**HISTORICAL AND GEOGRAPHICAL TRENDS IN INCIDENCE OF HEPATITIS C VIRUS (HCV) INFECTION AMONG PEOPLE WHO INJECT DRUGS: THE INC3STUDY**

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**Introduction**: The hepatitis C virus (HCV), identified in 1989, is a highly infectious blood-borne virus that disproportionately affects people who inject drugs (PWID) globally. The current study uses pooled biological and behavioral data from 8 individual prospective studies of PWID to describe geographic and temporal trends in HCV incidence and identify predictors of infection across Baltimore, San Francisco, Montreal, Sydney, Amsterdam, and Melbourne.

**Methods**: We used life-table methods to construct observed HCV incidence curves, estimate overall and temporal HCV incidence trends, and compare differences in cumulative HCV incidence by risk factor, across cities.

**Results**: Of 5,248 participants followed prospectively across 1985 and 2011, 1,981(38%) met inclusion criteria. Illicit drugs injected included heroin (28%), [meth]amphetamines (11%), cocaine (7%), and other opiates (4%) and varied by city. During 2,322.70 person-years of observation (pyo), 499 persons seroconverted (overall incidence 21.5/100 pyo (95% CI: 19.7, 23.5). Overall incidence was lowest in Melbourne (7.5/100 pyo) and Amsterdam (13.1/pyo), moderate in the Sydney (community: 18.5/100 pyo and prison: 20.4/100 pyo) and highest in North America (Montreal: 23.5/100 pyo; San Francisco: 24.7/100 pyo; Baltimore: 32.6/100 pyo). Downward trends were noted in most cities except Montreal and San Francisco where incidence remained stable and high. Predictors of injection differed across cities. Incidence was greater among females in Sydney (Risk Ratio [RR]: 2.1, 95%CI: 1.3, 2.8) and among heroin injectors (RR 5.2, 95%CI: 1.3, 21.2). In San Francisco, injection equipment sharing resulted in greater HCV incidence (RR: 2.0, 95%CI: 1.3, 3.0). Unstable housing (RR: 1.8, 95%CI: 1.2, 2.8) and injecting other opiates (RR: 2.7, 95CI%: 1.6, 4.5) were associated with higher HCV incidence in Montreal. No significant differences were noted for Amsterdam or Melbourne.

**Conclusion**: Important differences in structural-level factors (i.e., harm reduction strategies, drug availability, HCV prevention programs) across cities are a plausible explanation for large differences in HCV incidence geographically.

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