Strategies to enhance prevention of HCV infection and re-infection in PWID

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Cornerstones of HCV prevention

- Syringe service programs (SSPs)
- Medication-assisted substance use treatment (MAT)
- HCV treatment as prevention
- Prevent the onset of injection drug use

Syringe service programs & HCV

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High syringe coverage and HCV seroconversion

- SR/MA of 17 studies in Europe, N America, Australia
- High NSP coverage was defined as
  - obtaining 100% of needles/syringes from a safe source
  - reporting obtaining ≥100% of sterile needles/syringes per injecting frequency
  - regular attendance at least once per week at an NSP
  - obtaining most needles/syringes from an NSP in the last 6 months
- RR(HCV seroconversion) associated with high NSP coverage
  - RR 0.77 (0.38, 1.54)
- European studies of high NSP coverage
  - RR 0.24 (0.24, 0.8)

Platt, LM et al. (2016). Cochrane Database of Systematic Reviews.

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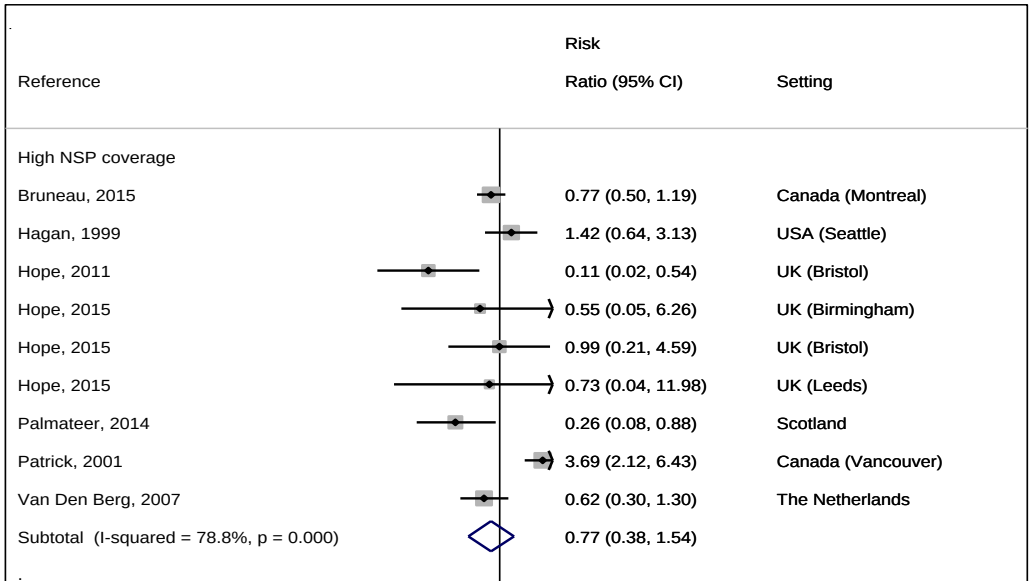

Platt, LM et al. (2016). Cochrane Database of Systematic Reviews.

Confounding in studies of SSPs

- Studies in Vancouver and Seattle showed that SSPs attract and retain the highest risk PWID
  - Frequent, daily injection
  - Unsafe injection
- Lack of precision in measurement of confounders & inadequate control for confounding
  - Bias in the direction of the confounding

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Schechter MT et al., 1999; Hagan H et al., 2000.

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Inception bias in studies of SSPs

- **Inception bias** occurs when the timing of the enrollment of participants in the study does not coincide with the timing of the intervention
  - There is no reason to believe that the effect of SSP is constant over time in an individual or in a community
  - RCTs enroll participants and then assign to *begin to use* interventions
- **When do SSPs have their greatest impact on HCV**?
  - We don't really know – nearly all studies of SSPs and HCV seroconversion have compared **prevalent SSP users to non-users**
  - It is likely that the longer SSPs exist in a community, the more SSP users and non-users become similar in terms of access to clean materials

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Misspecification of the causal exposure in studies of SSP & HCV seroconversion

- High SSP coverage is defined in relation to syringes in most studies
  - UNAIDS recommends 200/syringes/PWID/year
  - Bruneau et al., INHSU 2016 – injection material coverage
- Majority of HCV infections are attributable to cooker/cotton sharing
- Therefore defining high SSP coverage in terms of syringes/PWID is incorrect
  - Works for HIV, not for HCV

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Risk of HCV seroconversion in relation to sharing[a] injection equipment

