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Combined coverage of harm reduction interventions and rates of primary and recurrent HCV infection in a community-based cohort of people who inject drugs

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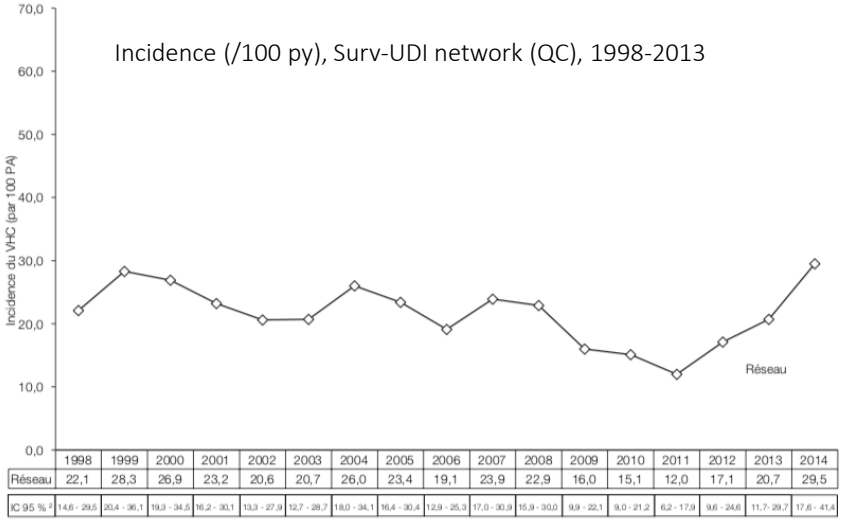
Disclosures

- Julie Bruneau receives advisor fees from Gilead Sciences and Merck and a research grant from Gilead Sciences, outside of this current work.

Background: HCV among PWID

Incidence (/100 py), Surv-UDI network (QC), 1998-2013

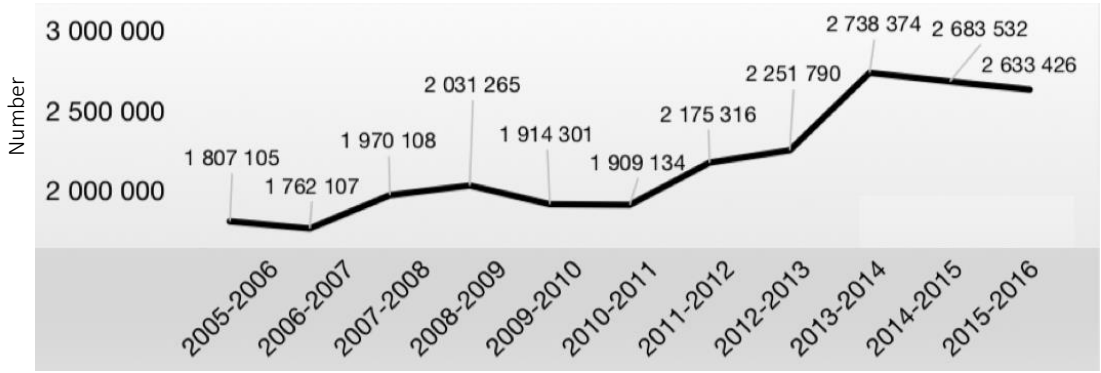


	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Réseau	22,1	28,3	26,9	23,2	20,6	20,7	26,0	23,4	19,1	23,9	22,9	16,0	15,1	12,0	17,1	20,7	29,5
IC 95 %	14,6 - 29,5	20,4 - 36,1	19,3 - 34,5	16,2 - 30,1	13,3 - 27,9	12,7 - 28,7	18,0 - 34,1	16,4 - 30,4	12,9 - 25,3	17,0 - 30,9	15,9 - 30,0	9,9 - 22,1	9,0 - 21,2	6,2 - 17,9	9,6 - 24,6	11,7- 29,7	17,6 - 41,4

Montréal:
72% Ab+
(2013)

