Buprenorphine

New treatment of opioid addiction in primary care

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Abstract

Objective To review the use of buprenorphine for opioid-addicted patients in primary care.

Quality of evidence The MEDLINE database was searched for literature on buprenorphine from 1980 to 2009. Controlled trials, meta-analyses, and large observational studies were reviewed.

Main message Buprenorphine is a partial opioid agonist that relieves opioid withdrawal symptoms and cravings for 24 hours or longer. Buprenorphine has a much lower risk of overdose than methadone and is preferred for patients at high risk of methadone toxicity, those who might need shorter-term maintenance therapy, and those with limited access to methadone treatment. The initial dose should be given only after the patient is in withdrawal. The therapeutic dose range for most patients is 8 to 16 mg daily. It should be dispensed daily by the pharmacist with gradual introduction of take-home doses. Take-home doses should be introduced more slowly for patients at higher risk of abuse and diversion (eg, injection drug users). Patients who fail buprenorphine treatment should be referred for methadone- or abstinence-based treatment.

Conclusion Buprenorphine is an effective treatment of opioid addiction and can be safely prescribed by primary care physicians.

Résumé

Objectif Faire le point sur l'usage de buprénorphine en cas de dépendance aux opiacés en médecine primaire.

Qualité des preuves On a recherché dans MEDLINE les articles traitant de la buprénorphine publiés entre 1980 et 2009.

Principal message La buprénorphine est un agoniste partiel des opiacés qui soulage les symptômes de sevrage et de besoin impérieux de drogue pendant au moins 24 heures. La buprénorphine présente un risque de surdose beaucoup plus faible que la méthadone et on l'utilise de préférence à la méthadone chez les patients qui ont un risque élevé de toxicité à la méthadone, chez ceux qui pourraient bénéficier d'un traitement d'entretien à court terme et chez ceux qui n'ont pas facilement accès à un traitement par la méthadone. La dose initiale ne devrait être administrée que lorsque le patient est déjà en sevrage. Pour la plupart des patients, la dose quotidienne varie entre 8 et 16 mg. Elle devrait être administrée quotidiennement par le pharmacien, avec une introduction graduelle de doses à apporter à la maison. On devrait introduire plus lentement ces doses chez les patients davantage susceptibles d'en abuser ou de les détourner. En cas d'échec du traitement à la buprénorphine, le patient devrait être redirigé en vue d'un traitement à la méthadone ou un traitement fondé sur l'abstinence.

Conclusion La buprénorphine constitue un traitement efficace de la dépendance aux opiacés, qui peut sans danger être prescrit par le médecin de première ligne.

KEY POINTS North America has witnessed a marked increase in prescription opioid misuse and addiction in the past 10 years, accompanied by increases in overdose deaths. These increases parallel the rise in the use of controlled-release opioids for chronic pain. Despite the great need for opioid addiction treatment, access to methadone treatment is limited. Treatment access would expand considerably if family physicians began to prescribe buprenorphine, a safe and effective alternative to methadone. This article reviews the use of buprenorphine in primary care.

POINTS DE REPÈRE Au cours des 10 dernières années, l'Amérique du Nord a connu une forte augmentation d'abus et de dépendance aux opiacés sous ordonnance ainsi qu'une augmentation des décès par surdose. Ces augmentations ont évolué parallèlement à l'accroissement de l'usage d'opiacés à libération contrôlée pour soulager la douleur chronique. Même s'il y a un grand besoin de traitement de la dépendance aux opiacés, l'accès au traitement par la méthadone est limité. L'accès au traitement serait considérablement meilleur si les médecins de famille décidaient de prescrire de la buprénorphine, une alternative à la méthadone qui est sécuritaire et efficace. Cet article fait le point sur l'usage de la buprénorphine en médecine de première ligne.

