Comprehensive needle and syringe program and opioid agonist therapy reduce HIV and HCV acquisition among people who inject drugs in different settings: a meta-analysis of emulated trials

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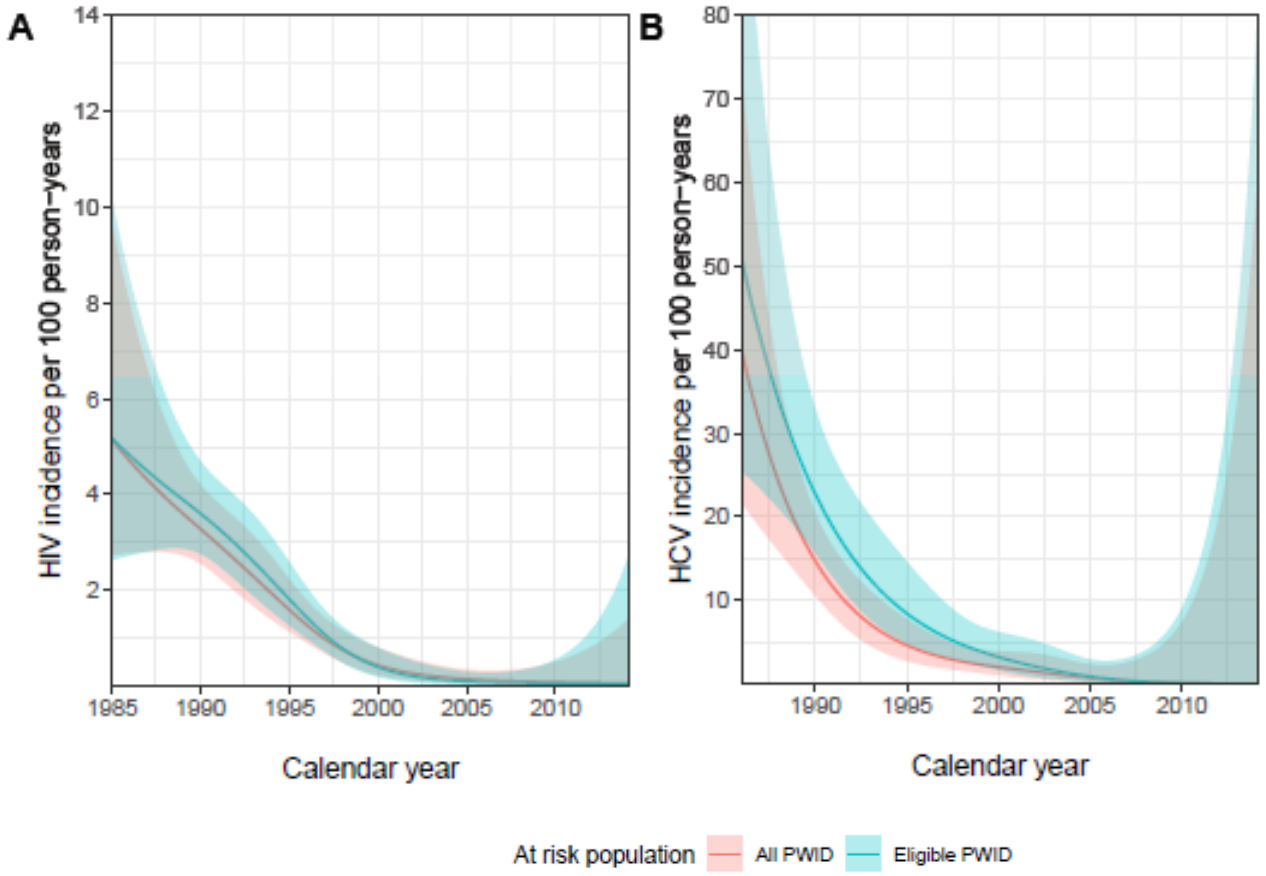
Introduction