Leclerc et al 2018

Syringe distribution by injection material access centres (Quebec, 2005-2016)



INSPQ 2017

Risk behaviours

- Needle sharing : primary risk factor of HCV infection
  - 20% (past 6m, urban PWID)
- High injection frequency
  - ↑ Manipulations → HCV
  - Cocaine injection: 75% (past 6m, Montreal)

SurvUDI - *Leclerc et al 2018*

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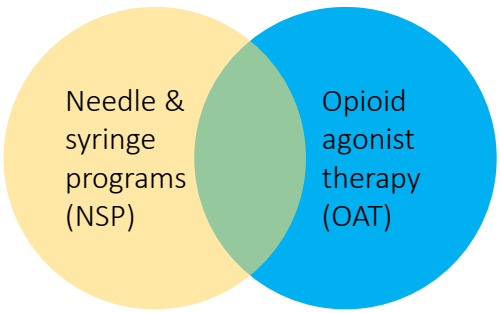
Harm reduction among PWID



Platt et al 2017

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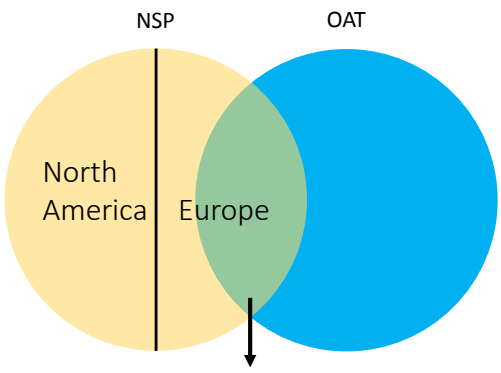
Harm reduction among PWID

Cochrane Library
Cochrane Database of Systematic Reviews



OAT associated with 50% reduced risk of HCV
(RR=0.50, 95% CI: 0.4-0.6)

OAT DOSE | OAT + NSP? | REINFECTION?

Platt et al 2017

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Aims

1. Estimate the rate of HCV infection and its association with NSP/OAT coverage among PWID in Montreal;
2. Compare estimates among HCV-naïve and previously-infected PWID

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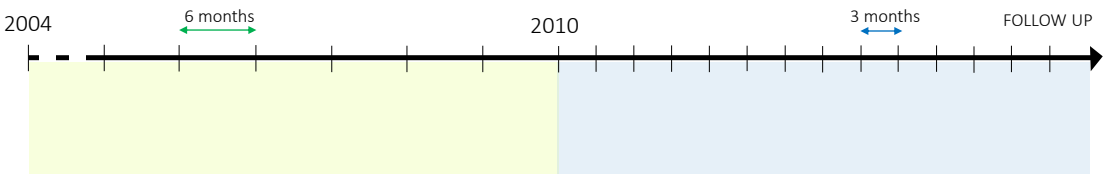
Methods

HEPatitis COhort (HEPCO)



Design: Prospective longitudinal open cohort study

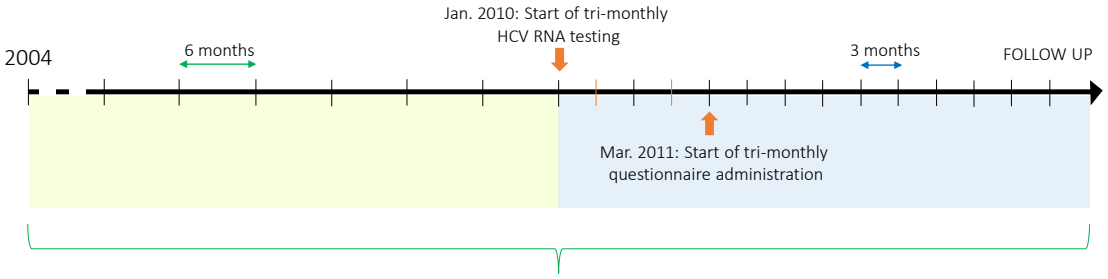
Aim: To identify individual and contextual determinants of HCV infection among PWID

