

Editorial

Buprenorphine in primary care: perspectives on clinical and research priorities

Buprenorphine and the opioid epidemic

After leading the world in opioid consumption and manufacturing, the USA is beginning to gain ground in responding to its opioid epidemic, in part by broadening efforts to provide opioid use disorder (OUD) treatment in office-based primary care. We discuss the USA experience with OUD medication treatment, previously termed medication-assisted treatment (MAT), particularly buprenorphine (BUP) in primary care and the role of integrated behavioural health care in providing the ‘assisted’ component of MAT. This topic is relevant to our international audience given evidence that prescription opioid dose is rapidly increasing in Germany, France, the Netherlands and Spain (1). Trends in opioid use will likely trigger parallel increases in OUD throughout Europe.

Since 2000, the United States Drug Addiction Treatment Act has allowed primary care physicians to prescribe BUP in an outpatient setting for treatment of substance use disorders (2). BUP has been transformative for safer OUD treatment due to BUP’s ceiling effect. Methadone has a roughly linear opioid response to dose and thus relatively greater overdose risk. However, as a partial agonist with different affinity for the mu and kappa opioid receptors, a patient using BUP will achieve an upper limit of an opioid effect regardless of increasing BUP dose. This ceiling effect limits BUP’s reward potential and thus is considered a safer medication than methadone. Because of this greater safety profile, BUP can now be prescribed in any setting by any physician, nurse practitioner, or physician assistant who takes a United States Drug Enforcement Administration (DEA) waiver training, passes the test, and registers with the DEA and Substance Abuse and Mental Health Services Administration (SAMHSA).

Medication-First model

In the USA, the State of Missouri’s Medication-First model incorporates individual and community recovery. The model’s main elements are prevention, treatment, recovery, sustainability and community impact. Together with overdose education and naloxone distribution, early access to BUP is a highly effective means of harm reduction. Following naloxone overdose reversal, BUP promotes rapid entrance of patients into treatment and long-term OUD maintenance. Both are on the continuum of harm reduction. BUP controls the cravings associated with OUD, and, it allows the neurotransmitters to normalize and the brain to heal (3). Once this healing process occurs, a person not only has an immediate means of changing behaviour, but a person can also engage more fully in psychotherapy that supports insight and behavioural change that address many of

the underlying causes of substance use disorders (4). The other key elements of the Missouri model include recovery and housing support and also education and advocacy for system change based on real-time data. A primary goal of the model is promotion of prescribing BUP to primary care providers.

Increasing BUP through primary care

SAMHSA has invested significantly in promoting BUP training and reports over 66,000 waived physicians as of 2019. Waiver training is required in response to the Harrison Act of 1914 and is 8 hours for physicians, 24 hours for physician assistants and nurse practitioners. Free waiver training can be done in-person, online, or in a mixed modality. After completing training, providers must register with SAMHSA and the DEA and maintain an active record of patients receiving BUP. While this workforce expansion grants far greater access to OUD treatment it is still well below the needed capacity, given estimates that 5 million persons in the USA are dependent on prescription opioids (5). In addition, the number of waived providers is a poor estimate of access because a large proportion of providers (25%) do not prescribe (6), or prescribe to just a handful of patients (7). In a survey of physicians, not limited to primary care, Huhn and Dunn (8) found that not believing in agonist therapy, inability to take on more patients, and concerns about insufficient reimbursement to be key barriers. Among primary care physicians, access to behavioural health providers, other specialists and time constraints are major barriers to BUP prescribing (7). However, even if all primary care providers were prescribing BUP and managing the maximum number of patients, barriers to access, including costs to patients, may remain due to the size of the dependent population. From 2007 to 2014, claims for OUD treatment increased more than 3000% (9) and have continued to rise through 2015 (10). Thus there is a clear and urgent need for expanding access and an appropriate point for care is in the generalist clinic.

