Addictive Behaviors Reports 17 (2023) 100490

Contents lists available at ScienceDirect

Addictive Behaviors Reports

journal homepage: www.elsevier.com/locate/abrep

Changes in daily dose in open-label compared to double-blind: The role of clients' expectations in injectable opioid agonist treatment

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ARTICLE INFO

Keywords:
Opioid use disorder
Injectable opioid agonist treatment
Person-centered care
Drug preference
Diacetylmorphine
Hydromorphone

ABSTRACT

Introduction: Though double-blind studies have indicated that hydromorphone and diacetylmorphine produce similar effects when administered through injectable opioid agonist treatment (iOAT) programs, participant preference may influence some aspects of medication dispensation such as dose.

Methods: This is a retrospective longitudinal analysis. Participants (n = 131) were previously enrolled in a double-blind clinical trial for iOAT who continued to receive treatment in an open-label follow up study. Data included medication dispensation records from 2012 to 2020. Using linear regression and paired t-tests, average daily dose totals of hydromorphone and diacetylmorphine were examined comparatively between double-blind and open-label periods. A subgroup analysis explored dose difference by preference using the proxy, blinding guess, a variable used to facilitate the measurement of treatment masking during the clinical trial by asking which medication the participant thought they received.

Results: During the open-label period, participants prescribed diacetylmorphine received 49.5 mg less than during the double-blind period (95% CI −12.6,-86.4). Participants receiving hydromorphone did not see a significant dose decrease. Participants who guessed they received hydromorphone during the clinical trial, but learned they were on diacetylmorphine during the open-label period, saw a decrease in total daily dose of 78.3 mg less (95% CI −134.3,–22.4) during the open-label period.

Conclusion: If client preference is considered in the treatment of chronic opioid use disorder, clients may be able to better moderate their dose to suit their individual needs. Together with their healthcare providers, clients can participate in their treatment trajectories collaboratively to optimize client outcomes and promote person-centered treatment options.

1. Introduction

Opioid use disorder (OUD) contributes to significant health burdens on communities including opioid related emergency department visits (Belzak & Halverson, 2018), infective endocarditis (Larney et al., 2017), increased rates of HIV and HCV infections (Degenhardt et al., 2017) and unintentional fatal overdoses (Degenhardt et al., 2019). People who use illicit opioids are exposed to disproportionate levels of risk, including ongoing exposure to the toxic unregulated drug supply and limited access to programs that provide safer alternatives (Park et al., 2020). As overdose rates remain high across North America (Hedegaard et al., 2021; Government of British Columbia, 2022) calls to supplement and diversify current modalities of opioid agonist treatment (OAT) provision look to expand access and engagement of people with OUD (Palis et al., 2022; Park et al., 2020; Schottenfeld & O'Malley, 2016). Though there is no single solution, pharmacological interventions and access to psychosocial supports are known to decrease morbidity and mortality, improve physical and mental health, reduce the use of illicit opioids, and work to keep clients in treatment (Mattick et al., 2014; Sordo et al., 2017; Wakeman et al., 2020). Treatment engagement for chronic health conditions, such as OUD, requires improving accessibility and desirability and considering the complex dynamics in the provision of addiction care.

Over the course of the last few decades, several European countries

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https://doi.org/10.1016/j.abrep.2023.100490
Received 15 October 2022; Received in revised form 3 April 2023; Accepted 11 April 2023
Available online 14 April 2023