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North America has witnessed a marked increase in prescription opioid misuse and addiction in the past 10 years, accompanied by increases in overdose deaths.[1-3] These increases parallel the rise in the use of controlled-release opioids for chronic pain.[4] Despite the great need for opioid addiction treatment, access to methadone treatment is limited; only an estimated 23% of opioid-addicted patients in Canada were taking methadone in 2003, a lower proportion than in Western European countries.[5]

Treatment access would expand considerably if family physicians began to prescribe buprenorphine, a safe and effective alternative to methadone. In France, family physicians prescribe buprenorphine to 65 000 patients, whereas specialized clinics prescribe methadone to only 6000 to 7000 patients.[6] Cohort studies and controlled trials have demonstrated that buprenorphine treatment of opioid addiction is safe and effective when prescribed by primary care physicians in community settings.[7-21]

Although methadone might have a higher treatment retention rate than buprenorphine,[18,22,23] buprenorphine is also a very effective treatment of opioid addiction. Also, buprenorphine might be more effective in patients addicted to prescription opioids than it is in those addicted to heroin[24] (which might reflect the greater social stability of oral prescription users compared with heroin users); it could, therefore, be very useful to family doctors. The primary advantage of buprenorphine is its safety: large observational studies have found that buprenorphine has a much lower risk of overdose than methadone,[6,25] and this makes it safer for use in primary care.[26] An analysis of French overdose deaths between 1995 and 1998 found an average annual death rate of 0.47% for patients taking methadone, compared with 0.05% for buprenorphine.[27]

Buprenorphine is a safe and effective alternative to methadone treatment of opioid dependence. This article reviews the use of buprenorphine in primary care.

Quality of evidence

MEDLINE was searched from 1980 to 2009, using the terms *buprenorphine, methadone, addiction, opioid, primary care,* and *overdose*. Randomized controlled trials, cohort studies, and large observational studies were included. We also considered guidelines from other jurisdictions as well as our collective clinical experience.

Clinical features of prescription opioid addiction

Typically, patients addicted to prescription opioids are young (younger than 45 years of age) and have a history of addiction to opioids, alcohol, cocaine, or other drugs. They often have an underlying anxiety or mood disorder, such as posttraumatic stress disorder.

If they are being prescribed opioids for underlying pain conditions, patients addicted to opioids tend to be taking doses well beyond what would usually be required (**Table 1**). They might attempt to maximize the opioid's psychoactive effect and avoid withdrawal symptoms by binging on the opioid, crushing or injecting oral tablets, and accessing opioids from multiple physicians or the street. If their personal physicians are the main source of the opioid, they frequently request higher doses and early refills. They often report withdrawal symptoms and difficulties at home or at work.

Opioid-addicted patients with concurrent pain sometimes experience *withdrawal-mediated pain* at the end of a dosing interval. Withdrawal–mediated pain is intense and is accompanied by myalgia, dysphoria, drug craving, and other withdrawal symptoms. In contrast, pain that is unrelated to withdrawal increases gradually as the analgesic wears off and is not accompanied by dysphoria or myalgia.

Table 1. Clinical features of prescription opioid addiction

FEATURE	EXAMPLES
Unsanctioned use	Frequently loses prescription Frequently takes more than prescribed Binges rather than using on schedule
Alters the route of delivery	Injects, bites, or crushes oral formulations
Accesses opioids from other sources	Purchases the drug from the street or family and friends Seeks prescriptions from multiple doctors Goes to walk-in clinics and emergency departments
Drug seeking	Takes a high or rapidly escalating dose despite stable pain condition Complains aggressively about the need for higher doses Harasses staff for faxed prescriptions or fit-in appointments Claims nothing else "works"
Accompanying conditions	Has current or past addiction to alcohol, cocaine, or other drugs Has underlying mood or anxiety disorders not responsive to treatment
Repeated or severe withdrawal symptoms	Experiences marked dysphoria, myalgia, gastrointestinal symptoms, cravings
Social features	Has deteriorating or poor social function Has family members expressing concern
Patient's views on their opioid use	Sometimes acknowledges being addicted Strongly resists tapering or switching to a different opioid Admits to mood-leveling effects or distressing withdrawal symptoms

Case

Mr H. is a 36-year-old man who injured his back 3 years ago while lifting heavy machinery at work. He has had chronic low back pain since then and has been unemployed and supporting himself through Workplace Safety and Insurance Board benefits. He has had trouble sleeping and has been depressed and anxious since he stopped working. He was initially started on acetaminophen-oxycodone (325 mg/5 mg) tablets, 1 tablet 4 times daily, but this was only partially helping his pain and he was switched to 10 mg of sustained-release oxycodone 4 times daily. His dose has been escalating over the past 2 years and he is now taking 80 mg of sustained-release oxycodone 4 times daily. He often asks his doctor's receptionist to fit him in for early renewal of his medications.