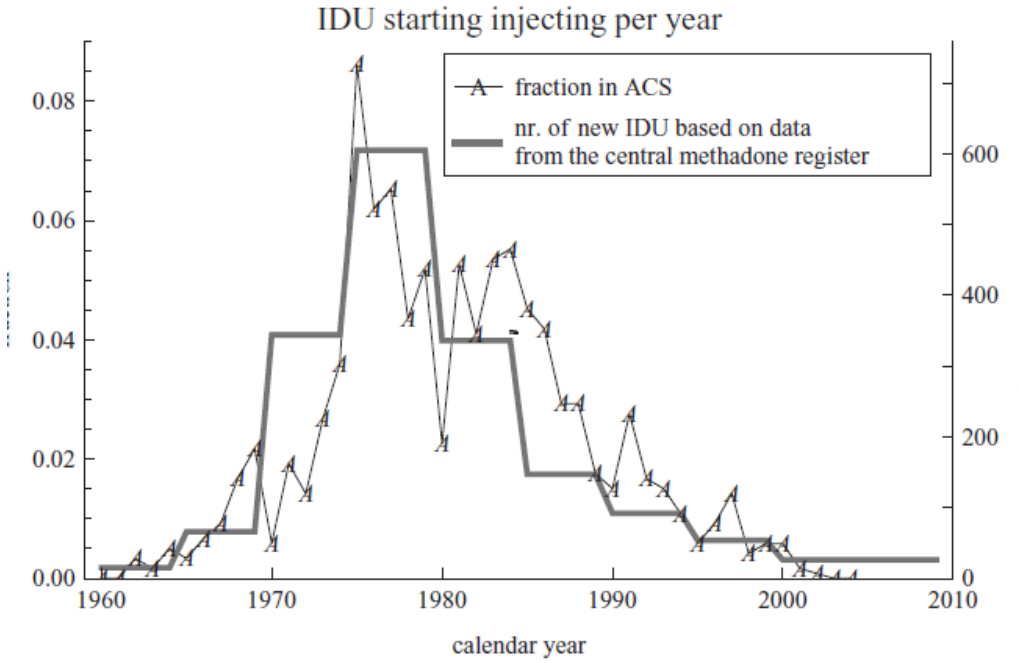
Harm reduction programs for people who inject drugs (PWID) in Amsterdam

1979: Methadone bus
Opiate Agonist Therapy (OAT)

1984: Needle and Syringes Program (NSP)
by Junkiebond (NGO)

Declining HCV and HIV incidence and numbers of PWID





van Santen et al, Addiction 2021; de Vos et al, Addiction 2013

RESEARCH REPORT

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Full participation in harm reduction programmes is associated with decreased risk for human immunodeficiency virus and hepatitis C virus: evidence from the Amsterdam Cohort Studies among drug users