and Canada began offering injectable diacetylmorphine (i.e., pharmaceutical grade heroin) for the treatment of OUD as a way to engage people in treatment by providing their preferred medication safely (Room, 2002). Randomized clinical trials showed this form of injectable opioid agonist treatment (iOAT) to be a clinically effective, safe alternative (Ferri et al., 2011). IOAT has also been demonstrated to be a cost-effective way to decrease illicit opioid use and retain clients in treatment (Bansback et al., 2018; Dijkgraaf et al., 2005; Nosyk et al., 2012). To increase accessibility and diversity of options, studies in Canada showed a short-acting opioid, hydromorphone (an opioid analgesic licensed in many countries for acute pain management), to be non-inferior to diacetylmorphine in a double-blind randomized trial (Oviedo-Joekes et al., 2016). Where available, iOAT medications are provided in a specific setting for consumption under the observation of health care providers. Following an induction protocol to reach a safe and effective dose, iOAT doses are individualized in consultation with the prescriber, the client and the nurse (Oviedo-Joekes et al., 2019b). Clients are offered a range of other medical and non-medical services, either on site or by referral, depending on their respective needs (Canadian Research Initiative in Substance Misuse, 2019). Currently, iOAT medications do not include long-acting depot injections (Haight et al., 2019; Johnson et al., 2022) or other forms of short-acting medications (e.g., morphine or fentanyl), though other options might become more accessible in the future.

The two licensed iOAT medications approved by Health Canada for the treatment of OUD, hydromorphone and diacetylmorphine (Health Canada, 2019, 2022), have been found to produce similar effects clinically and subjectively when offered double-blind (Brands et al., 2004; Dunn et al., 2018; Wallenstein et al., 1990) and have demonstrated non-inferiority without breaking blinding (Oviedo-Joekes et al., 2016). While these studies contribute to the body of evidence for treatment effectiveness, they also enable iOAT to welcome people into care by offering them the ability to choose their preferred medication (Room, 2002). Multiple treatment options open the door to client preference. For example, 83.2% of participants in one double-blind study indicated they preferred one medication (diacetylmorphine) over the other (hydromorphone) (Oviedo-Joekes et al., 2016). This measured aspect of preference may have influenced the on average higher health scores experienced by those whose drug of choice aligned with what they thought they were receiving during the trial (Oviedo-Joekes et al., 2017).

Though double-blind studies provide robust evidence of treatment effectiveness, an important part of treatment outcomes involves the consideration of participants' expectations (Colagiuri & Boakes, 2010; Fairbairn et al., 2008; Oviedo-Joekes et al., 2017; Schnoll et al., 2008). Client preferences have been known to influence how individuals select, respond to, and accept one medication over another and have important impacts on treatment adherence (Sanders et al., 2013). Involving clients in shared decision-making has been shown to improve client-provider therapeutic relationships (Palis et al., 2020) and promote client autonomy, self-confidence, and independence in the treatment of substance use disorders (Marchand et al., 2019; Marshall et al., 2021). In line with recent work that describes the role of drug preference when improving interventions and services for people who use opioids (Buresh et al., 2019; Ferguson et al., 2022; Morales et al., 2019), providing clients with the opportunity to inform both medication and dose is an integral part of providing person-centered care.

While studies on methadone have assessed the impact of client's perceptions on treatment outcomes (Nosyk et al., 2021; Walcher et al., 2016), injectable hydromorphone and diacetylmorphine have yet to be explored. The present study explores differences in the individualized iOAT daily dose clients received during the blinding and after the medication was provided open-label. This research question has meaningful potential to help inform policy makers and clinical teams in addiction, strengthen the evidence for inclusive practice through shared decision-making, and benefit current or potential services users.

2. Methods

2.1. Design, setting and participants

This is a retrospective longitudinal inferential study involving participants from the Research on the Utilization of Therapeutic Hydromorphone (RUTH) study, conducted in Vancouver, Canada from 2016 to 2019. Details of this study have previously been described elsewhere (Oviedo-Joekes et al., 2019b). Briefly, RUTH was a longitudinal cohort study of people receiving open-label injectable diacetylmorphine or injectable hydromorphone involving participants that took part in the Study to Assess Longer-term Opioid Medication Effectiveness (SALOME) trial who were offered open-label injectable hydromorphone or diacetylmorphine once the trial ended. SALOME was a double-blind, phase III, non-inferiority randomized clinical trial that tested if injectable hydromorphone compared to injectable diacetylmorphine. Treatments for the double-blind SALOME trial and the open-label RUTH study were delivered by Providence Health Care's Crosstown Clinic. For the present analysis, Crosstown clinic dispensation records were obtained. The study period for this analysis includes the SALOME Phase I double-blind period (2012 – 2014), the open-label RUTH cohort study (2016 – 2019), and Crosstown Clinic Dispensation Records (2012 – 2020).