Role of buprenorphine in primary care

Most family physicians will prescribe buprenorphine primarily for opioid-dependent patients who are already in their practices. Prescribing opioids to an addicted patient can be frustrating and time-consuming, and (in our experience) it usually has poor outcomes. In contrast, patients' mood, functioning, pain, and withdrawal symptoms usually improve with buprenorphine, making the patient-doctor interaction more satisfying and therapeutic. Physicians should refer patients who do not respond to buprenorphine treatment to a specialized methadone program. This stepped-care approach exposes patients to the safest drug first (buprenorphine), transferring them to another drug if necessary.[28]

Case continued

Mr H. denies injecting the oxycodone, but admits that he often crushes the tablets and has on 1 occasion snorted a crushed tablet. He finds that he needs more and more oxycodone to get the same pain relief; his pain remains at 5 or 6 out of 10. When the oxycodone wears off, he experiences marked worsening of the pain ("12 out of 10"), along with depressed mood, myalgia, sweating, and diarrhea. He feels as though he needs to take the oxycodone just to feel "normal."

Indications for buprenorphine treatment

Table 2 outlines the indications for buprenorphine, methadone, and detoxification. Buprenorphine maintenance should be considered over detoxification or methadone in patients who meet 1 or more of the following criteria:

Quickly relapsed after a trial of detoxification. Such quick relapse suggests that the patient needs treatment with either methadone or buprenorphine.

Adolescents, young adults, and others who might not need long-term opioid agonist treatment. Buprenorphine has a milder withdrawal syndrome and might be easier to discontinue than methadone.[29] For this reason it could be the first choice for patients who have good prognoses and might be able to successfully taper off buprenorphine after several months.

At higher risk of methadone toxicity. Higher-risk patients include older patients, those taking benzodiazepines or other sedating drugs, heavy drinkers, patients with chronic obstructive pulmonary disease or other respiratory illnesses, and patients with lower tolerance to opioids (eg, taking weak opioids, such as codeine, or nondaily doses of oral opioids).

Socially stable oral prescription opioid users. For such patients, methadone take-home restrictions will be problematic (eg, patients with full-time family or work responsibilities or limited access to transportation).

Limited or no access to methadone. Patients living, for example, in rural or northern communities might have limited or no access to methadone treatment.

Pregnant patients with no access to methadone treatment. Methadone maintenance is currently the standard of care for opioid addiction during pregnancy. However, buprenorphine could be an alternative to methadone maintenance treatment in pregnancy, especially for patients who do not have access to

Table 2. Indications for detoxification, buprenorphine, or methadone

DETOXIFICATION	BUPRENORPHINE MAINTENANCE	METHADONE MAINTENANCE
Patient preference Good prognostic factors* Has not tried detoxification or has tried previously and had a good response	Failed or had adverse effects with methadone Quickly relapsed after detoxification Good prognosis*; might not need long-term opioid agonist treatment At higher risk of methadone toxicity†	Failed or had adverse effects with buprenorphine Quickly relapsed after detoxification Intravenous buprenorphine abuse High risk of treatment dropout (socially unstable injection opioid user)

*Good prognostic factors include younger age, recent history, not addicted to other drugs, socially stable, oral use and no intravenous use, and no concurrent active psychiatric disorders.

†Those at higher risk of methadone toxicity include older patients, heavy drinkers, patients taking higher or unstable doses of benzodiazepines or other sedating drugs, those with respiratory illness (eg, chronic obstructive pulmonary disease), and those with lower opioid tolerance.

methadone (eg, lack of services in a certain geographical location). Buprenorphine-naloxone in combination is contraindicated in pregnancy because the safety of naloxone in pregnancy has not been established. However, buprenorphine without naloxone has been shown to be safe and effective in pregnancy.[30,31] Buprenorphine should only be prescribed for pregnant women after a detailed discussion of risks, benefits, and treatment options. Buprenorphine without naloxone can be obtained on a case-by-case basis through Health Canada's Special Access Programme (**www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/index_e.html**).

Case continued

Mr H. has tried to taper off his oxycodone multiple times without success. Each time he has relapsed after a few days. He does not want to go into a formal withdrawal management program, and he lives 2 hours away from the nearest methadone treatment centre.