Setting: Montreal, QC, Canada

Eligibility: drug injection (within past 6m), age ≥18

Recruitment: Combination of street-level strategies and community program referrals

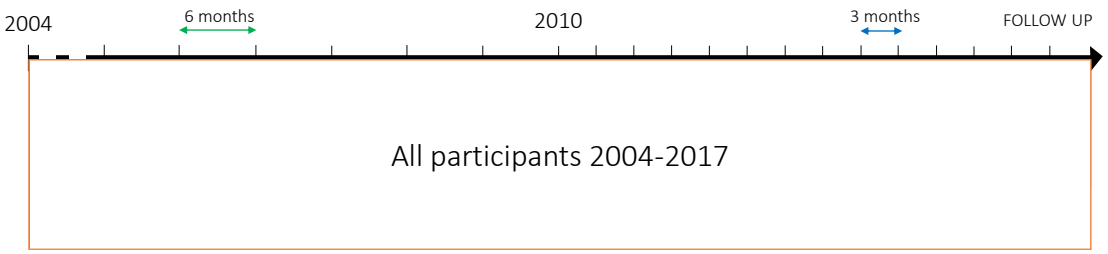
Procedures: Detailed sociodemographic and behavioural questionnaire administered by trained interviewers, HCV testing (every 6/3 months)



HCV antibody testing for primary HCV incidence among Ab-negative

HCV RNA testing for recurrent HCV incidence among Ab+/RNA-

FOR THIS ANALYSIS:



- Recent opioid use/OAT (6m) at enrolment
- Ab+/RNA-negative met clinical definitions of treatment-induced (SVR) or spontaneous viral clearance

Exposure variables: opioid agonist treatment

Self-report: Yes/No + current dose

- Not on treatment
- High dose (≥60 mg/day methadone / ≥16 mg/day suboxone)
- Low dose (<60 mg/day methadone / <16 mg/day suboxone)

Based on clinical guidelines and increasing evidence that OAT is effective provided it relieves withdrawal & craving

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Exposure variables: needle-syringe program coverage

CACTUS	PHARMACIES
ANONYME	SHOOTING GALLERY
SPECTRE	SECONDARY DISTR.
DOPAMINE	FRIEND/PARTNER
DANS LA RUE (POPS)	DEALER
RELAIS METHADONE	BOUGHT ON STREET
CLINIC/CLSC	FOUND
OUTREACH WORKER	OTHER

previous 3/6m

100% SAFE SOURCES
vs
<100% SAFE SOURCES

Consistent with Bruneau et al (2011)

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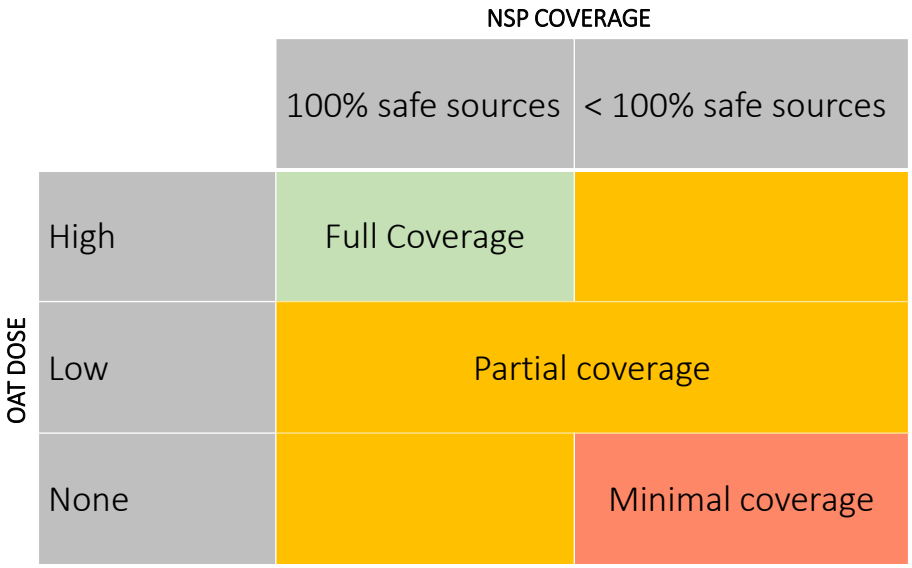
Combined harm reduction coverage