Unintended consequences of increased access to BUP

While increases in treatment-seeking for OUD are warranted and a reflection of greater access, most of what is known about treating OUD comes from studies of heroin or illicit opioid use. And while BUP has a much lower risk for overdose, it can be abused and diverted. Li and colleagues (6) highlight evidence that BUP, even when combined with naloxone, has subjective effects similar to other mu-opioid receptor agonists. Emergency department visits involving

BUP increased nearly 4-fold between 2006 and 2010 but remained well below those visits associated with other narcotics (11). Data from the USA and multiple European countries reveal abuse and diversion of BUP is not uncommon, including doctor-shopping, and greater availability has been associated with increases in mortality related to BUP combined with benzodiazepine and alcohol use (6). In addition to abuse, non-medical use to self-manage withdrawal contributes to diversion (6). While BUP is clearly an appropriate harm reduction response to the opioid epidemic, it is not a panacea and it is not without risks. And while harm reduction is necessary, it is not sufficient. It is saving lives, but it does not explicitly speak to long-term treatment goals.

How can research inform best practice with OUD medications?

Much of the research on BUP has been limited to short-term treatment trials and research is needed to identify prescribing patterns and patient characteristics associated with retention in treatment over many years. While national guidelines exist on BUP initiation, maintenance, and tapering (4,12), there are no guidelines on who should be tapered off BUP and when taper should be attempted.

Determine risk factors for treatment drop-out and relapse

Greater access, particularly through primary care office-based treatment, should be paired with research to determine how best to manage relapse, and to identify the patient characteristics associated with BUP adherence and taper. OUD often co-occurs with psychiatric disorders and research is needed to determine the role of these comorbid conditions on relapse. Although BUP has been shown to improve treatment-resistant depression (13), it is not clear if this benefit is retained over many years. Psychosocial determinants of health such as housing security, food security, poverty, education, social support, race, gender, and employment, are likely associated with BUP outcomes but there are no large scale, long-term studies in primary care to adequately assess these relationships.

Implementation and evaluation

Implementation research is critical to increase adoption of BUP and to improve compliance with prescribing guidelines given evidence that only 50% of prescribers are following SAMSHA guides (14). Hsu et al. (2018) (15) describes a comprehensive primary care model which produced better treatment retention at lower cost. Evaluation studies are warranted to determine which models of care (e.g. team-based prescribing involving the primary care physician, pharmacist and behavioural health specialist versus physician and behavioural health) produce increased access, improve adherence and reduce unintended adverse outcomes (16,17). In addition, evaluation studies are needed to assess whether training residents is associated with a greater likelihood of including BUP in their practice.

Research to determine optimal dosing and long-term management

There is little discussion, much less recommendations, regarding long-term treatment for OUD. Currently, recommendations state that a patient should be retained on BUP as long as 'they are receiving benefit from treatment' (14). Physicians should be suspicious of falling into prescribing patterns not based on evidence of efficacy and long-term sequelae. Research can inform best practices by

defining success in OUD and pain management based on function, quality of life, and improvements in social determinants of health. Clinicians need better indicators on length of treatment, possible transitions from high-potency agonist to lower power antagonists to antagonists to medication-free treatment and therapeutic support. Clinicians also need recommendations on use of OUD medications that may be episodic, rather than scheduled, depending on a patient's life situation and exposure to opioids and other addictive substances.

Does the source of opioids matter, OUD versus prescription opioid use disorder?

Prescription opioid use disorder (POUD) is four times more prevalent than heroin/illicit OUD (18), and meta-analysis estimates nearly 5% of all patients using prescription opioids for 7 days or more will develop iatrogenic POUD (19). Because much of the existing studies on treating OUD have either enrolled patients who developed problems with heroin or from non-medical use of prescription opioids, longitudinal outcomes research is necessary to establish an evidence base for the effectiveness of BUP in chronic pain patients with POUD. We need studies that characterize barriers to seeking care in pain patients with POUD and this research should establish the most effective maintenance dose, determine patient characteristics associated with treatment drop-out and evaluate benefits and risks related to tapering off BUP.

Conclusions

Primary care providers have prescribed a large percent of the opioids in the USA under the false evidence that long-acting formulations were safe and addiction was rare in chronic pain patients. Now primary care physicians are being tasked with increasing access to OUD treatment. Generally this is in the interest of patients, but rapid expansion of BUP prescribing should be coupled with research that supports evidence-based prescribing. BUP is the right treatment to reduce harm. However, expansion should be coupled with continued research and careful assessment of patient and population-level outcomes while also (and seemingly paradoxical), efforts are needed to identify and overcome barriers to treatment. Collaboration between primary care clinicians, behavioural health providers, researchers and policy makers is crucial to providing safe, effective, and adequate OUD treatment in primary care. All of these stakeholders have a part to play, in fact, a responsibility to inform current and future prescribing practices.

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