2.2. Treatment

Participants began treatment after an initial clinical induction phase spanning three days that involves communicative collaboration between the physician, the nurse, and the client to reach an initial safe and effective dose (Oviedo-Joekes et al., 2019b). Medications were self-administered (intravenously or intramuscularly) up to three times per day under the observation of registered nurses. Each visit required a minimum of three hours between doses. Participants could receive a maximum daily dose of 500 mg/day for hydromorphone or 1000 mg/day for diacetylmorphine. During SALOME, medications were prescribed in diacetylmorphine milligrams to maintain double-blinding, with a 2:1 ratio. Once in open-label, participants could increase their daily dose of hydromorphone beyond the trial protocol limits, if needed. At the time of this study, only hydromorphone was licensed in Canada for OUD. Diacetylmorphine was provided under the special access program and therefore subject to additional regulatory and prescribing restrictions (e.g., dose limits). While receiving injectable treatment, participants were offered a wide array of services, either on site or by referral. Services included, but were not limited to counseling, nutritionists, primary care, and infectious disease specialists.

2.3. Data collection

This study uses data from RUTH (open-label), SALOME (double-blind), and dispensation records from Crosstown Clinic. Databases include the daily prescribed and received dose of injectable diacetylmorphine or hydromorphone. Prescribed doses refer to the amount of drug in milligrams a participant is prescribed by a physician or nurse. Received doses refer to the amount of drug in milligrams that a participant physically administered. These amounts can differ as participants or nurses can make daily adjustments in dose if necessary, though they are only able to reduce the amount received. Increases in doses required a new prescription.

RUTH (open-label) participants consented to have their Crosstown clinical data (i.e., daily dose) linked with their records from the SALOME (double-blind) clinical trial (i.e., study questionnaires and daily dose). In addition, participants consented to have their open-label RUTH study questionnaire data linked to their Crosstown clinical data. RUTH questionnaires recorded participants' behaviors from the previous 30 days to the day the questionnaire is performed on the following topics: sociodemographics, substance use patterns, physical and mental health, and participant experience of treatment, including dose satisfaction and

a Visual Analog Scale (VAS) drug-liking score that rated six perceived drug effects from 0 to 100, where higher scores indicate a larger magnitude of the perceived effect. To measure treatment masking during the double-blind SALOME trial, participants were asked what treatment they thought they had received at the end of the 180-day treatment period. This variable, blinding guess, included five response options: a) heroin definitely, b) heroin possibly, c) hydromorphone definitely, d) hydromorphone possibly, and e) not sure (Oviedo-Joekes et al., 2016). For the purpose of this analysis, blinding guess choices were grouped by likelihood of drug (definitively and possibly heroin or hydromorphone), and the unsure. All data were linked using a unique participant identifier to preserve confidentiality.

2.4. Data analysis

A total of 115 (87%) out of 131 eligible participants were included in this study. Of the 16 (13%) participants not included, six (37%) had dispensing discrepancies, two (12%) switched to oral medication, and eight (50%) were removed as they received daily-total doses of hydromorphone that were higher than the maximum recommended dose during the open-label period. Descriptive statistics were used to present daily totals of prescribed medication, demographic information, and longitudinal data of identified characteristics (e.g., chronic medical problems, housing, health scores) that may have a clinical association with receiving iOAT. As in prior analyses, data from days with co-prescription of oral medications (e.g., hydromorphone, methadone, morphine) and the first 30 days of treatment were removed from the analysis. The latter was to account for initial dose adjustments to appropriately meet the participant's needs (Oviedo-Joekes et al., 2019a).

