arthur Kim, Meghan Morris, Lisa Maher, Andrew Lloyd, Greg Dore, Jason Grebely, Margaret Hellard, Paul Dietze, Julie Bruneau, Naglaa Shoukry, Maria Prins, and Kimberly Page

**Background**: Opioid agonist therapy (OAT) has been shown to reduce hepatitis C virus (HCV) incidence by 50% among people who inject drugs (PWID). Recent research suggests that the protective effect of OAT may be attenuated in females compared to males. This study assessed sex disparities in HCV incidence among PWID exposed to OAT and factors independently associated with decreased protective efficacy.

**Methods**: Inc3 pooled biological and behavioural data from 10 prospective observational studies examining incident HIV and HCV infections in high-risk cohorts. This study synthesised data from seven of the ten cohorts. Cox proportional hazards regression models with random effects for handling clustered survival data were used to identify predictors of incident HCV infection. Entry in each study to the estimated date of HCV infection was used to calculate person-year observation (PYO) and adjusted hazard ratios (aHRs) among participants who reported recent (last 12 months) OAT (methadone, buprenorphine or buprenorphine-naloxone).

**Results**: Among 701 participants exposed to OAT observed over 3,003 visits and 1,427 person-years observation (PYO), HCV incidence was 16.5 PYO (95%CI 13.1-20.7) in females and 7.6 PYO (95%CI 6.0-9.5) in males (F:M aHR 1.80, 95%CI 1.37-2.22, p<0.001). Factors associated with HCV acquisition among females exposed to OAT included non-white race (aHR 1.79, 95%CI 1.25-2.56, p=0.001), recent unstable housing (aHR 4.00, 95%CI 3.62-4.41, p<0.001), recent daily or more frequent injection (aHR 1.45, 95%CI 1.01-2.08, p=0.042) and recent receptive syringe sharing (aHR 1.43, 95%CI 1.33-1.53, p<0.001).

**Conclusion**: Among respondents exposed to OAT, HCV incidence among females was twice that compared to males. Independent associations with attenuated effect included bio-social (non-white race), structural (unstable housing), and behavioural (frequent injecting and receptive syringe sharing) factors. Structural and behavioural
interventions that target women are needed to bolster the efficacy of OAT in females in order to prevent HCV transmission.

**Disclosure of Interest Statement:** InC3 was funded by the National Institute on Drug Abuse (NIDA) R01DA031056. JB, MH, PD, GD and JG have received funding from Gilead Sciences Inc. and/or AbbVie and/or Bristol-Myers Squibb and/or Cepheid and/or Merck/MSD for work on HCV treatment unrelated to this study. PD has received funding from Indivior for work unrelated to this study. Authors (LG, AE, JI, JT, NS, MP, MDM, AL, LM and KP) have no commercial or other associations that might pose a conflict of interest. LG is supported through an Australian Government Research Training Program Scholarship. JI, PD, MH, AL, GD, JG and LM are supported by Australian National Health and Medical Research Council (NH&MRC) Fellowships. KP is supported by 3R01DA016017, 1ULTR001449 and U54GM104944.