	Pooled RR	95% CI	PAR%[b,c]
Syringe sharing	1.9	1.5 – 2.5	25%
Drug cooker sharing	2.4	1.9 – 3.1	43%
Filtration cotton sharing	2.6	1.9 – 3.6	42%
Rinse water	2.0	1.5 – 2.6	31%

a. Sharing defined as re-use of a syringe, cooker etc. that could result in HCV transmission

b. Population Attributable Risk Percent is the proportion of HCV infections in the underlying PWID population that is attributable to each injection behavior. Depends on the prevalence of the exposure in the PWID population. Should only be calculated when evidence supports causal relation.

c. PAR% = prevalence(exposure in the controls or population) x (RR-1/RR)

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Pouget R. et al., Addiction, 2013 SR/MA of 21 studies

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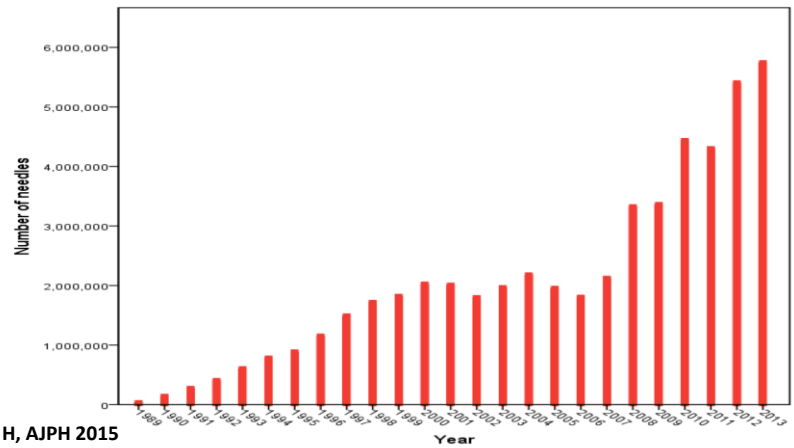
High syringe coverage does not equal high equipment coverage

Syringes distributed, Seattle 1989 - 2013

400-600 syringes/PWID/year



Burt R & Thiede H, AJPH 2015

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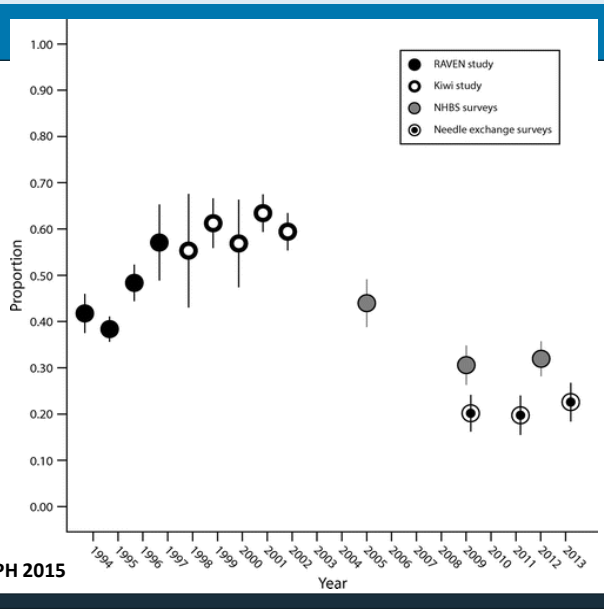
Syringe sharing, Seattle PWID 1994-2013



400-600 syringes/PWID/year

Source: Burt R & Thiede H, AJPH 2015

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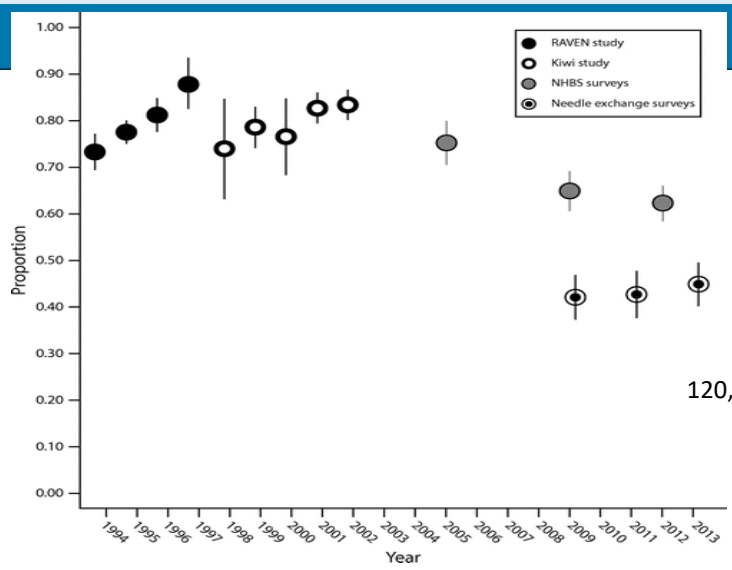
Cooker/cotton sharing Seattle PWID 1994-2103



120,000 cookers distributed/year =
7-10 cookers/PWID/year

Burt R & Thiede H, AJPH 2015; personal communication, R. Burt & M Hanrahan, 2016.