Linear regression analysis and paired t-tests were used to explore associations between received medication and dose between double-blind and open-label periods. To address potential explanatory factors that might have differed between study periods, the blinding itself was also tested with paired t-tests by medication received, and a subgroup analysis by blinding guess in the double-blind study was performed. In an effort to explore additional explanations for differences in dose, open-label potency ratios for diacetylmorphine and hydromorphone were calculated. Average total daily dose and percentile ranks of observations were described and compared against the ratios currently being used in clinical practice (Oviedo-Joekes et al., 2011). For the subgroup analysis, we included the eight participants whose doses of hydromorphone fell outside of current protocol boundaries. These observations were imputed with the maximum daily-total allowed plus one mg. (i.e., 501 mg a day). All analyses were conducted using R (Version 1.4.1106).

3. Results

Of the 115 participants included in the analysis, 67 received diacetylmorphine and 48 received hydromorphone in both double-blind and open-label periods. The mean age was 44.6 years, 70.4% identified as male, and 31% identified as Indigenous; 38.9% of participants indicated satisfaction with dose, and the mean days of use of any illicit opioids was 6.1 days (Table 1). Characteristics of participants did not significantly differ between the diacetylmorphine and hydromorphone groups.

3.1. Double-blind vs. open-label

Table 2 shows double-blind and open-label daily-total doses in milligrams and the dose difference in milligrams by medication type. We compared the daily-total average dose received during the open-label RUTH study period to the daily-total average dose received during SALOME. During the open-label period, participants getting diacetylmorphine received 49.5 mg less (95% CI −12.6, −86.4) on average than during the double-blind period. No significant decrease was noted in the participants receiving hydromorphone, even after performing a

Table 1
Open-label Study (RUTH) Participant Characteristics and Outcomes Receiving Injectable Diacetylmorphine or Hydromorphone in Both Double-blind (SALOME) and Open-label Periods.

	Diacetylmorphine (n = 67)	Hydromorphone (n = 48)	Total (n = 115)	p-value
Socio-demographics and relevant factors:				
Age	44.5 ± 8.9	44.8 ± 9.8	44.6 ± 9.2	0.89[a]
Gender				0.11[b]
Female	19 (28.4)	12 (25.0)	31 (27.0)	
Male	48 (71.6)	33 (68.8)	81 (70.4)	
Transgender	0 (0.0)	3 (6.3)	3 (6.3)	
Ethnicity				0.99[b]
Indigenous	21 (31.3)	15 (31.3)	36 (31)	
Non-indigenous	46 (68.7)	33 (68.7)	79 (69)	
Double-blind study factors: Stable housing[d]				0.17[b]
Yes	25 (37.3)	24 (50.0)	49 (42.6)	
No	42 (62.7)	24 (50.0)	66 (57.4)	
Lifetime chronic medical problem[e]				0.91[b]
Yes	37 (55.2)	26 (54.2)	63 (54.8)	
No	30 (44.8)	22 (45.8)	52 (45.2)	
VAS Drug Liking[f]	63.5 ± 33.3	59.7 ± 33.7	62 ± 33.3	0.56[a]
Related Adverse Events(per person)[g]				<0.01[b]
Yes	55 (82.1)	22 (45.8)	77 (67)	
No	12 (17.9)	26 (54.2)	38 (33.0)	
Related Serious Adverse Events (per person)[h]				<0.01[b]
Yes	10 (14.9)	0 (0.0)	10 (8.7)	
No	57 (85.1)	48 (100.0)	105 (91.3)	
Open-label study factors: Stable housing[d]				0.51[b]
Yes	32 (47.8)	20 (41.7)	52 (45.2)	
No	35 (52.2)	28 (58.3)	63 (54.8)	
Health Scores				
Physical health[i]	24.5 ± 10.0	23.8 ± 9.4	24.2 ± 9.7	0.73[a]
Psychological health[j]	8.1 ± 6.3	8.8 ± 5.9	8.4 ± 6.1	0.54[a]
Substance use: Days of use in the prior month[k]				
Alcohol	1.9 ± 4.1	3.1 ± 6.9	2.4 ± 5.4	0.29[a]
Any illicit opioid	4.8 ± 6.5	8.0 ± 8.3	6.1 ± 7.3	0.03[a]
Any illicit stimulant	9.6 ± 10.6	11.7 ± 10.9	10.5 ± 10.7	0.32[a]
Satisfaction with dose[l]				0.01[c]