Pharmacology

Table 3 outlines the pharmacology of buprenorphine. It is a partial μ receptor agonist with a low intrinsic activity at the receptor site. Clinically this gives it a "ceiling effect": its opioid agonist effects plateau at higher doses (hence the low risk of overdose). Buprenorphine attaches tightly to opioid receptors and dissociates slowly from them, giving it a 2- or 3-day duration of action. Because of its slow onset of action, opioid-dependent patients do not experience sedation or euphoria when taking the appropriate dose. Its high receptor affinity causes it to displace other opioids from endorphin receptors,[32] triggering withdrawal in patients who are physically dependent on opioids.

Buprenorphine is available as a combined product of buprenorphine and naloxone in a 4:1 ratio. Unlike methadone, wthat is dispensed in 100 mL of orange juice, buprenorphine is a tablet that can be easily crushed and injected. Naloxone, an opioid antagonist, has poor oral bioavailability, but will precipitate withdrawal in opioid-dependent patients if used intravenously,[33] thereby discouraging intravenous abuse. Naloxone does not interfere with the pharmacokinetics or effectiveness of buprenorphine when the combination formulation is taken sublingually.[10,34,35]

Benefits and adverse effects

Buprenorphine has side effects similar to other opioids, including sedation, constipation, and nausea. Buprenorphine has several advantages over methadone besides a lower overdose risk. It does not prolong the QT interval[36,37] and it is less likely to cause erectile dysfunction.[38,39] Buprenorphine patients perform better than methadone-maintained patients on cognitive and psychomotor tests,[40,41] and the cognitive effects of concurrent benzodiazepine use are less pronounced than they are with methadone.[42]

All buprenorphine-exposed neonates need to be observed for neonatal abstinence syndrome. Research studies have demonstrated that exposure to buprenorphine in utero is associated with milder and shorter neonatal withdrawal than seen with methadone maintenance treatment.[43-45] The safety of buprenorphine during lactation remains uncertain. Buprenorphine has been detected in breast milk in amounts similar to maternal serum levels; however, as buprenorphine undergoes a high first-pass metabolism and has poor oral bioavailability, infants are exposed to substantially lower amounts through breastfeeding. Furthermore, neonatal abstinence syndrome presentation and management are not altered by breastfeeding. Women need to consider the benefits of breastfeeding for their babies against the potential risk of exposure to a small proportion of buprenorphine in breast milk.[45,46]

Table 3. Summary of buprenorphine pharmacology

FEATURE	RESULT
Very tight binding to opioid receptors	Displaces other opioids from opioid receptors Triggers withdrawal in patients physically dependent on opioids Blocks the analgesic action of other opioids
Slow dissociation from opioid receptors	Long duration of action Relieves withdrawal and cravings for 24 h or longer
No bioaccumulation	Allows quick titration to effective dose
Partial agonist with ceiling effect	Very low risk of overdose Might be less effective than higher doses of methadone
SL and IV absorption; poor oral absorption	Can be abused intravenously
Combined with naloxone	When injected, naloxone will trigger withdrawal in patients physically dependent on opioids; this serves as a deterrent to IV use

IV—intravenous, SL—sublingual.

Special considerations

Availability. **Table 4** lists the criteria for buprenorphine coverage under provincial drug plans. Currently only Ontario and Quebec provide coverage for family physicians' prescriptions.

Table 4. Buprenorphine coverage under different provincial drug plans

PROVINCE OR PROGRAM	CURRENT COVERAGE
British Columbia	None
Alberta	Restricted to methadone prescribers
Saskatchewan	None
Manitoba	None
Ontario	If methadone has failed, is not tolerated, or is contraindicated When methadone treatment is not accessible (waiting list > 3 mo) If at high risk of methadone toxicity (elderly, benzodiazepine user, heavy drinker, low opioid tolerance, respiratory illness, taking medications that interfere with methadone metabolism) Only 8-mg tablets are covered All physicians can prescribe (but should have training)
Quebec	If methadone has failed, is not tolerated, or is contraindicated When methadone treatment is not available or accessible
New Brunswick	Restricted to methadone prescribers Only if methadone is contraindicated
PEI	None
Nova Scotia	Restricted to methadone prescribers Only if methadone is contraindicated
Newfoundland and Labrador	None
NIHB Program	None

NIHB—Non-Insured Health Benefits.

