Shall we screen for cardio-metabolic risks in methadone and buprenorphine treatment for opiate dependence?

Abstract
Recent evidence suggests that buprenorphine, the partial opiate receptor agonist, exhibits equal efficacy as methadone in reducing withdrawal and craving for opiates in opioid dependence. Very few studies examine the benefits of screening for combined cardiovascular and metabolic risk factors in methadone and buprenorphine maintenance options for opioid dependence. We explore the feasibility whether outcome may improve through developing cardio-metabolic screening strategy in treatment facilities for opioid addiction.

Keywords: methadone, buprenorphine metabolic cardiovascular risks

Introduction
Buprenorphine vs Methadone for opioid dependence
Converging evidence suggests the efficacy of methadone maintenance therapy [MTT] for the treatment of opiate dependence. Methadone was seen as an opioid substitute for heroin dependence. Converging evidence suggests the efficacy of methadone maintenance therapy [MTT] for the treatment of opiate dependence. Methadone is the most prescribed opioid agonist in the treatment of opioid dependence. The safety margins and the likelihood of abuse of buprenorphine have been highly favourable for buprenorphine, especially when formulated with naloxone as a sublingual formulation.

In contrast to methadone, buprenorphine behaves as a partial mu-opiate agonist and kappa antagonist, for the treatment of opiate dependence. Buprenorphine is favoured over pure opioid antagonist, naltrexone due to its partial opioid agonist properties. Intriguing enough, the Positron Emission Tomography [PET] study of mu-opioid receptor found that 16 mg oral dosage of buprenorphine reduced mu-opioid receptor availability by 79-95%. Opioid dependent subjects. The threshold blockade of opioid receptor is related to reduced craving for opioids. The mix agonist-antagonist activities of buprenorphine explain the efficacy of buprenorphine based treatment option in managing opioid dependence. The safety margins and the likelihood of abuse of buprenorphine have been highly favourable for buprenorphine, especially when formulated with naloxone as a sublingual formulation.

Marketed as [Suboxone] in a 4:1 ratio offers safeguard against medical diversion through intravenous self-administration. When buprenorphine/naloxone is taken sublingually as prescribed, the naloxone exerts no clinically significant effect, leaving the opioid agonist effects of buprenorphine to predominate. When buprenorphine/naloxone is parenterally administered in patients physically dependent on full agonist opioids, the opioid antagonism of naloxone causes withdrawal effects, thus reducing the abuse potential of the drug combination. Abuse-detergent and tamper-proof modes of delivery of buprenorphine represent new advances in opioid treatment.

Abbreviations: MTT, methadone maintenance therapy; PET, positron emission tomography; DATOS, drug abuse treatment outcomes studies; NTORS, national treatment outcome research study; ATOS, australian treatment outcome study; QTC, quantum tunneling composite; TDP, torsades de pointes; BMI, body mass index.
Harm reduction and avoidance, coupled with abstinence-based goal, has become the guiding principle underlying opioid treatment. Three major studies have documented the efficacy of methadone and buprenorphine in opioid dependence. Three longitudinal outcome studies: Drug Abuse Treatment Outcomes Studies [DATOS] in the United States,° National Treatment Outcome Research Study [NTORS] in the United Kingdom,° and the Australian Treatment Outcome Study [ATOS],° found that buprenorphine or methadone maintenance treatment can effectively reduce opioid abuse and misuse and minimize the harmful effects in the medical and psychosocial and medical arenas.

Screening for cardio-vascular risks in opioid treatment

The past few years witnessed alarming rise in methadone-related deaths along with marked increase in the misuse and abuse of prescribed opiates e.g. oxycotin for non-malignant pain syndrome. In reviewing the contributory factors, two patterns of methadone-related deaths emerge. Early mortalities from methadone fatalities appear to be due to respiratory arrest during methadone induction; however, cardiac sudden death may also be an important factor. Methadone can induce QTC prolongation and the uncommon but potentially fatal ventricular arrhythmia, Torsades de Pointes, albeit uncommon, is potentially fatal. Buprenorphine, on the higher cardiac risk of significant QTC prolongation. The final common symptom history of syncope and seizure, drug-drug interaction e.g. of QTC interval: electrolyte imbalance, previous history of any angina, ratio should be discussed thoroughly with the potential MTT clients corrected QTC interval is > 450 ms but less than 500 ms. Risk-benefit all opiate dependence individuals being considered for MTT. If the mean BMI of MTT study reported that the means BMI shifted gradually towards the upper one third of the population are overweight as defined by inactivation of the sodium channel can result from a mutation in the single gene coding for a specific subtype of potassium channel: hERG [human ether-a-go-go related gene] or coding for a variant of the sodium channel SCN5A. The binding affinity of opioid agonists and partial agonists for potassium channel can be evaluated with electrophysiological technique of measuring the changes in potassium channel coded by hERG gene has been localized on chromosome 7 and plays an important role in cardio-electric coupling. The binding affinity of methadone to the potassium channel is stereospecific, since the [R] isomer blocks the hERG current 3.5 fold more potently than the [S] isomer.°

Very few studies have directed towards the issue of weight, diet and physical activity in opioid dependence. Our Medline search finds very few systematic studies on BMI [Body Mass Index] in methadone or buprenorphine treatment in opioid dependence. There is a paucity of data on the body composition: BMI, waist circumstance, relative proportion of body fat in the opiate dependence cohort. Two European studies suggested that the increase in weight gain reflecting improved nutritional status after entry to the MTT program.°° Our 1 yr follow up of MTT study reported that the means BMI shifted gradually towards the recent trend in body weight and BMI in the general population in that approximately 50% of the population are overweight as defined by BMI=25.0 but less than 30.0. The recent renaissance of interest in screening and interventions to modify cardio-metabolic risk factors in opioid addiction has stimulated us to examine the cardiovascular risk factors along with metabolic risks in the area of diabetes and obesity prevention. We find very few published studies originating from Canada in this area. Our methadone/buprenorphine opioid treatment team in Ontario has recently found that the 43 % of the sample of methadone clinic in subjects are overweight and obese: the results are summarized in the Figure 1.°°

Figure 1 BMI distribution in Methadone Outpatients.°°

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A one-year follow up found a significant increase was noted in their mean BMI [increase from 24.1, SD=4.1 to 26.3, SD=4.8], mean body mass [from 71.8 kg, SD=14.4 to 78.3 kg, SD=15.9], % fat [from 25.3% of total body mass, SD=10.0 to 30.6%, SD=9.3], and basal metabolic rate [from 1593.4, SD=267.0 to 1635.5, SD=288.6] and a significant decrease in % of muscle mass [from 71.0% of body mass, SD=9.6 to 65.8%, SD=8.9], in % of water [from 52.0%, SD=6.1 to 48.8%, SD=5.5] and in % bone mass [from 3.7%, SD=0.5 to 3.5%, SD=0.5]. We interpret the rise in BMI from normal value to overweight category to the increment in % of body fat, raising the issue of cardio-metabolic risk factors in opiate dependence. The change of subjective sleep quality is related to cocaine abuse, but unrelated to change in body composition.

Conclusion
A recent Cochrane meta-analysis concludes that the strength of evidence does not support the effectiveness of QTC screening for preventing cardiovascular morbidity or mortality in methadone maintenance. In this respect buprenorphine has a definitive cardiovascular safety profile in the treatment of opioid dependence. Future endeavours should focus on the evaluating the benefits of developing QTC screening strategies and clarifying the relative benefits and harm reduction.

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Conflict of interest
The author declares no conflict of interest.

References