**ILLICIT FENTANYL USE INDEPENDENTLY PREDICTS HCV SEROCONVERSION AMONG A COHORT OF PEOPLE WHO USE DRUGS ON THE US-MEXICO BORDER**

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**Background:**
Broad markets shift away from heroin to illicitly manufactured fentanyl (IMF) are transforming the risk environment for people who inject drugs (PWID) in North America. IMF causes large increases in overdose mortality, but its role in infectious disease transmission is unknown. We examined whether IMF use predicts HCV incidence among a cohort of PWID in the US-Mexico border region.

**Methods:**
PWID residing in San Diego, CA and Tijuana, Mexico were recruited into a prospective cohort in 2 waves from 10/20-10/21 and 02/22-06/22, undergoing semi-annual interviewer-administered surveys, HIV and HCV serology through 02/24. Excluding baseline HCV-seropositive individuals, Cox regression was conducted to examine predictors of incident HCV infection considering fentanyl use as a fixed or lagged time-dependent covariate and with shared frailty based on recruitment group.

**Results:**
Of 398 PWID at baseline, 67% resided in Tijuana, 70% were male, median age was 43, 42% reported receptive needle sharing, 25% reported using IMF and HIV prevalence was 9%. Participants contributed a median of 6 semi-annual study visits (IQR:4-6). HCV incidence was 14.26 per 100 person-years (95% CI: 11.49-17.02) and did not differ by city of residence. Fentanyl use, both at baseline and time-varying (lagged by 12 months) was associated with HCV seroconversion, with the latter having a univariate hazard ratio (HR) of 1.68 (95%CI: 1.12-2.53), which remained independently associated with seroconversion after controlling for receptive needle sharing, sex and age (adjHR1.54; 95%CI:1.01-2.34).

**Conclusion:**
We provide evidence of a novel association between fentanyl use and HCV seroconversion among PWID in Tijuana-San Diego. Qualitative studies show that the short half-life of many IMF analogues has destabilizing effects on the lives of PWID— increasing the need for repeat dosing and risky behaviors such as sharing syringes and smoking materials. New harm reduction approaches may be needed in the fentanyl era to reduce HCV transmission.

**Disclosure of Interest Statement:**
Authors declare no conflicts of interest.