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The association between nicotine dependence and physical health among people receiving injectable diacetylmorphine or hydromorphone for the treatment of chronic opioid use disorder☆

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A B S T R A C T

Introduction: People with chronic opioid use disorder often present to treatment with individual and structural vulnerabilities and remain at risk of reporting adverse health outcomes. This risk is greatly compounded by tobacco smoking, which is highly prevalent among people with chronic opioid use disorder. Despite the known burden of tobacco smoking on health, the relationship between nicotine dependence and health has not been studied among those receiving injectable opioid agonist treatment. As such, the present study aims to explore the association between nicotine dependence and physical health among participants of the Study to Assess Longer-Term Opioid Medication Effectiveness (SALOME) at baseline and six-months.

Methods: SALOME was a double-blind phase III clinical trial testing the non-inferiority of injectable hydromorphone to injectable diacetylmorphine for chronic opioid use disorder. Participants reporting tobacco smoking were included in a linear regression analysis of physical health at baseline (before receiving treatment) and at six-months.

Results: At baseline, nicotine dependence score, lifetime history of emotional, physical, or sexual abuse and prior month safe injection site access were independently and significantly associated with physical health. At six-months nicotine dependence score was the only variable that maintained this significant and independent association with physical health.

Conclusions: Findings indicate that after six-months, the injectable treatment effectively brought equity to patients' physical health status, yet the association with nicotine dependence remained. Findings could inform whether the provision of treatment for nicotine dependence should be made a priority in settings where injectable opioid agonist treatment is delivered to achieve improvements in overall physical health in this population.

1. Background

Chronic opioid use disorder (OUD), particularly the injection of illicit street opioids, is known to exact a number of harms on the individual, including the risk of infectious disease such as human immunodeficiency virus (HIV) and hepatitis C (HCV), as well as the risk of fatal and non-fatal overdose, social disintegration, violence and incarceration (Roxburgh, Darke, Salmon, Dobbins, & Jauncey, 2017; van der Zanden, Dijkgraaf, Blanken, van Ree, & van den Brink, 2007). The burden of chronic opioid use disorder on communities includes death,

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public disorder, and health and criminal justice costs (Birnbaum et al., 2011).

Opioid agonist treatment (OAT) with long-acting oral opioids such as methadone is effective at managing cravings and symptoms of withdrawal, reducing the use of street opioids, and at attracting and retaining patients in treatment (Mattick, Breen, Kimber, & Davoli, 2009; Mattick, Breen, Kimber, & Davoli, 2014). However many individuals will not be retained in treatment long-term or will continue to inject illicit opioids even while engaged in oral treatment (Johnson et al., 2000; Mino, Page, Dumont, & Broers, 1998). Evidence from five randomized controlled trials (RCT) in Europe (Demaret et al., 2015; Haasen et al., 2007; March, Oviedo-Joekes, Perea-Milla, & Carrasco, 2006; Strang et al., 2010; van den Brink et al., 2003) and two in Canada (Oviedo-Joekes et al., 2009; Oviedo-Joekes et al., 2016) has demonstrated that for those that continue injecting despite access to available treatments, injectable opioid agonist treatment (iOAT), namely the provision of injectable diacetylmorphine (DAM; pharmaceutical grade heroin) or hydromorphone (HDM, a licensed opioid) under the supervision of registered nurses, offer safe, effective, and cost-effective treatments (Nosyk et al., 2012).

These clinical trials have recruited opioid users that have been injecting street opioids long-term, many of whom have had multiple prior treatment attempts and have not been effectively reached by the addiction treatment system for a number of years. While take home maintenance doses of DAM have been prescribed in the United Kingdom, iOAT is most commonly provided in clinics, self-administered under the supervision of nurses (Hartnoll et al., 1980). This direct observation is known to ensure patient safety, and daily contact with health care providers brings the opportunity to build relationships and offer comprehensive care. This approach has been effective at attracting and retaining patients in much needed, structured care at rates significantly higher than those in first-line treatments such as oral methadone (Ferri, Davoli, & Perucci, 2011). Studies of iOAT have further demonstrated broadly similar benefits with regards to reductions in street heroin use, and in secondary outcomes such as physical and mental health and social functioning (Strang et al., 2015).

Because of the profile of patients included in iOAT clinical trials (i.e. people that have been injecting illicit opioids for many years and continue doing so despite available treatments), participants had high rates of chronic conditions and infectious diseases (e.g. HIV, HCV, cardiovascular disease, cancer etc.) (Buster, Rook, van Brussel, van Ree, & van den Brink, 2002; Haasen et al., 2007; Oviedo-Joekes et al., 2015; van den Brink et al., 2003). At the time of recruitment, participants presented with a wide array of individual and structural vulnerabilities known to be associated with poor physical health including unstable housing conditions, high rates of physical, sexual, and emotional abuse, and the use of other substances (Oviedo-Joekes et al., 2015).