(continued on next page)

Table 1 (*continued*)

	Diacetylmorphine (n = 67)	Hydromorphone (n = 48)	Total (n = 115)	p-value
Yes	28 (50)	9 (23.1)	37 (38.9)	
No	27 (48.2)	27 (69.2)	54 (56.8)	
Unknown	1 (1.8)	3 (7.7)	4 (4.2)	
Missing	11	9	20	
VAS Drug Liking (T12) [f]	77.0 ± 21.2	64.1 ± 29.2	71.7 ± 25.5	0.01[a]

Data shown are mean ± standard deviation or number (%).
[a] Unequal variance two sample *t*-test.
[b] Chi-Square p-value.
[c] Fisher Exact p-value.
[d] At first visit in open-label study. Unstable housing is single resident occupancy hotel rooms with restrictions or couch surfing, and street housing defined as outdoor, in vehicles or in public places.
[e] Measured once, at the beginning of the double-blind trial, when all baseline measures were taken.
[f] Visual Analog Scale (VAS) scores range from "not at all" [0] to "extremely" [100] and measures the experienced opioid drug effects. Double-blind VAS scores at six months. Total n = 105; diacetylmorphine = 62; hydromorphone = 42. Open-label VAS scores at 12 months (T12) correspond to the year 2017. Total n = 102; diacetylmorphine = 60; hydromorphone = 42.
[g] Drug reactions per person with at least one event; data collected during the double-blind period only.
[h] Drug reactions per person with at least one event; measured in phase one; systematic data collected during the double-blind period only.
[i] OTI (Opioid Treatment Index) total health scores range from 0 to 51, higher scores suggest more physical conditions.
[j] MAP (Maudsley Addiction Profile) psychological health scores range from 0 to 40, higher scores indicate poorer psychological health.
[k] Average number of days in prior 30 before the interview across the 18 months duration of the study.
[l] Dose satisfaction for this study were included in follow up number six and was categorized as a) Yes: yes, at every time point, b) No: no at least in one time point and c) unknown (for participants who never provided an answer but had an average dose in the prior 30 days). Participants with no average dose (i.e., not retained) are not included.

Table 2
Double-blind (SALOME) and Open-label (RUTH) Daily-Total Doses and Dose Difference in Milligrams by Medication Type.

Group	n	SALOME dose in mg	RUTH dose in mg	Difference in mg (RUTH – SALOME)
Diacetylmorphine	67	509.9 ± 190.1	460.4 ± 186.7	−49.5 (-86.4, −12.6)*
Hydromorphone	48	243.8 ± 81.6	248.7 ± 96.8	4.9 (–22.5, 32.3)
Hydromorphone sensitivity analysis	56	267.4 ± 99.9	284.8 ± 126.3	17.4 (-8.7, 44.4)

mg: milligrams.
Data shown are mean ± standard deviation and 95% confidence interval.
(*) Indicates the difference in dose received within groups is significant at $p < 0.05$.
Differences within groups calculated using *t*-test.
Sensitivity analysis included eight participants who received daily-total doses of hydromorphone that were greater than the maximum allowed dose per protocol in the open-label period.

sensitivity analysis that included the eight observations that fell outside of recommended prescribing dosages.

3.2. Blinding guess

Table 3 displays the doses of diacetylmorphine and dose difference for participants receiving diacetylmorphine in the double-blind SALOME trial and diacetylmorphine in the open-label RUTH study by blinding guess. Participants receiving double-blind diacetylmorphine, but thought they were definitively or possibly receiving hydromorphone, saw a significant decrease in daily-total average dose of 78.3 mg less (95% CI −134.3, –22.4) during the open-label RUTH period when compared to the double-blind period.

Table 3
Diacetylmorphine Dose and Dose Difference in Milligrams for Participants Receiving Diacetylmorphine in double-blind (SALOME) and Diacetylmorphine in open-label (RUTH) periods by Blinding Guess.

