Evaluation of in-hospital buprenorphine/naloxone initiation for opioid use disorder: study protocol and rationale

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Background

Opioid Use Disorder

- More than 10,000 people in British Columbia (BC) experienced an opioid overdose between Jan 1, 2015 and Nov 20, 2016, resulting in the declaration of a public health emergency in 2016.[1]
- Patients with opioid use disorder (OUD) are often hospitalized for complications related to their opioid use; however, many do not receive timely treatment of their underlying OUD.[2,3]
- Initiating treatment for hospitalized patients with substance use disorders can improve outcomes, including completion of medical treatment, successful transition to outpatient care and decreased utilization of emergency services.[4]

Opioid Agonist Therapy

- Opioid agonist therapy (OAT) decreases morbidity and mortality in patients with OUD, but remains substantially underutilized.[5,6]
- Buprenorphine/naloxone (bup-nlx) has overtaken methadone as first-line due to its more favourable safety profile and convenience of use.[5,6]
- Typically, concern about bup-nlx precipitating opioid withdrawal requires patients already be in withdrawal before initiating bup-nlx. However, novel induction strategies, such as bup-nlx microdosing, are increasingly used to minimize opioid withdrawal during induction.

Table 1. Key Properties of Buprenorphine/Naloxone and Methadone [5-7]

	Buprenorphine/naloxone	Methadone
Efficacy	• ↓ mortality and morbidity compared to placebo • Ceiling effect due to partial agonist activity	• ↓ mortality and morbidity compared to placebo • No maximum dose; may be more effective in severe OUD
Safety	• Lower risk of overdose • Milder side effect profile • Fewer drug interactions • Lower potential for diversion and problematic use	• Higher risk of overdose • Risk of cardiac arrhythmias due to QTc prolongation • Many drug interactions • Higher potential for diversion and problematic use
Ease of use	• Induction is shorter but may cause precipitated withdrawal • Permits flexible and take-home dosing regimens	• Requires several weeks to titrate to therapeutic dosage • Daily witnessed ingestion generally required

Rationale for this Study

- There is some evidence describing inpatient bup-nlx initiation; however, this may not be applicable to our population in Vancouver, BC.
  - A single-centre study in Massachusetts found that hospitalized patients initiated on bup-nlx in hospital were more likely to continue OAT in the community, compared to patients receiving detoxification.[8]
  - A single-centre randomized study in Connecticut established that bup-nlx initiation in Emergency improved engagement in addictions care at 30 days, compared to brief intervention and referral.[9]
- Data is lacking to inform choice of ideal bup-nlx induction strategy, particularly for hospital inpatients.

Research Objectives

Primary Objective

- Determine the rate of successful initiation of bup-nlx for OUD for inpatients at a tertiary care hospital in Vancouver, BC.

Secondary Objectives

- Identify predictive factors of successful in-hospital bup-nlx initiation.
- Determine rate of treatment retention on OAT after hospital discharge among patients successfully initiated on bup-nlx in hospital.
- Characterize adverse effects and use of hospital resources among patients initiated on bup-nlx in hospital.

Methods

Design

- Methodology: Retrospective, hospital-based chart review cross-linked with a province-wide community prescription database (PharmaNet).
- Population: Adults initiated on bup-nlx for OUD during an admission at Vancouver General Hospital from January 1, 2018 to December 31, 2018.
- Anticipated sample size: 100 patients.

Table 2. Study Inclusion and Exclusion Criteria

Inclusion	Exclusion
• At least 18 years of age • Bup-nlx initiated for OUD during admission and received at least 1 dose	• Received bup-nlx within 1 month prior to admission • Received bup-nlx for indications other than OUD • Discharged directly from Emergency

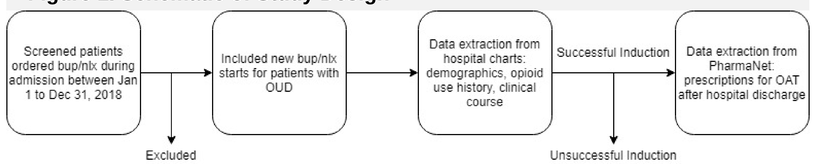
Outcome Definitions

- Successful initiation: Active order for bup-nlx upon hospital discharge.
- Predictive factors: Pre-specified factors of interest include history of injection drug use, pre-admission prescription opioid use and bup-nlx induction strategy. Other factors to be explored include housing status and access to a family physician.
- Treatment retention rate: Proportion of patients who were successfully initiated on bup-nlx with active OAT prescriptions on PharmaNet at 1 week, 1 month, 3 months and 6 months after discharge

Analysis

- Descriptive statistics to determine rate of successful in-hospital bup-nlx initiation and treatment retention following discharge.
- Multivariate logistic regression analysis to determine level of correlation between pre-specified predictive factors and successful bup-nlx initiation.

Figure 1. Schematic of Study Design



Discussion

Strengths

- Addresses an important knowledge gap in our health system's response to the opioid crisis.
- Provides insight into real-world effectiveness of local efforts to increase evidence-based treatment of OUD.
- Linkage with community prescription data permits characterization of treatment retention on OAT after discharge from hospital care.

Limitations

- Retrospective study design may result in incomplete data gathering.
- Use of prescription fill data may not capture patient non-compliance or receipt of OAT in long-term care, medical facilities and outside of BC.
- Unable to corroborate treatment retention on OAT with clinical outcomes such as OUD remission or relapse.

Future Research Areas

Treatment Selection Based on Predictive Factors

Predictive factors of successful bup-nlx initiation may guide strategies to optimize treatment selection and induction in hospitalized patients.

Optimal Induction Method

Comparing different bup-nlx induction methods used in hospital practice may provide insight into their advantages and disadvantages.

Direct Referral to Outpatient Clinics

Direct outpatent clinic referral may improve treatment retention in the community, but is outside the scope of this project. Investigation into feasibility of streamlined referrals for outpatient follow-up may be beneficial.

Acknowledgments

This project was supported by a VCH Research Institute Research Challenge grant, funded by the Robert H.N. Ho Enhancing Patient Care Fund.

Thank you to the BC Ministry of Health for their assistance with a Health Data Request for this project. All inferences, opinions and conclusions drawn in this poster are those of the authors, and do not reflect the opinions or policies of the Data Stewards.

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