Training. Physicians prescribing buprenorphine can be trained in its use with a workshop or online course (**Box 1**). While the drug itself is safe and easy to prescribe, training is recommended because most family physicians are unfamiliar with the components of opioid agonist treatment (eg, take-home doses, regular urine drug screens).

Box 1. Resources for physicians

Training courses

- Online course: Suboxone Training Program, Schering-Plough (**www.suboxonecme.ca**)
- Online and in-person: Centre for Addiction and Mental Health in Toronto, Ont (**www.camh.net**)

Clinical guidelines available on the Internet

Canada

- Quebec: Collège des médecins du Québec, Ordre des pharmaciens du Québec. *La buprénorphine dans le traitement de la dépendance aux opioïdes. Lignes directrices.* Montreal, QC: Ordre des pharmaciens du Québec; 2009. (**www.opq.org**)
- Ontario: Centre for Addiction and Mental Health guidelines are in progress. (**www.camh.net**)

United Kingdom

- Ford C, Morton S, Lintzeris N, Bury J, Gerada C. *Guidance for the use of buprenorphine for the treatment of opioid dependence in primary care.* 2nd ed. London, UK: RCGP Drug and Alcohol Misuse Training Programme; 2004. (**www.rcgp.org.uk/pdf/drug_buprenorphine.pdf**)

Australia

- Lintzeris N, Clark N, Muhleisen P, Ritter A, Ali R, Bell J, et al. *Clinical guidelines: buprenorphine treatment of heroin dependence.* Canberra, Australia: Commonwealth of Australia; 2006. (**www.health.vic.gov.au/dpu/downloads/bupguide)**

United States

- Center for Substance Abuse Treatment. *Clinical guidelines for the use of buprenorphine in the treatment of opioid addiction. A treatment improvement protocol (TIP), series 40.* Rockville, MD: US Department of Health and Human Services; 2004. (**www.samhsa.gov**)

Physician support and advice

- Clinicians can contact the Toronto Centre for Substance Use in Pregnancy at St Joseph's Health Centre with additional questions regarding the use of buprenorphine during pregnancy (telephone 416 530-6860)
- Physician Clinical Support System (**www.pcssmentor.org**)

Dose titration

If patients take buprenorphine while they have another opioid in their systems, they might experience withdrawal. This occurs as a result of the buprenorphine displacing the original opioid from the opioid receptors, triggering acute withdrawal in patients who are physically dependent. Symptoms of precipitated withdrawal peak within 1.5 to 3 hours of the buprenorphine dose, and can take up to 12 hours to resolve.[29,47] This can be prevented by administering the first buprenorphine dose after the patient's last opioid dose has worn off, when the patient is in moderate opioid withdrawal (**Box 2**). Physicians who are unfamiliar with opioid withdrawal might consider using the Clinical Opiate Withdrawal Scale (COWS) to help them decide when to give the first dose of buprenorphine (**www.csam-asam.org**).[48] The initial buprenorphine dose is 2 to 4 mg. The first day's total dose should be no more than 8 mg, with daily increases of 2 to 4 mg as necessary.[46] The optimal dose relieves cravings and symptoms of withdrawal for a full 24 hours, without causing sedation. The usual therapeutic range is 8 to 16 mg daily, to a maximum of 24 mg a day.[46]

While induction in the physician's office is usually recommended, preliminary research has found that home induction is safe and might be more practical and acceptable to patients.[49] If home induction is used, patients should be advised to take the first dose only when they are in withdrawal and to call the doctor's office if they have concerns. It is probably best to do home inductions earlier on in the week so that patients can then be reassessed in a day or two in the office for dose adjustments and also so that the office is open for any patient queries. Patients should be warned that they might experience some sedation during the titration phase and they should avoid driving or taking sedating medications.

