

Research and Clinical care in the supervised model of care with injectable opioids in Vancouver



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Acknowledgements



- Study participants
- Frontline workers at the Crosstown clinic
- Research team
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- Also:
 - Health Canada and its many divisions
 - PHC/UBC Research Ethic Board
 - Data and Safety Monitoring Board
 - Community Advisory Board

Background



- Six RCT have tested injectable diacetylmorphine (the active ingredient in heroin) as a second-line treatment for severe opioid use disorder. Including one in Canada.
- Injectable diacetylmorphine improved treatment outcomes: greater reduction in the use of street heroin, involvement in illegal activities, overall health and retention, compared with control groups (mostly oral MMT).
- The positive findings have not in general persuaded policy makers to support many existing programs, nor to roll-out the treatment more widely to bring into care those not doing well with first-line treatments (e.g., methadone, buprenorphine).

SALOME rationale



- Health Canada denied compassionate access for diacetylmorphine in May 2008:
 - *“In the course of reviewing your request, we determined that there are other options (i.e., marketed drugs) that we would consider alternative to diamorphine at this time”.*
- The injectable side of the clinic closed and patients were transferred to oral methadone. PHC kept the site open.
- NAOMI provided hydromorphone to a 25 participants (to test for heroin metabolites in urine):
 - blinding was not broken;
 - almost identical treatment effect compared to diacetylmorphine (however, study not powered to test this hypothesis).
 - Similar profile that diacetylmorphine
 - Licensed opioid in Canada for analgesia

Supervised model of care



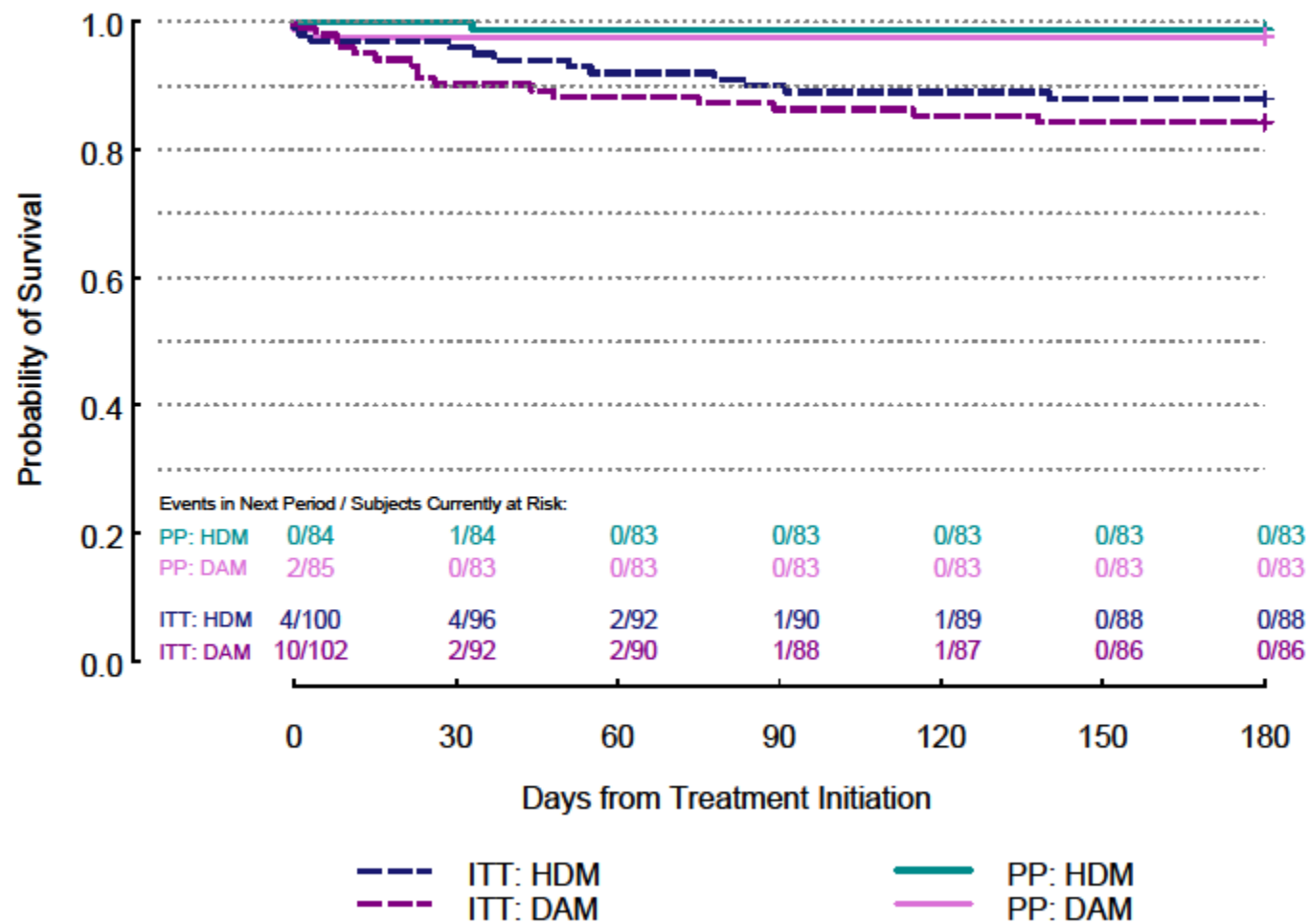
- Medication is dispensed and self-administered by injection **under supervision.**
- The supervision ensures **safety** of the patients (e.g., overdoses) and the community (e.g., secure the medication)
- For some, injectable diacetylmorphine seems to provide enough motivation to attend and comply with much needed **structured treatment**
- The supervised model of cares provides a tremendous opportunity to **offer comprehensive care.**