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Outcome variable: time-to-HCV infection

- Primary HCV = Ab+ test among Ab-negative
- Recurrent HCV = RNA+ test among Ab+/RNA- defined as having cleared the virus

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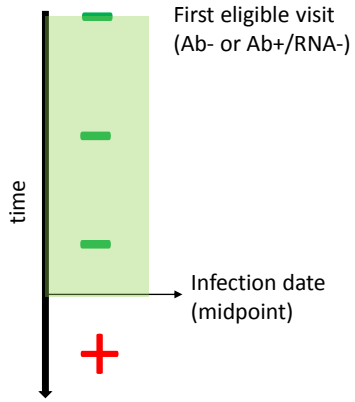
Analyses

- Time-to-event methods
- Time-updated Cox regression models
  - Adjusted for age (<30, ≥30), gender (m/f), past-month cocaine injection (y/n)
  - Stratified by Ab-status



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Results

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Study sample

	GROUPS AT RISK		
	GLOBAL	PRIMARY (Ab-)	RECURRENT (Ab+/RNA-)
Unique participants	422	238	205
Person-years of follow-up	1183.5	526.2	657.3
Median follow-up time	25.2m	21.4m	26.2m

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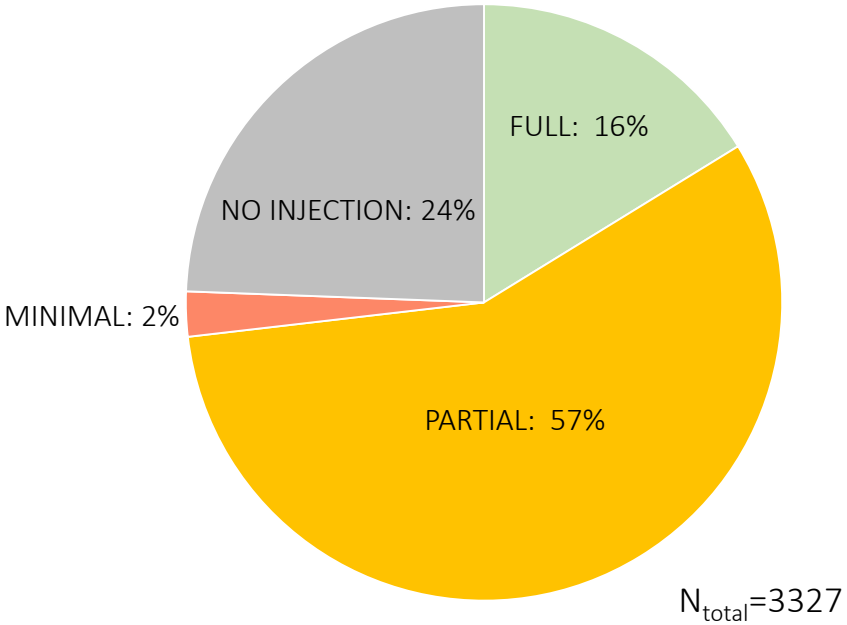
Harm reduction coverage (% visits)



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Characteristics of eligible HEPCO participant-visits

	OVERALL
Median age	40.8
Male gender	81.7%
Caucasian	88.6%
Drugs injected, past month:	
Heroin	30.6%
Cocaine	38.2%
Prescription opioids	11.8%
Days injected, past month (median)	6.7

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HCV Incidence Rates

	GLOBAL
Cases:	106
Rate:	9.0 cases / 100 py
95% CI*:	(7.4-10.8)

*Assuming a Poisson distribution

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Associations (aHR) between NSP/OAT coverage and time-to-HCV infection