Blinding Guess Group	n	SALOME Diacetylmorphine dose in mg	RUTH Diacetylmorphine dose in mg	Difference in mg (RUTH – SALOME)
Diacetylmorphine Definitively or Possibly	23	535.8 ± 163.2	512.8 ± 198.9	–22.9 (-82.1, 36.2)
Hydromorphone Definitively or Possibly	30	528.7 ± 187.9	450.4 ± 170.9	−78.3 (-134.3, –22.4)*
Unsure	14	427.1 ± 224.1	395.6 ± 187.8	−31.5 (-132.9, 70.0)

Diacetylmorphine; mg: milligrams.
Data shown are mean ± standard deviation and 95% confidence interval.
(*) Indicates the difference in dose received within groups is significant at $p < 0.05$.

3.3. Difference in diacetylmorphine dose by prescriber and participants' characteristics.

To further explore the data, the difference in in average daily-total diacetylmorphine dose received in the open-label (cohort study) and the blinding period (randomized study) was categorized as dose decrease or increase (negative or positive milligrams if the participant received lower or higher dose during the open-label period, respectively). Analyses were conducted with the observed diacetylmorphine differences by prescriber during the open-label period, but they were not significant (Fisher's exact test). Diacetylmorphine dose difference was also considered by client characteristics. Overall, no statistical significance was found among the main study variables with few exceptions. For example, there was a reported decrease in use of any opioids in the 30 days prior to the schedule research interview of −8.84 mg (95% CI −14.18, −3.50). In addition, participants who had chronic medical problems at baseline in the double-blind trial (SALOME) received −55.1 mg less (95% CI −108.2, −1.9) during the open-label RUTH study in average daily-total dose received when compared to SALOME. Those who report not having a chronic medical condition received −42.7 mg. difference, although it was not significant (95% CI −96.1, 10.7).

3.4. Potency ratio

Potency ratios between diacetylmorphine and hydromorphone open-label were in the range of 1.4:1 and 1.6:1. Lower potency ratios were observed on the lower dosage percentiles and stabilized at around 1.6:1 starting at mid-range doses (i.e., 270 mg for hydromorphone and 430 mg for diacetylmorphine). These observed potency ratios for diacetylmorphine to hydromorphone are lower than the observed potency ratio of 2:1 in previous clinical trials. Potency ratios between hydromorphone and diacetylmorphine can be found in Table 4.

4. Discussion

The present study demonstrates that clients receiving injectable diacetylmorphine throughout a double-blind study period reduced their

Table 4
Potency Ratios Between Hydromorphone and Diacetylmorphine by Prescribed and Received Doses in Milligrams.

Statistics (n)	Hydromorphone in mg (n = 127)	Diacetylmorphine in mg (n = 123)	Ratio for diacetylmorphine to hydromorphone
Dose Prescribed[a]			
10th percentile	203.1	265.1	1.3
25th percentile	254.0	361.0	1.4
50th percentile	317.8	501.0	1.6
Mean	333.7	524.3	1.6
75th percentile	419.4	651.0	1.6
90th percentile	501.0	826.9	1.7
Dose Received[b]			
10th percentile	156.4	220.3	1.4
25th percentile	196.3	294.0	1.5
50th percentile	273.1	431.2	1.6
Mean	286.9	455.6	1.6
75th percentile	370.2	589.0	1.6
90th percentile	480.4	730.8	1.5

Hydromorphone and Diacetylmorphine; mg: milligrams.
[a] Dose Prescribed is the amount of drug in milligrams a participant was prescribed by a prescriber.
[b] Dose Received is the amount of drug in milligrams that a participant physically administered.

daily dose once they received it open-label. When assessed for intra-group characteristics or systematic errors, no differences in dose were found to be clinically and statistically significant outside of blinding guesses. These findings have implications around the role of client expectations and perceptions in medication administration, client engagement with healthcare providers, and treatment success. To our knowledge, this is the first study to demonstrate that clients receiving iOAT treatment may moderate their dose if expectations of medication preference are being met.