People with opioid use disorder (OUD) remain at a higher risk of reporting adverse health outcomes as compared to the general population (Schuckit, 2016). This risk is greatly compounded by tobacco smoking (Chisolm et al., 2013; Hurt et al., 1996). For example, a recent 15-year population based study found that smoking related conditions comprised 40% of all deaths among people with OUD. Further, those with opioid use disorder (OUD) had a significantly higher risk of mortality from all 19 tested smoking related conditions (i.e. cardiovascular, respiratory diseases and cancers) when compared to the general population (Callaghan, Gatley, Sykes, & Taylor, 2018). The observed relationship between tobacco smoking and health among people with OUD is particularly concerning given the high prevalence of smoking in this population. For example, prior studies of patients receiving treatment with oral methadone or buprenorphine in the United States and Europe have shown tobacco smoking rates to be significantly higher than in the general population, ranging between 80–100% (Nahvi, Richter, Li, Modali, & Arnsten, 2006; Pajusco et al., 2012; Richter, Gibson, Ahluwalia, & Schmelzle, 2001).

Despite the burden of tobacco smoking on the health of people with OUD the relationship between nicotine dependence and physical health has not been studied among iOAT patients, who have high daily treatment adherence, especially in the first year of treatment. This is of particular interest given iOAT patients present to treatment with several chronic health conditions, besides OUD and often face a number of vulnerabilities that have known implications for health. As such, iOAT patients present a population for whom targeted smoking cessation interventions may play a key role in supporting improvements in physical health. The present study aims to explore the association between nicotine dependence and physical health scores among participants of the Study to Assess Longer-Term Opioid Medication Effectiveness (SALOME) RCT at baseline and after six months receiving iOAT, accounting for other factors with known relationships to physical health in this population. These findings could, for the first time inform whether the provision of treatment for nicotine dependence should be made a priority in settings where iOAT is delivered to achieve improvements in overall physical health in this population.

2. Material and methods

2.1. Setting, participants, study design

SALOME was a double-blind phase III RCT involving 202 long-term street opioid injectors in Vancouver (Canada) not benefiting from available treatments. Full details regarding screening procedures and recruitment, participant profile, design, and main results are published elsewhere (Oviedo-Joekes et al., 2015; Oviedo-Joekes et al., 2015; Oviedo-Joekes et al., 2016). SALOME participants were randomly assigned to receive injectable diacetylmorphine (n = 102) or hydromorphone (n = 100) up to three times daily for six months under the supervision of registered nurses. Both HDM and DAM were provided under identical conditions at the Crosstown Clinic, with no differences in dose prescribed, or the provision of treatment services (i.e. all participants had access to the same set of comprehensive services). The SALOME trial demonstrated the non-inferiority of injectable HDM to injectable DAM, with no differences in primary (i.e. street opioid use) or secondary outcomes (e.g. dose, retention, adherence) tested at six months. Moreover, patients did not guess what drug they were receiving beyond what is expected by chance (i.e., the blinding was not broken). In addition, subgroup analyses have revealed no significant differences in treatment outcomes between HDM and DAM when comparing men and women, and Indigenous and non-Indigenous participants (Oviedo-Joekes et al., 2017 and Palis et al., 2017). Baseline and six-month data were collected through self-report questionnaires by a research team independent of the clinical team. Participants were asked whether they were current tobacco smokers. Participants responding “no” were excluded from the present analysis.

2.2. Study measures

2.2.1. Dependent variable

At both baseline and six months, physical health score was derived from the health domain of the Opiate Treatment Index (OTI). The OTI presents a comprehensive, standardized set of measures for six independent outcome domains: health, drug use, HIV risk taking, social functioning, criminality and psychological adjustment. The health domain is specifically designed with items reflecting areas within which opioid users tend to develop health problems (González-Saiz & García-Valderrama, 2012). It has been used extensively in studies of patients receiving OAT, and in assessing health in prior clinical trials of patients receiving diacetylmorphine (Haasen et al., 2007; March et al., 2006; Verthein, Haasen, & Reimer, 2011) since it was developed in 1992. A more recent review has demonstrated high internal consistency ($\alpha = 0.71$), and high correlation with the global assessment of functioning scale, (GAFS) which is part of the multiaxial system (Axis V) of the DSM-IV (González-Saiz & García-Valderrama, 2012).