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Thoughts on SSPs and HCV seroconversion

- Difficult to find published data on injection material coverage either among individuals or the community
  - Interesting to relate to HCV epidemiology
- Differences in equipment (non-syringe) sharing explain SSP effect?
  - North America vs Europe?
- Studies to examine injection material coverage (syringes, cookers, cottons, etc.) as the SSP exposure of interest

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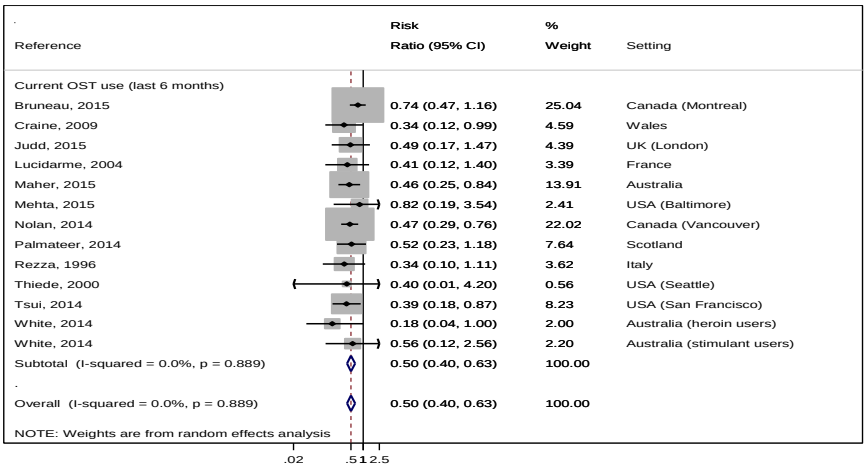
Medication-assisted substance use treatment & HCV

Current OST reduces HCV incidence by 50%



Platt, L, et al., 2016. Cochrane Database of Systematic Reviews.

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Limitation to MAT impact on HCV incidence

- Low proportion of PWID at risk of HCV and in OST/MAT
  - If 10% are in OST/MAT, then 5% of infections may be prevented
  - If 20% are in OST/MAT, then 10% of infections may be prevented
- Tsui et al., 2014 paper on MAT and HCV in San Francisco PWID < 30
  - 4.2% in maintenance treatment
- Unpublished data from opioid/opiate injectors 18-29 in rural NY state
  - 5% in maintenance treatment
- Expansion of buprenorphine dispensing is happening

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Preventing re-infection post HCV treatment

Reinfection post SVR

Asher AK et al., 2016 – 10% of clinicians at AASLD willing to treat active PWID, citing reinfection & treatment cost

Author, year	Sample	Rate per 100 low risk PWID PY	Rate per 100 high risk PWID PY
Aspinall, 2013	SR/MA 5 studies	2.4/100 PY	6.1/100PY
Simmons et al., 2016	SR/MA of 12 studies	1.9	
Weir et al., 2016	277 PWID	1.7	5.7
Midgard et al., 2016	138 PWID abstinent at start of treatment	1.7	4.9

MIdgard H et al, J Hepatol 2016.

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Prevention of reinfection

- Most of studies of DAAs have excluded active injectors
  - Others have restricted enrollment to PWID in MAT
  - Selection bias an issue in estimating risk of reinfection in a broad HCV elimination strategy
- Publications say very little about any active measures to prevent reinfection
- Opportunity to study prevention of reinfection
  - Adaptive designs acknowledge heterogeneity in response to interventions
  - "Personalized" prevention

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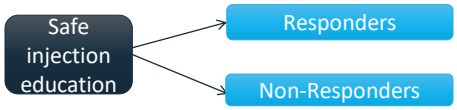
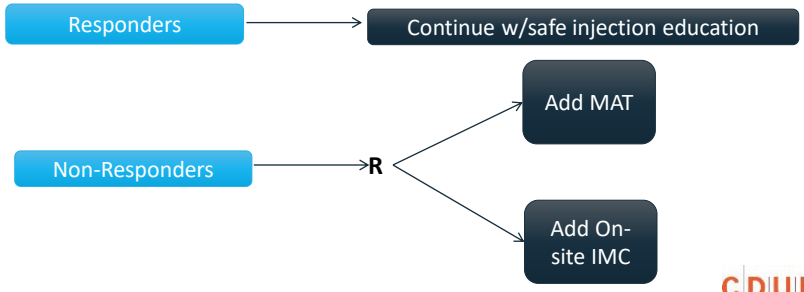
Adaptive interventions

- What is the best initial intervention?