STRATIFIED ANALYSES = GLOBAL ANALYSIS

Associations (aHR*) between combined harm reduction coverage and time-to-HCV infection

NSP

100% safe sources	1.00 (ref)
<100% safe sources	0.79 (0.41-1.52)
No injection	**0.34 (0.15-0.76)**

OAT

High	1.00 (ref)
Low	**2.90 (1.15-6.53)**
None	**4.26 (1.95-9.31)**
No injection	1.04 (0.36-3.05)

*Adjusted for age (<30, ≥30), gender (m/f), past-month cocaine injection (y/n)

Associations (aHR*) between combined harm reduction coverage and time-to-HCV infection

Full	1.00 (ref)
Partial	**3.31 (1.53-7.17)**
Minimal	2.43 (0.81-7.25)
No injection	0.95 (0.32-2.78)

*Adjusted for age (<30, ≥30), gender (m/f), past-month cocaine injection (y/n)

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Discussion

- Harm reduction similarly associated with HCV regardless of Ab+/- status
- High-dose OAT coverage is particularly important to reduce drug-related harms
- Low % report full coverage of combined harm reduction
  - 1/3 of partially covered report 100% safe sources + no OAT
    - Could indicate a difficulty in accessing OAT
- Consistent with previous North American studies, NSP coverage was not significantly associated with HCV infection
  - HCV efficiently transmitted in a stimulant-injecting population
  - Measurement: 100% safe sources variable not detailed enough to capture coverage / injection

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Strengths

- Prospective, longitudinal cohort design with long follow-up of community-dwelling participants
- Frequent (tri-monthly) RNA testing

Limitations

- Self-reported coverage
- No genotyping info to distinguish reinfection from reactivation
- Loss-to-follow-up
- Residual confounding

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Public health implications

- Given the high rate of HCV recurrence observed and low % reporting full harm reduction coverage, scale-up of strategies (OAT*) may be necessary to curtail ongoing HCV epidemics, even in the DAA era
- NSP material needs to remain responsive to needs of PWID within the context of evolving drug trends
- Within cocaine-injecting settings (where OAT may not be indicated), innovative approaches are needed to address HCV transmission (e.g. SIS), including those targeting upstream social vulnerability and stigma

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Acknowledgements

COLLABORATORS

- Julie Bruneau
- Marie-Pierre Sylvestre
- Didier Jutras-Aswad
- Élise Roy
- Adelina Artenie
- Stine Hoj
- Brendan Jacka
- Emmanuel Fortier
- Iuliia Makarenko

HEPCO COHORT

- Rachel Bouchard
- Maryse Beaulieu
- Elyse Boucher
- Serge Côté
- Sira Diarra
- Marie-Lyne Girard
- Marie-Eve Turcotte
- Geng Zang

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Supplementary slides

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Associations (aHR) between NSP coverage and time-to-HCV infection

	Global Infection	Primary Infection	Recurrent Infection
100% SAFE SOURCES	1.00 (ref)	1.00 (ref)	1.00 (ref)
< 100% SAFE SOURCES	0.79 (0.41-1.52)	0.84 (0.36-1.96)	0.80 (0.29-2.27)
No injection (past 3/6m)	**0.34 (0.15-0.76)**	0.37 (0.11-1.26)	**0.29 (0.10-0.85)**

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Associations (aHR) between OAT coverage and time-to-HCV infection

	Primary infection	Recurrent infection	Global infection
HIGH DOSE	1.00 (ref)	1.00 (ref)	1.00 (ref)
LOW DOSE	**2.75 (1.15-6.53)**	2.72 (0.74-10.02)	2.50 (0.78-8.05)
NOT ON OAT	**4.14 (1.90-9.04)**	**3.54 (1.09-11.53)**	**4.63 (1.63-13.17)**
NO INJECTION	1.01 (0.35-2.96)	1.04 (0.20-5.33)	0.86 (0.21-3.57)