SALOME

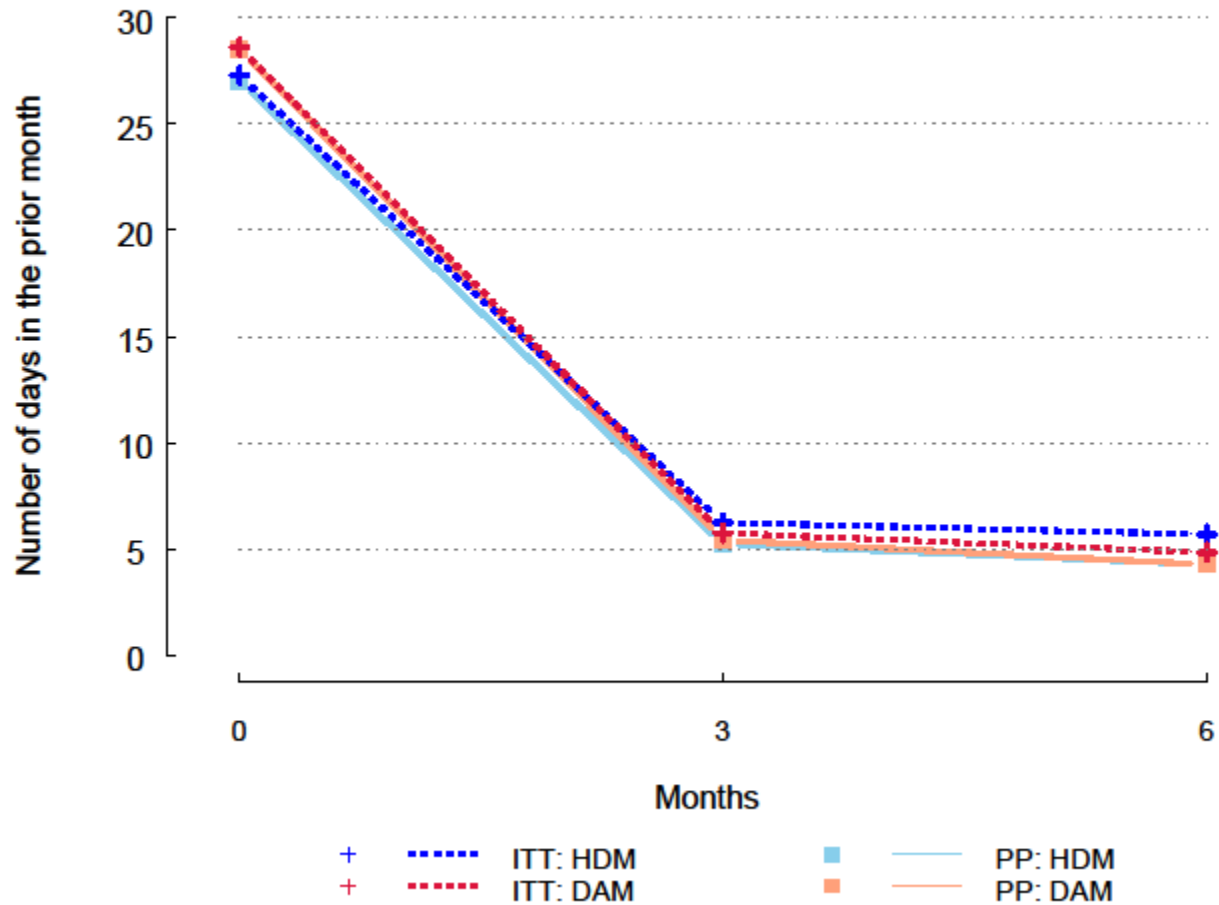


- Tested the ***non-inferiority*** of hydromorphone compared to diacetylmorphine for long-term opioid dependence in a double-blind Randomized Clinical Trial.
- Non-inferiority trials are designed to test treatments that offer ***ancillary advantages*** over those that have shown to be effective in previous superiority studies.
- Ancillary advantage of hydromorphone: is currently ***licensed*** for analgesia.

Time to First 30-Day SALOME Treatment Interruption



Total Street Acquired Opioid Use