Participants in this study were formerly enrolled in the double-blind SALOME trial where the overall preference before the study began was for injectable diacetylmorphine (83.2%) over injectable hydromorphone, and only if diacetylmorphine was not available, they would accept hydromorphone (Oviedo-Joekes et al., 2017). In addition, previous work indicated that participants in the double-blind (SALOME) trial were more likely to suspect they were receiving hydromorphone if they did not like the drug effect regardless of which drug they were receiving (Oviedo-Joekes et al., 2017). This study is uniquely positioned to explore expectations due to the double-blind vs. open-label nature of the data. Given the majority of participants specified they would prefer to receive diacetylmorphine, we suggest that clients whose medication expectations were not being met (i.e., in cases where the client wanted diacetylmorphine, but they thought they were receiving hydromorphone) lowered their dose once diacetylmorphine became an available option through open-label prescribing. These results are supported by a previous double-blind study that determined participants who thought they were receiving diacetylmorphine reported higher drug scores and drug effects than those on hydromorphone, even when they were receiving a placebo (Dunn et al., 2018). These findings are in line with research that identifies how personal experience might influence the way clients perceive and engage with different forms of treatment (Ridge et al., 2009). As the availability of illicit substances changes rapidly, the system will need to adapt, integrate, and diversify aspects of opioid preference into available treatment options, including the provision of fentanyl (Ferguson et al., 2022; Morales et al., 2019).

Though doses of diacetylmorphine decreased in this study, clients receiving hydromorphone saw a small increase in dose during the open-label period. While not verifiable in this present analysis, this phenomenon could be explained by the observed potency ratio of 1.6:1 recorded during in the open-label study. This ratio is lower than the expected 2:1 ratio that was previously observed in the double-blind period. Clinical guidelines show that diacetylmorphine's potency ratio does not follow a linear relationship compared to other opioids (Office Fédéral de la Santé Publique, 2004) and similarly it was found to differ across dose levels in the present analysis. In addition, hydromorphone was a licensed opioid for opioid use disorder during the open-label study period, but diacetylmorphine was not licensed in Canada. Because of hydromorphone's regulatory status, prescribers were able to prescribe doses beyond clinical trial protocols for a small number of clients. Regardless of this elevation in overall milligrams received of hydromorphone, the increase was not found to be significant. Other possible explanations for the difference in dose may have been adverse events (e.g., histamine reactions). During the open-label study (RUTH), data on adverse events were not systematically collected due to the proficiency with which the double-blind trial (SALOME) documented previous events. However, during the double-blind study (SALOME), average daily-total dose did not appear to play a direct role in the relationship with adverse events and data from three iOAT studies showed that people with higher reported adverse events did not receive lower doses (Oviedo-Joekes et al., 2019b). Clients receiving iOAT medications have individualized doses that stabilize over time, and many factors contribute to received client doses, including clients that present with multiple health conditions which require caution in dosing practices (MacDonald & Oviedo-Joekes, 2022). In this study, those who reported chronic medical health problems had significantly lower doses, as expected. Given these considerations, we are confident that the discrepancy in dose for those receiving diacetylmorphine before and after blinding was driven by client preference.

The association between medication expectation during the double-blind (SALOME) period and open-label (RUTH) dose for diacetylmorphine might suggests that addiction service engagement may be influenced by the effects of personal preference and the experience of being included in treatment decision-making. Previous research identifies that the creation of customized care plans with healthcare providers and service users is a foundational part of person-centered care and has been known to promote client autonomy (Martins et al., 2021), increase client engagement (Park et al., 2020), lower the severity of substance use and psychiatric problems (Joosten et al., 2009), and strengthen therapeutic-relationships by fostering mutual respect and trust (Marchand et al., 2020; Palis et al., 2020). Shared decision-making that incorporates client preference has the potential to avoid treatment incongruencies between the expectations and the application of treatment. Incompatible treatment options might put clients in high-risk situations (e.g., engaging with the illicit opioid market) if client needs are not met (Meyer et al., 2022). As lack of medication preference has been associated with an increase in odds of experiencing overdose events (Whiteside et al., 2018), failing to provide the option for clients to access their preferred treatment in a regulated and supportive environment may be causing undue harm.