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	À RISQUE DE VHC PRIMAIRE		À RISQUE DE VHC RÉCURRENTE	
	100% SOURCES SÉCURITAIRES	**< 100% SOURCES SÉCURITAIRES**	**100% SOURCES SÉCURITAIRES**	**< 100% SOURCES SÉCURITAIRES**
TAO ÉLEVÉE	**Complete:** 1.00 (ref)		**Complete** 1.00 (ref)	
TAO FAIBLE	**Partial:** 2.98 (0.92-9.63)		**Partial:** **3.25 (1.16-9.10)**	
TAO AUCUNE		**Minimal:** 1.58 (0.32-7.86)		**Minimal:** 3.70 (0.82-16.64)

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Characteristics	Full coverage N=540 (16.2%) n (%)	Partial coverage N=1772 (53.3%) n (%)	Minimal coverage N=203 (6.1%) n (%)	No injection N=812 (24.4%) n (%)
Age at baseline				
Median (Q1-Q3)	39.9 (32.0-47.7)	39.4 (30.5-46.9)	44.2 (36.7-47.1)	42.5 (34.0-39.3)
Aboriginal, Inuit or Metis				
Yes	15 (2.8)	95 (5.4)	1 (0.5)	22 (2.7)
Ethnicity				
Caucasian	491 (90.9)	1525 (86.4)	201 (99.0)	715 (88.3)
Gender				
Male	418 (77.4)	1438 (81.2)	175 (86.2)	686 (84.5)
HIV status				
Positive	11 (2.0)	110 (6.2)	11 (5.4)	50 (6.2)
Housing				
Unstable[c]	93 (17.3)	468 (26.4)	56 (27.6)	201 (24.8)
Recent incarceration[d]				
Yes	32 (5.9)	148 (8.4)	13 (6.4)	65 (8.0)
Cocaine injection[a]				
Yes	248 (45.9)	903 (51.0)	121 (59.6)	NA
Prescription opioid injection[a]				
Yes	130 (24.1)	706 (39.8)	39 (19.2)	NA
Heroin injection[a]				
Yes	281 (52.0)	712 (40.2)	24 (11.8)	NA
Cocaine & opioid[e] injection[a]				
Yes	124 (23.0)	416 (23.5)	20 (9.9)	NA
Days injected[a]				
Median (Q1-Q3)	8.0 (2.0-24.25)	10.0 (2.0-30.0)	2.0 (1.0-8.0)	0 (0.0)
Sources of needle-syringes[b]				
100% safe	540 (100.0)	1620 (91.4)	0 (0.0)	NA

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Reinfection?

High-risk studies							
Weir et al 2014	277	4.5 (410.0)	Terminology	0	7 (0)	7	17.07 (8.29–34.82)
Ruzic et al 2013	20	5 (100.0)	–	0	0	0	0.00 (.00–36.99)
Hilsden et al 2013	23	1.8 (35.5)	Risk factors	0	1 (0)	1	28.17 (4.99–143.49)
Edlin et al 2013	15	NR (45.1)	Terminology	0	1 (0)	1	22.17 (3.92–115.43)
Conway et al 2013	70	2.0 (138.6)	Genotyping	0	4 (4)	4	28.86 (11.28–71.85)
Deshaies et al 2013	20	1.6 (31.7)	Genotyping	0	2 (1)	2	63.09 (17.48–203.15)
Grady et al 2012	42	2.0 (110.6)	Sequencing	0	1 (0)	1	9.04 (1.60–49.45)
Manolakopouos et al 2012	61	2.0 (122.0)	Genotyping	0	5 (4)	5	40.98 (17.63–92.36)
Grebely et al 2010	35	2.0 (62.5)	Genotyping and risk factors	0	2 (1)	2	32.00 (8.82–109.38)
Currie et al 2008	9	3.6 (38.0)	Terminology	0	1 (0)	1	26.32 (4.66–134.95)
Backmund et al 2004	18	2.8 (48.8)	Genotyping	0	1 (1)	2	40.98 (11.31–137.65)
Dalgard et al 2002	27	4.9 (118.0)	Genotyping	0	1 (1)	1	8.47 (1.50–46.45)
Marco et al 2013	101	1.4 (148.5)	Genotyping and risk factors	0	6 (5)	6	40.40 (18.65–85.34)
Bate et al 2010	53	3.4 (180.4)	Genotyping	5 (5)	4 (4)	9	49.89 (26.47–92.08)