Box 2. Initial buprenorphine titration

Before starting

Before the first dose of buprenorphine, the patient needs to be in opioid withdrawal. The timing of the last opioid dose before the office visit should be as follows:

- Short-acting opioids—12 h or more
- Longer-acting opioids—24 h or more
- Methadone—36 h to 3 d

Initial dose

Dispense 2-4 mg only if the patient has symptoms of withdrawal

- 2 mg if at higher risk (eg, older, lower tolerance, taking benzodiazepines)
- 4 mg for lower-risk patients

Observe for 2 h, then dispense according to symptoms:

- Withdrawal symptoms resolved
  - -Discharge with prescription for 2-4 mg/d, depending on initial dose
- Withdrawal symptoms only slightly better
  - -Dispense another 4 mg
  - -Discharge with prescription (8-12 mg/d, dispensed daily)
  - -Follow up in 1-4 d to reassess dose
- Withdrawal symptoms substantially worse (precipitated withdrawal)
  - -Symptomatic treatment (eg, dimenhydrinate, naproxen)
  - -Repeat induction the next day

Discharge and follow-up

- Advise patient to avoid alcohol or sedating drugs and to avoid driving until tolerant to dose
- If possible, schedule a follow-up visit 1-4 d after start of induction to reassess dose
- For the first week, provide telephone or in-person access to a nurse or physician for dose adjustments and support
  - -Increase dose by 4-8 mg for withdrawal symptoms and cravings
  - -Optimal dose relieves cravings and withdrawal for 24 h
- Usual range is 8-16 mg/d; maximum daily dose is 24 mg

Case continued

Mr H. takes his last dose of oxycodone on Sunday morning and shows up at his family physician's office on Monday morning reporting diarrhea, nausea, myalgia, and cravings. He is given a prescription for 1, 8-mg buprenorphine tablet and instructed to return to the office with the medication. He is given half a tablet (4 mg) sublingually in the office and is reassessed 2 hours later. He reports feeling better but still has some withdrawal symptoms. He is given another 4-mg sublingual dose to bring his total daily dose to 8 mg. He is given a prescription for 8 mg sublingually, once daily for the next 2 mornings, to be observed in the pharmacy. At his follow-up visit on Thursday, he describes withdrawal symptoms 12 hours after taking each dose. His dosage is increased to 12-mg sublingually, once daily, and a follow-up visit is booked for the following Wednesday. At that visit, he states that the 12-mg dose relieves withdrawal symptoms for 24 hours. He is given a prescription for daily observed dosing with a Sunday take-home dose.

Less-than-daily dosing

Less-than-daily dosing (eg, double the daily dose given every 2 days), which is outlined in **Box 3**, is as effective as daily dosing in reducing opioid use.[50] It is preferred by patients who are not eligible for take-home doses, as they must otherwise visit the pharmacy daily.[51-53]

Opioid detoxification with buprenorphine

Buprenorphine detoxification (**Box 4**) is more effective than nonopioid treatments for relieving opioid withdrawal symptoms[54-56] and retaining patients in treatment.[50,57,58] However, it is less effective than buprenorphine maintenance treatment.[59-61] Detoxification might be considered for patients with good prognostic factors (**Table 2**) who do not need or want maintenance treatment. Detoxification should in

Box 3. Less-than-daily dosing

Prescribe

Prescribe less-than-daily dosing after 1 mo on daily dose and 2 wk on stable dose

Revert

Revert to daily dosing if patient experiences considerable sedation with higher dose or uncomfortable withdrawal symptoms despite maximum dose (32 mg)

Examples

Four times/wk: eg, convert 8 mg/d to 16 mg on Monday, 16 mg on Wednesday and Friday, and 8 mg on Sunday
Three times/wk: eg, convert 8 mg/d to 16 mg on Monday, 16 mg on Wednesday, and 24 mg on Friday

most cases be immediately followed by an addiction treatment program, as by itself it is unlikely to be effective. Patients should be warned that they quickly lose tolerance with abstinence and can overdose if they relapse to their previous dose.

Tapering

Patients who have been on a stable buprenorphine dose and are doing well might choose to taper off buprenorphine for financial or personal reasons (**Box 4**). Tapering has a high risk of relapse and works best for patients with a short history of addiction and a strong support network, who have not used unauthorized drugs for months and who do not have active mood or anxiety disorders. The taper should be put on hold or reversed if the patient relapses or experiences severe withdrawal symptoms or cravings.