- What is the best subsequent intervention for non-responders?



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Preventing the onset of injection

Transition to injection in the era of prescription opioids

- Case control study design
- 18-29 year old opioid/opiate users in rural New York state
- Cases are injectors, controls have never injected
- Recruited via respondent driven sampling
  - Enrolled 128 between April and July, 2017
- Urine screening at enrollment
  - Must be positive for opioids or opiates indicating use within the past 3-4 days
- Preliminary analysis of 27 controls and 101 cases

H. Hagan, in preparation. Funded by New York State Department of Health AIDS Institute

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Cases (injectors) vs. controls (non-injectors)

	Injectors (n=101)	Non-injectors (n=27)	p
% Female	38 (38%)	10 (37%)	NS
Mean age	25.7	23.7	**<.001**
Mean yrs using opioids	8.1	5.1	**<.001**
Mean yrs injecting	3.7	--	
Anti-HCV positive	64 (63%)	3 (11%)	**.011**
Urine positive for:			
Cocaine	41 (41%)	7 (26%)	NS
Prescription opioids	6 (6%)	5 (19%)	**.04**
Buprenorphine	31 (31%)	5 (19%)	NS
Heroin	96 (95%)	26 (96%)	NS
Methamphetamine	28 (28%)	3 (11%)	.06
Severity of dependence > 3	99 (98%)	20 (74%)	**<.001**

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Recruitment of non-injectors in an opioid epidemic

Prevalence ~ Incidence x Duration

Prevalence of non-injectors in an opioid epidemic **~** Incidence of non-injection use of opioid/opiates **x** Duration of interval from onset of opioid/opiate use to injection

Dependence
Drug availability
Peer norms
Network features
Concern about risks

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"Break the Cycle" or "Change the Cycle"

- Peer-driven, one-session intervention to reduce initiation into injection
- Targets **current injectors**
- Supports them to **avoid**:
  - Speaking positively about injecting to non-injectors
  - Injecting in front of non-injectors
  - Showing non-injectors how to inject
  - Helping with first injection
- Results:
  - 72% reduction in initiation by self-report
- Rural New York young opiate/opioid users:
  - 1/3 of injectors learned to inject by watching videos online
  - 60% were taught by a friend or acquaintance

Hunt N et al., Drug Alcohol Rev 1999; Strike C et al., Drug and Alcohol Dependence 2014.

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Peer influence on injection

Injectors			Non-injectors	
Did anyone encourage you to inject the first time?			**Has anyone ever tried to encourage you to inject?**	
	Yes	62 (48%)	Yes	13 (48%)
How much did this influence your decision?			**Has anyone ever discouraged you from injecting?**	
	Not at all	2 (3%)	Yes	22 (81%)
	A little bit	13 (22%)	**Have you ever witnessed someone injecting drugs?**	
	A lot	45 (75%)	Yes	21 (75%)
Did anyone discourage you from injecting the first time?			**Would most of the people you know who inject be**	
	Yes	43 (34%)	**willing to inject someone for the first time?**	
How much did this influence your decision?			Yes	21 (75%)
	Not at all	38 (88%)		
	A little bit	5 (12%)		
	A lot	0 (0%)		

Concerns about HIV, HCV & overdose

	Non-injectors	Injectors
How worried are you about getting HIV?		
Not at all	22 (81%)	52 (52%)
A little or somewhat worried	2 (8%)	34 (33%)
Very worried	3 (11%)	15 (15%)
How worried are you about getting HCV?		
Not at all	16 (59%)	26 (26%)
A little or somewhat worried	9 (37%)	46 (46%)
Very worried	2 (7%)	29 (29%)
How worried are you about overdosing?		
Not at all	14 (52%)	52 (52%)
A little or somewhat worried	9 (33%)	34 (34%)
Very worried	4 (15%)	15 (15%)
Ever overdosed	3 (11%)	58 (57%)

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  - So helpful & willing to contribute

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