SIMMONS et al 2016

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Recent studies among active PWID

- Aspinall2013: 6.4/100py among individuals reporting IDU after tx-induced HCV clearance
- Weir2016: For PWID who have been hospitalised for an opiate or injection related cause post SVR (11%), the risk of HCV reinfection was greater [AHR = 12.9, 95% CI 2.2–76.0, p = 0.002] and the reinfection rate was 5.7/100 py (95% CI 1.8–13.3).
- Martinello2017: 7.4 per 100 py (95% CI 4.0, 13.8). Reinfection incidence was significantly higher among participants who reported injection drug use at end of or post-treatment, irrespective of HIV status (15.5 per 100 py, 95% CI 7.8, 31.1).
- Midgard2016: Individuals who had relapsed to IDU after treatment (incidence rate 4.9/100 PY; 95% CI 2.3–8.9).

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<table>
<tr><th>3327</th><th>100% Safe Sources</th><th>< 100% Safe Sources</th><th>No injection (p6/3m)</th></tr>
<tr><td>High</td><td>Full coverage
n=540 (16%)</td><td></td><td rowspan="2">No injection, not on OAT
n=341 (10%)</td></tr>
<tr><td>Low</td><td colspan="2">Partial coverage
n=1894 (57%)</td></tr>
<tr><td>None</td><td></td><td>Minimal coverage
n=81 (2%)</td><td>Not injecting nor on OAT
n=471 (14%)</td></tr>
</table>

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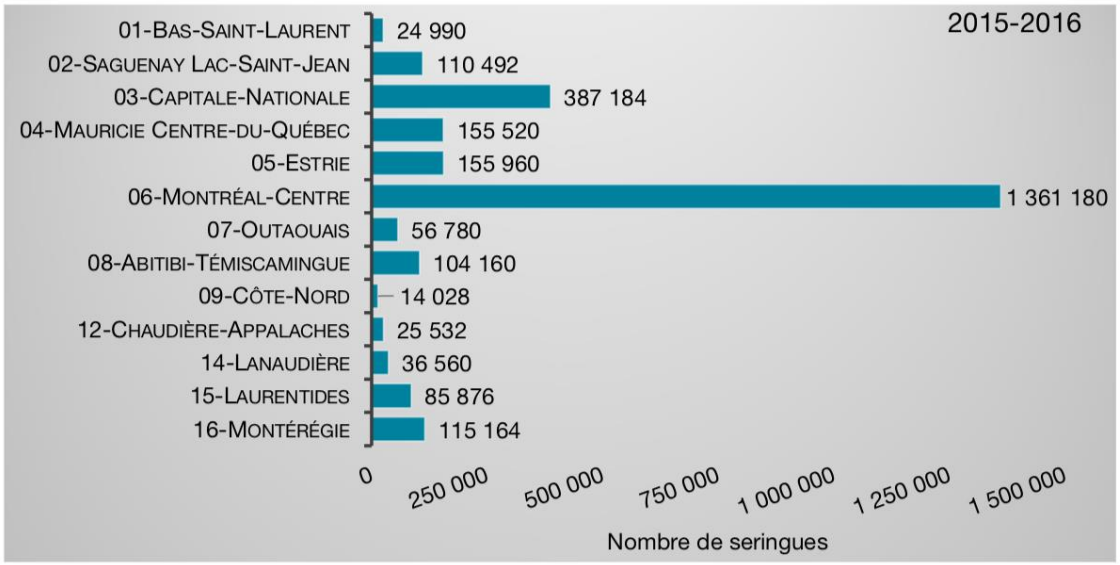

Figure 4 Seringues remises par les DSP aux CAMI selon les régions, 2015-2016

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