Primary efficacy outcomes according to analysis population a six months



HDM
Estimates (95% CI)

DAM

Difference: DAM minus HDM (two-sided 90% CI)

Days of street heroin use in the prior month

ITT 5.50 (3.81 to 7.34) 3.15 (1.82 to 4.67)

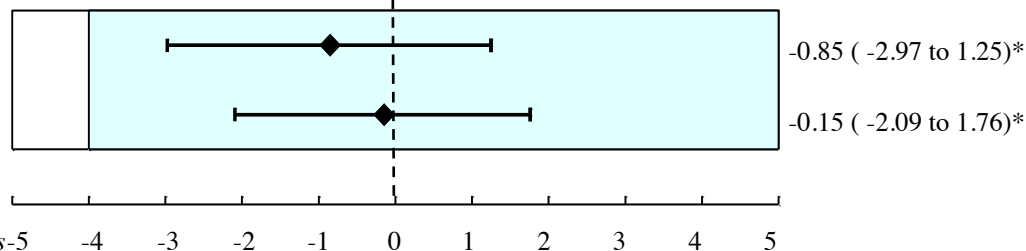
PP 4.08 (2.42 to 5.81) 2.64 (1.36 to 3.95)



Days of street opioid use in the prior month, including heroin

ITT 5.75 (4.07 to 7.62) 4.90 (3.34 to 6.79)

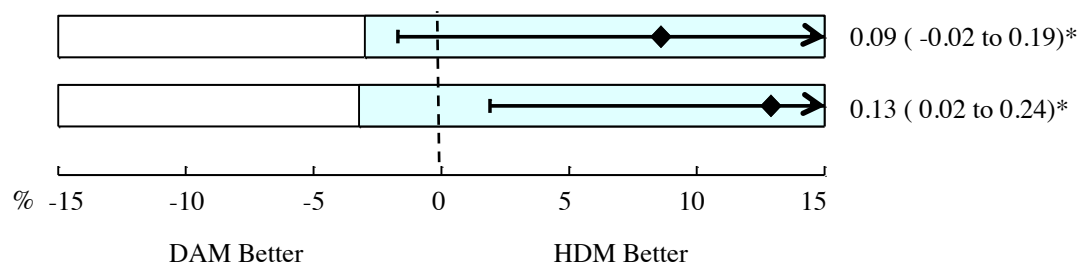
PP 4.34 (2.66 to 6.18) 4.20 (2.62 to 5.88)