Office visits

At each visit, the practitioner should inquire about substance use, mood, and functioning. Physician advice and support should be brief, practical, and solution-focused (**Table 6**).[62]

Take-home doses

Daily observed dispensing of buprenorphine followed by a gradual increase in take-home doses is the recommended policy in Australia, the United Kingdom, and other countries.[63-65] Prescribing take-home methadone doses contingent on drug-free urine samples is associated with reductions in opioid, cocaine, and benzodiazepine use.[66,67]

Take-home doses of buprenorphine should be granted for patients who do not have severe or unstable psychiatric disorders, who can safely store their medication, and who are not currently using other drugs problematically. Take-home doses can also be given if the drug use is occasional and without evidence of harm (eg, weekend cannabis users). The optimal take-home schedule is not known, and schedules should be based on individual clinical considerations. Take-home doses should be prescribed more slowly for patients at higher risk of diversion and intravenous use, such as patients with a history of intravenous drug use or other street or illicit drug use, or patients with evidence of current unstable drug use (**Table 7**).

Pharmacy visits can be reduced in such patients through less-than-daily dosing. Patients can be given take-home doses at a faster pace if they are at lower risk of diversion (ie, taking prescription opioids orally from 1 physician only, not abusing street drugs, and not selling or buying their opioids). Daily dispensing might be unnecessary for such patients and could cause them to reject buprenorphine treatment, particularly if they lack transportation or have daily work or family commitments.

In the product monograph, Health Canada recommends that buprenorphine be dispensed daily, except for weekends, for 2 months. Physicians who prescribe take-home doses before 2 months have passed should document their rationale for doing so, as they are prescribing "off label."

Box 4. Protpcols for detoxification and tapering

Rapid detoxification

- Titrate buprenorphine to 8-16 mg over 1-3 d
- Reduce dose by 2 mg every 1-3 d (inpatients) or 2 mg/wk (outpatients)
- Treat symptoms: diphenoxylate-atropine, dimenhydrinate, acetaminophen, trazodone
- **Precautions:** Always follow with addiction counseling
- Warn patients that they can overdose if they relapse to their usual opioid dose

Slow outpatient taper

- Rate: no faster than 2 mg every 2 wk
- Put taper on hold or reverse if patient experiences severe withdrawal, cravings, relapse, or depression
- Patient should have input into rate of taper

Table 6. Agenda for routine follow-up visits

TOPIC	ACTION
Buprenorphine	Inquire about withdrawal, cravings, opioid use, and side effects
Substance use	Ask about other substance use; review urine drug screen results
Social	Inquire about housing, relationships, job, or school; provide brief advice and support
Mental health	Inquire about anxiety and depression; prescribe appropriate pharmacotherapy
Physical health	Manage hepatitis C and other chronic illnesses
Preventive health	Ensure the patient undergoes age-appropriate screening and interventions

Urine drug testing

Urine drug screening (UDS) is recommended at each office visit, as UDS combined with self-report is more accurate than either method alone.[68] Infrequent UDS will fail to detect many cases of substance use, particularly if the use is less than daily.[69] Granting take-home doses in response to negative UDS results (contingency management) is effective in reducing drug use.[70]

Case continued

Two months later, Mr H. is doing well on 12 mg of sublingual buprenorphine daily and results of his

Table 7. Suggested take-home dose (carry) schedule

SCHEDULE	LOWER RISK OF IV USE OR DIVERSION*	HIGHER RISK OF IV USE OR DIVERSION
Rate of adding take-home doses	1 carry every 1-2 wk	1 carry every 3-4 wk
Maximum no. of carries	6/wk	6/wk
Time to reach maximum carries	6-12 wk	18-24 wk

IV—intravenous.
*No injection drug use, double-doctoring, or buying or selling drugs, and not addicted to other substances.

regular UDS have been negative for any unprescribed substances. He has discontinued all use of oxycodone. His mood is improved and, while he still has chronic low back pain, he feels that his pain is much better now that he has discontinued the oxycodone. Because he is now clinically stable and no longer using drugs problematically, his physician prescribes take-home doses for Monday and Thursday as well as Sunday.

Conclusion

Buprenorphine is a safe and effective treatment for primary care patients who are addicted to prescription opioids. Family physicians can safely prescribe buprenorphine in an office-based setting. Patients who fail to respond to buprenorphine treatment should be referred for methadone treatment.

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Contributors
All authors contributed to concept and design of the study; data gathering, analysis, and interpretation; and preparing the manuscript for submission.

Competing interests
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