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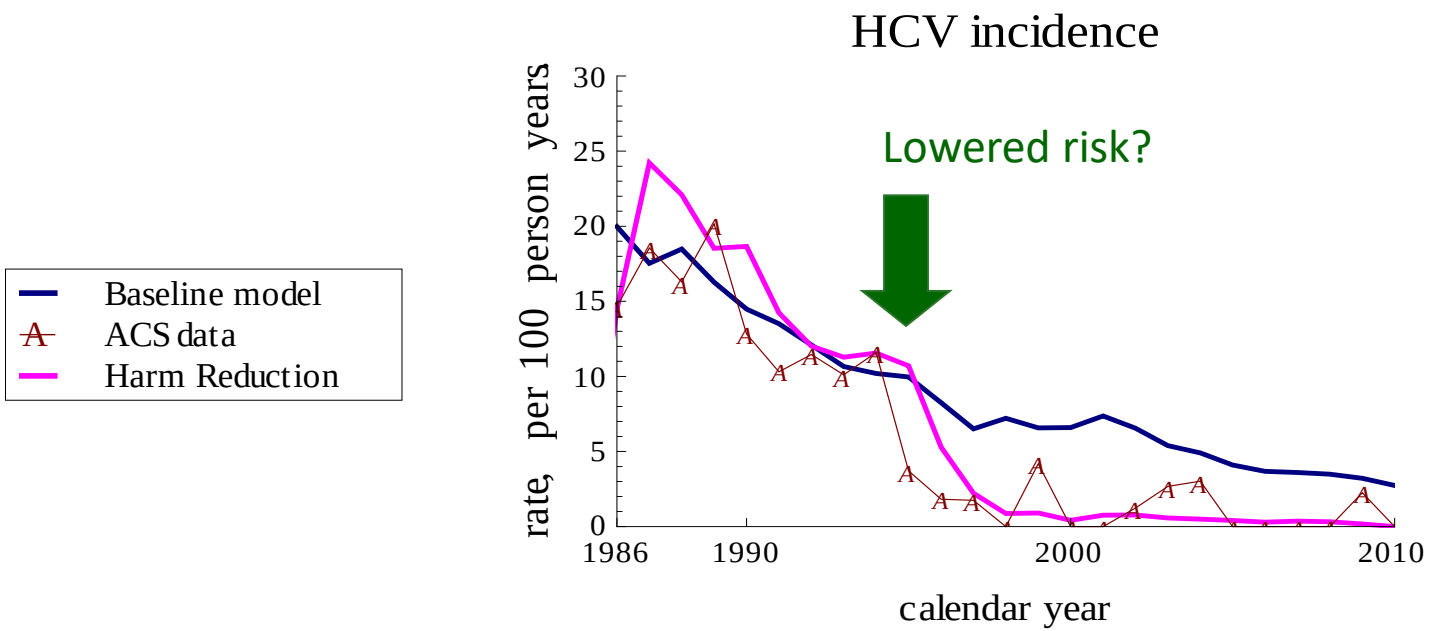


van den Berg et al, Addiction 2007; de Vos et al, Addiction 2013

Background current study

Weak evidence for effect harm reduction on infection risk?

Observational cohort studies:

- Insufficient adjustment for confounding and selection bias

Randomized controlled trial woul[illegible]est possible evidence for a causal effect of harm reduction on infection risk

- Unethical to include an arm without [illegible]duction pograms as the benefits of these programs across a range of outc[illegible]nized

Harm reduction programs for PWID in Amsterdam revisited

Re-use of cohort data using novel methods for causal inference

Novel method: Emulated trial using data from observational studies

Key finding: Harm reduction works in Amsterdam!

Comprehensive NSP and OAT reduced risk of acquisition of

- HIV by 45%
- HBV by 72%
- HCV by 84%

van Santen, Addiction 2021

Background: Evidence from one setting sufficient?

Re-use of cohort data from 3 settings

- The Netherlands, Canada and Australia were all early adopters of harm reduction for PWID

- Their respective HIV and hepatitis C (HCV) epidemics and populations of PWID differ e.g.
  - HIV never successfully introduced among PWID in Australia
  - Drug consumptions rooms were available much earlier in he Netherlands than in Australia and Canada
  - Coverage of harm reduction components differed between countries
  - Different market for illicit drugs

Objective

Determine the effect of comprehensive NSP/OAT participation on HIV and HCV infection risk using observational cohort data from Vancouver, Amsterdam and Melbourne