Proportion of urinalyses positive for street heroin metabolites in the 6th month visit urine sample

ITT 0.21 (0.13 to 0.30) 0.30 (0.20 to 0.40)

PP 0.19 (0.11 to 0.28) 0.32 (0.22 to 0.42)



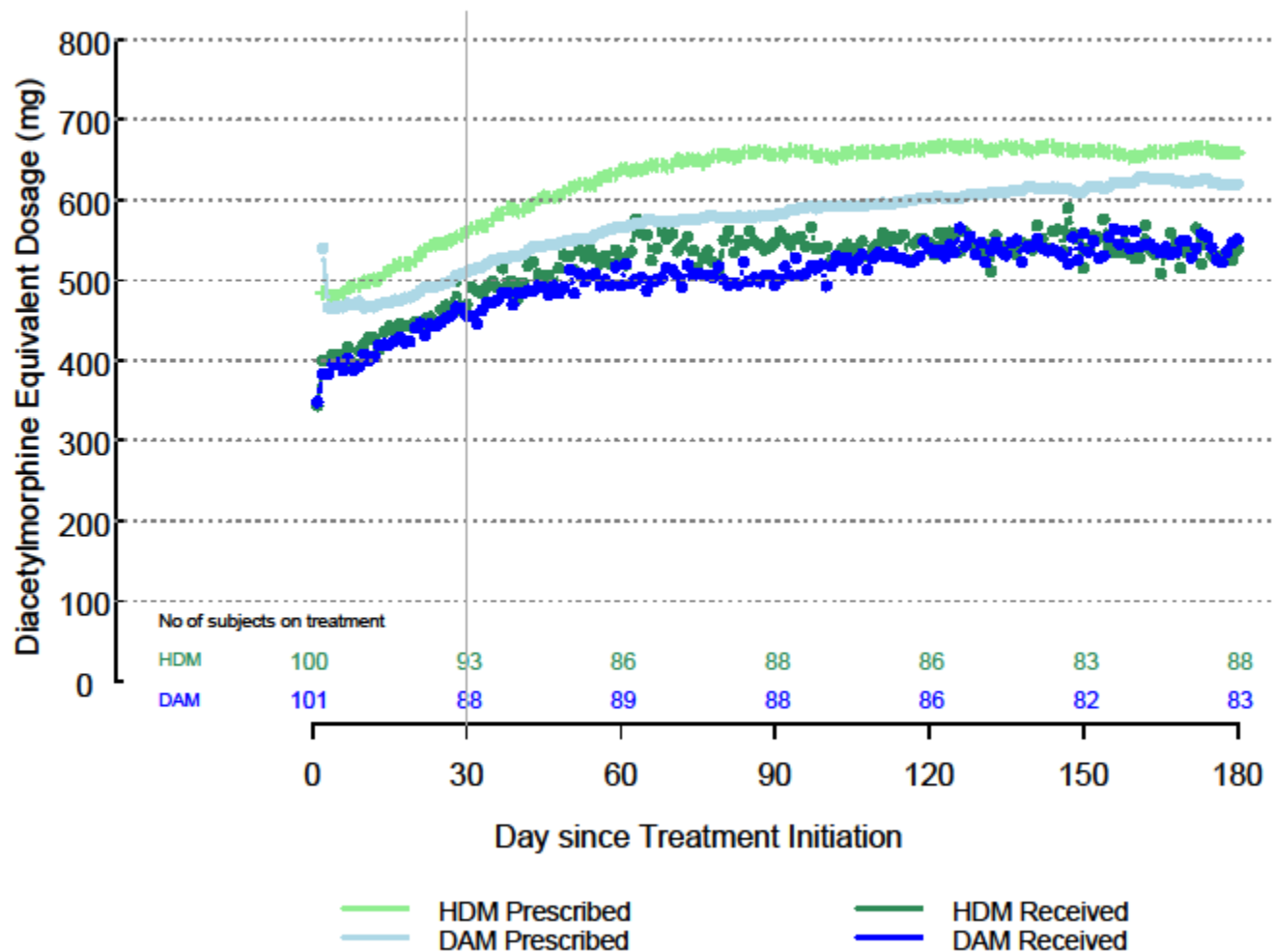
HDM= hydromorphone, injectable; DAM= diacetylmorphine, injectable; CI = confidence intervals; ITT = Intention to Treat, included all participants randomized, using multiple imputation in case of missing data, except when data were missing due to death. PP = Per Protocol, included all participants receiving treatment with injectables at least 20 days in the month prior to the 6th month visit. Street opioid use includes illicit use of heroin, morphine, hydromorphone, and speedball (combined street opioids and stimulants). The CI comparison approach is used, in which non-inferiority was concluded when the lower bound of the 1-sided 95% CI (corresponding to a two-sided 90% CI) lies within the non-inferiority zone represented by the shaded area defined by the margin. For days of street heroin and opioid use the margin was -4 days. For the proportion of urinalyses positive for street heroin markers, the margin was -10% of the value for DAM (i.e. -0.03 for ITT and -0.32 for PP). For days of street heroin and opioid use, baseline values were adjusted. Asterisks indicate where non-inferiority was concluded.