The landscape of British Columbia's opioid epidemic demands the

immediate prioritization of systemic changes to care provision and an increase in access to services such as iOAT. British Columbia's fentanyl-related overdose deaths have increased (from 5% in 2012 to 84% in 2021), while deaths attributable to other opioids have steadily declined (Government of British Columbia, 2022). People with OUD need a myriad of safer alternatives, yet the availability of injectable diacetylmorphine and hydromorphone is limited in Canada due to financial, structural and practical barriers that further marginalize this community of opioid users by providing them with inferior care (Dasgupta et al., 2018). To safeguard best practices of person-centered care for people with OUD, it is critical for healthcare providers, prescribers and policy makers to consider the way in which client perceptions and preferences impact treatment engagement and overall wellbeing. The results indicate that the impacts of client preference should be further explored. Clients who lowered their injectable diacetylmorphine dose once they knew they were receiving the medication they favored reflects a complexity in treatment engagement that must be better understood through future research.

4.1. Limitations

The present study has many limitations, derived from the nature of it being a retrospective analysis (with data spanning eight years) and a study not designed or powered to test the questions explored in this paper. For example, we can only speculate that true client preference and expectation measures were accurately reflected by blinding guess. Additionally, the data used in this study were not designed to test potential meaningful factors by dose, as doses are individualized and our sample size is limited. As the array of available illicit opioids is constantly changing, our findings are not intended to be prescriptive regarding the treatments accessed by participants in the data (e.g., diacetylmorphine and hydromorphone). Situationally, the political, structural, and social phenomenon that shape the needs of communities of people who use opioids will vary. It is our intention that these findings present an opportunity to explore the potential benefits of encouraging the inclusion of client perspectives as a part of treatment access and person-centered care. This specific context should be considered when situating our findings in this study.

5. Conclusion

As treatment for OUD expands and diversifies, it is crucial for service providers, prescribers, and stakeholders to identify how client perceptions and expectations regarding treatment (e.g., hydromorphone or diacetylmorphine) might impact the dose received, and ultimately program adherence and client engagement. The implications of this study provide the opportunity to enhance person-centered care in upcoming and established iOAT sites. As this analysis shows, client perspectives may have an effect on treatment dose received. These findings are in line with the promotion of shared decision-making models that reflect an inclusive approach to encouraging individualized client care.

Funding

The RUTH Study was funded by a Canadian Institutes of Health Research Project Grant. Further financial support was provided by and the Canada Research Chairs Program (EOJ, MTS). All participants provided informed consent and were compensated monetarily for their time. The funding sources had no role in the study design, conduct or analysis of this study or the preparation, review or approval of this manuscript. All research activities were approved by the Providence Health Care Research Ethics Board (harmonized board of record) and Fraser Health Authority (harmonized partner board) [H20-00794]. This work was supported by the Canadian Institute of Health Research Project Grant [F15-00960] and Canada Research Chairs [F21-00475].

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgements

The authors respectfully acknowledge the unceded and traditional territory of the Coast Salish Peoples, including the traditional territories of xʷməθkwəy̓əm (Musqueam), Skwxwu7mesh (Squamish), and Səl̓ílwətaɬ (Tsleil-Waututh) Nations, upon which this research took place. We would like to thank all the clients, advisory committee members, experts, and stakeholders who generously gave their input throughout survey development. We acknowledge the study participants who shared their experiences and time. We also thank Providence Health Care Crosstown Clinic administrators and care providers for their commitment to delivering care with the fundamental philosophy of meeting clients where they are at. The authors gratefully acknowledge the RUTH, SALOME, and NAOMI study participants for their contributions of time and personal experiences over the many years. The authors also wish to acknowledge the broader clinical and RUTH research team members for their commitments to the study, and the funders for making this research possible.

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