Methods: study population and data

PWID at risk of infection from three cohort studies

ACS
Amsterdam Cohort Studies

VIDUS
The Vancouver Injection Drug Users Study

SuperMIX
The Melbourne Injecting Drug User Cohort Study

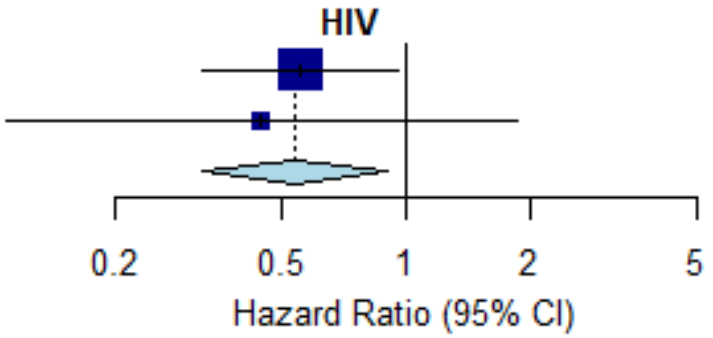
Study design: Emulating a target trial

Protocol component	Target trial	Emulated trial
Eligibility	• HIV or HCV antibody negative • Recent injecting • Opioid use disorder • ≥18 years old	Same as for the target trial *Opioid use disorder defined as any recent opioid use*
Follow up	Study enrolment (baseline) until the visit at which the participant deviated from their initial baseline intervention strategy, outcome occurrence, loss to follow-up, administrative censoring date or 2.5 years after baseline.	Same as for the target trial *Baseline was defined as the first visit the participant met the eligibility criteria, had an HIV or HCV test result and complete data was available.*
Intervention strategies	Three intervention arms: 1) No NSP/OAT 2) Partial NSP/OAT: <100% NSP coverage and/or no current OAT among participants reporting current injecting. 3) Comprehensive NSP/OAT: 100% coverage of NSP and current OAT among participants reporting recent injecting or, current OAT only when reporting no current injecting.	Two intervention arms: 1) No and partial NSP/OAT combined 2) Comprehensive NSP/OAT
Intervention assignment	Random assignment	Individuals were classified to each intervention strategy based on the observed data. We adjusted for baseline and time-varying confounders.
Casual contrast	Intention to treat and per protocol	Observational analogue of per-protocol analysis
Outcomes	HIV, HCV or HBV seroconversion	Same as for the target trial
Statistical analyses	Cox-proportional hazard models. Using inverse-probability weights (IPW) to adjust for baseline and time-varying confounders associated with baseline participation adherence in the per-protocol analysis. For both the ITT and per-protocol analysis include IPW to adjust for potential lost to follow up.	Separate for each cohort : marginal structural models using a sequential trial emulation approach, adjusting for confounders and loss to follow up. Combing data from the cohorts: pooled hazard ratios (HR) and 95%CI were calculated using random-effect models.

Results: Complete vs no/partial NSP/OAT participation

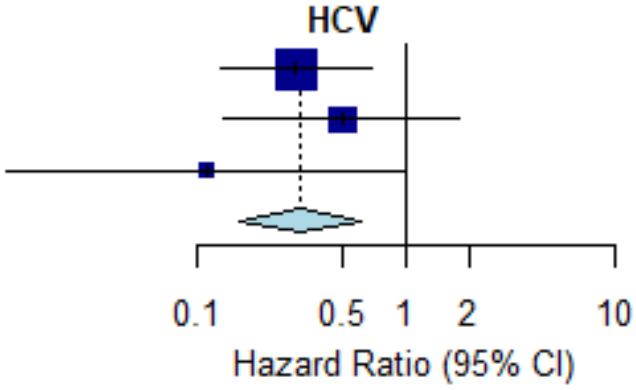
Cohort	HR (95% CI)
ACS	0.56 [0.32; 0.96]
VIDUS	0.45 [0.11; 1.85]
Total	0.54 [0.33; 0.90]

Heterogeneity: $\chi^2_1 = 0.08$ ($P = .78$), $I^2 = 0\%$



Cohort	HR (95% CI)
ACS	0.30 [0.13; 0.67]
SuperMIX	0.49 [0.13; 1.81]
VIDUS	0.11 [0.01; 1.01]
Total	0.31 [0.16; 0.60]

Heterogeneity: $\chi^2_2 = 1.35$ ($P = .51$), $I^2 = 0\%$



Conclusion

When applying a target trial approach to infer causality from observational data, we demonstrated that comprehensive NSP/OAT led to a substantial reduction of HIV and HCV acquisition compared to no/partial participation in different settings of high-income countries

These findings coupled with the fact that this intervention is associated with reductions in drug use, criminal activity and mortality, and engagement in care

- reinforce the critical role of access to harm reduction programs
- suggest that WHO should emphasize access to comprehensive NSP and OAT rather than each component separately

Given that most countries lack access to comprehensive NSP/OAT, and global HCV and HIV elimination is unlikely to be reached by 2030, increased coverage of these key interventions will be vital to preventing new infections

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