Secondary Outcomes



Secondary outcomes in the prior 30 days		HDM (95%CI)	DAM (95%CI)	Difference: DAM minus HDM (95%CI)
Proportion of participants receiving study medications ≥ 28 days				
	ITT	0.77 (0.69 to 0.85)	0.80 (0.72 to 0.88)	0.03 (-0.08 to 0.14)
	PP	0.92 (0.86 to 0.98)	0.94 (0.89 to 0.99)	0.02 (-0.05 to 0.10)
MAP physical health ^a				
	ITT	11.70 (10.28 to 13.13)	11.71 (10.23 to 13.19)	0.00 (-2.02 to 2.03)
	PP	12.12 (10.62 to 13.61)	11.98 (10.45 to 13.51)	-0.13 (-2.25 to 1.98)
MAP psychological health ^a				
	ITT	9.08 (7.58 to 10.58)	8.13 (6.55 to 9.71)	-0.95 (-3.09 to 1.19)
	PP	9.51 (7.90 to 11.13)	8.11 (6.50 to 9.72)	-1.40 (-3.65 to 0.85)
Days of illegal activities				
	ITT	3.76 (2.14 to 5.66)	2.78 (1.65 to 4.21)	-0.98 (-3.11 to 1.04)
	PP	3.73 (1.73 to 5.65)	2.78 (1.35 to 4.14)	-1.06 (-3.46 to 1.14)
Days of crack cocaine use				
	ITT	7.09 (5.04 to 9.72)	4.78 (3.17 to 7.02)	-2.31 (-4.73 to -0.21)*
	PP	6.43 (4.03 to 9.47)	4.87 (2.91 to 7.53)	-1.56 (-3.94 to 0.41)

Mean daily dose prescribed and received of DAM equivalent by arm



Adverse Events Summary



- All related AEs and SAEs were expected: mostly histamine reactions and oversedations.
- Hydromorphone had significantly less AEs and SAEs compared to diacetylmorphine.
- In the total 88,451 injections, there were 14 opioid overdoses that required narcan, and 11 seizures (in 4 patients), all successfully treated on site without hospitalization.

CONCLUSION



- In jurisdictions where **diacetylmorphine is currently not available** or for patients where it is contraindicated or unsuccessful, **hydromorphone could be offered as an alternative** within the supervised model of care.
- In a broader context, SALOME participants have provided **key evidence to support the supervised model of care:**
 - In a double-blind study, where participants did not guess the medication they were receiving beyond what is expected by chance, outcomes did not differ.