Supplementary material 2. Additional details on limitations and strengths of this study

Several limitations need to be acknowledged in interpreting our findings. First, given the cross-sectional nature of data, we could not make causal inferences. However, the two models we tested are plausible in light of theoretical considerations. Second, it is possible that participants might have underreported their incarceration experience due to social desirability bias. Despite this possibility, incarceration experience was associated with needle/syringe sharing, and the association between incarceration experience and HIV status was partially mediated by needle/syringe sharing. Third, the models for synergistically interacting epidemics and serially causal epidemics were non-nested models, precluding direct statistical comparisons to determine which one was better. More theoretical and empirical research is needed to adjudicate between these models of co-occurring risks. Fifth, we could not test the mutually causal model because of the difference in the timeframe between needle/syringe sharing (last time, usually within the previous three months) and the other two exposures (past-year violence victimisation and past-year incarceration experience). While it is possible that incarceration experience might have led to physical violence victimisation, the reverse is unlikely. In fact, family members were the commonly reported perpetrators of physical violence, again making it unlikely that incarceration experience might have led to physical violence victimisation. Sixth, we understand that our analysis is restricted to the examination of co-occurrence and interactions between individual-level exposures. However, a syndemic, being a population-level phenomenon, is best examined using data that consists of ecological variables only or both ecological and individual-level variables (*i.e*., multilevel data)[21]. Seventh, given that some subgroups of men who inject drugs (*e.g*., educated and those from high socioeconomic status) may not come to 'hotspots'–venues used for time-location sampling in the IBBS – we cannot generalise the results to all subgroups of PWID in India. Finally, another limitation is the exclusion of women who inject drugs from the original IBBS study. This exclusion limits our ability to examine gender differences in syndemic exposures and their impacts on HIV risk. Given that women who inject drugs often face higher rates of violence victimisation and women-specific barriers to accessing harm reduction services, future studies should prioritize including both men and women to provide a more comprehensive understanding of syndemics among PWID in India.

The present study has notable strengths as well. First, it is the largest probability-based study of a syndemic in a population of PWID to date[14]. The low non-response rate (10%) reinforces our ability to make population-level generalizations. Secondly, following prior work[23], we specified the adverse exposures as dichotomous variables so that we could compute statistical indices for assessing interaction on the additive and multiplicative scales. When we instead specified the exposures as continuous variables, we obtained similar findings. Thirdly, while our 2014/15 data may not fully reflect current conditions, our study remains relevant because it provides a baseline for understanding syndemic processes among PWID in India; PWID continue to have the highest HIV prevalence among key populations in India; it is the first large-scale, population-based examination of syndemics among PWID in India using appropriate statistical methods; key gaps we identify, such as lack of needle/syringe programmes in prisons, remain unaddressed; and our findings on synergistic interactions provide a basis for developing integrated interventions.