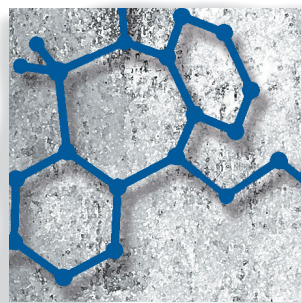


Treatment of opioid dependence with buprenorphine: current update

Michael Soyka, MD



Opioid maintenance treatment is the first-line approach in opioid dependence. Both the full opioid agonist methadone (MET) and the partial agonist buprenorphine (BUP) are licensed for the treatment of opioid dependence. BUP differs significantly from MET in its pharmacology, side effects, and safety issues. For example, the risk of respiratory depression is lower than with MET. The risk of diversion and injection of BUP have been reduced by also making it available as a tablet containing the opioid antagonist naloxone. This review summarizes the clinical effects of BUP and examines possible factors that can support decisions regarding the use of BUP or MET in opioid-dependent people.

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Introduction: extent of the problem

Opioid dependence results in clinically significant impairment. According to the tenth edition of the *International Classification of Diseases (ICD-10)*¹ and the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)*,² opioid dependence is a chronic medical disorder characterized by various somatic, psychological, and behavioral symptoms (three out of six or seven criteria must be fulfilled). Both of those classification systems follow a categorical approach. In contrast, the fifth edition of the *DSM (DSM-5)*³ takes a dimensional approach to substance-use disorders and lists 11 symptoms: a severe disorder is defined as the presence of at least six symptoms, a moderate disorder as the presence of 4 to 5, and a mild disorder as the presence of 2 to 3.

The risk of developing a substance-use disorder is related to several factors, such as the pharmacology of the drug, genetics, personality, family, and the individual microcosm (*Figure 1*). Opioid-dependence disorder is chronic and relapsing,⁴ and the mortality rate and rates of psychiatric and physical comorbidity are high.⁵⁻⁷ The Global Burden of Disease 2010 study estimated that opioid dependence accounted for 9.2 million disability-adjusted life years (DALYs) worldwide.⁷ According to estimates from the United Nations Office on Drugs and Crime (UNODC), 33 million people use opioids worldwide for nonmedical purposes.⁸ In Europe, the number of opioid users is estimated at 1.3 million people, and opioids are involved in 82% of fatal drug intoxications.⁵ Prevalence rates of opioid use in Europe appear to have

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Author affiliations: Medical Park Chiemseeblick, Bernau, Germany; Psychiatric Hospital, University of Munich, Munich, Germany

Address for correspondence: Michael Soyka, MD, Medicalpark Chiemseeblick, Rasthausstr. 25, 83233 Bernau, Germany (email: m.soyka@medicalpark.de)

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decreased over the past few years.⁹ Also, opioids other than heroin, eg, methadone (MET), buprenorphine (BUP), and fentanyl, have rather become the drugs of choice.⁹ From 2002 to 2013, the rate of heroin use increased in the United States (US) by 62%.¹⁰ In a 2014 survey in the US, about 914 000 individuals had used heroin in the past year and about 4.3 million people had used prescription opioids for nonmedical reasons.¹¹ From 2001 to 2013, related deaths increased threefold¹²; many of these deaths were a result of accidental poisoning of children.¹³

Opioid maintenance treatment is a well-established first-line approach for opioid dependence.¹⁴ Oral MET, BUP, or the combination of BUP and naloxone are frequently used.¹⁵⁻¹⁸ The efficacy of both MET and BUP is proven.^{16,19,20} A few long-term studies have been performed, mostly in patients in opioid maintenance.^{21,22} Other available medications, such as oral or depot naltrexone, slow-release oral morphine,²³ and injectable MET or heroin²⁴ are not part of this review.

Search strategy

This paper is an extension of previous work on the World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for treatment of opioid dependence.¹⁷ A PubMed search was performed with the

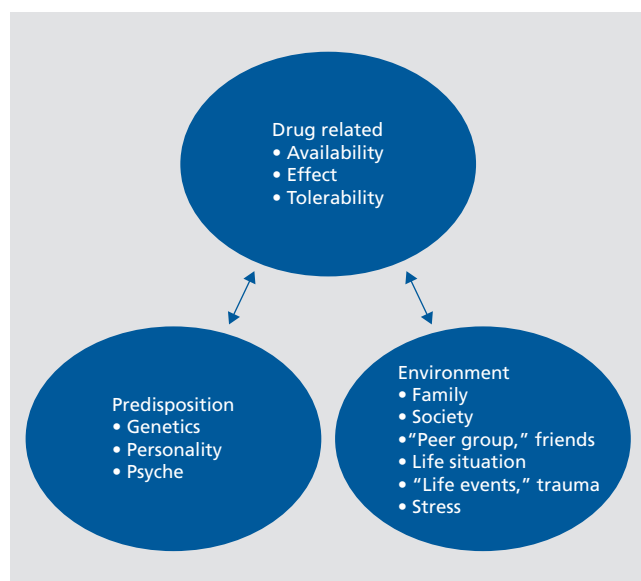


Figure 1. Factors contributing to the risk of developing a substance-use disorder.

search terms “opioid dependence,” “buprenorphine,” and “treatment” to identify additional and recent publications.

BUP in opioid maintenance treatment

MET, BUP, and BUP/naloxone are well-established first-line treatments for opioid dependence.^{14,17,25-28} For comprehensive reviews on this issue, see Mammen and Bell¹⁵ and Yokell et al.²⁹ In the United States, the Food and Drug Administration (FDA) approved BUP in October 2002 as a treatment for opioid addiction. The chemical structure of BUP is shown in *Figure 2*.

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Because of the rapid metabolization of BUP and because it is subject to extensive first-pass liver metabolism, bioavailability is low after oral administration, and BUP tablets are given sublingually. Unlike MET, BUP is a partial agonist at the μ -opioid receptor and an antagonist at the κ -opioid receptor; after sublingual administration, it has a long half-life (24 to 60 hours).³⁰ Its pharmacological profile is unique and differs from that of full opioid agonists. In the induction phase, BUP may precipitate withdrawal symptoms.³¹

The induction and titration phase (which is often too rapid, causing side effects, opioid withdrawal, and, consequently, low retention, or too slow, resulting in a significant dropout rate) for BUP is of special relevance for treatment retention and varies between countries.^{32,33} For opi-

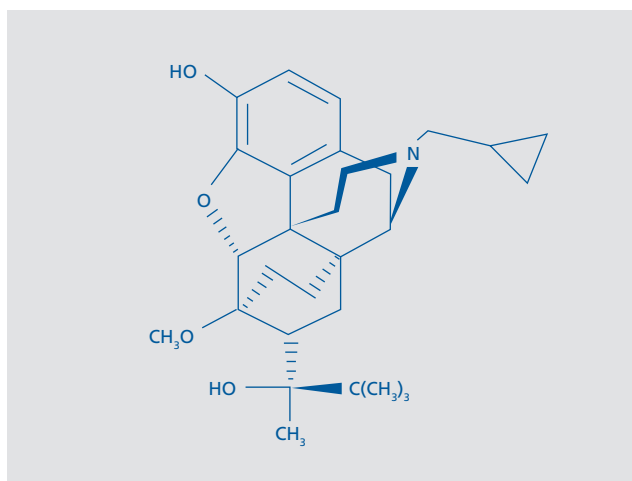


Figure 2. Chemical structure of buprenorphine.

oid maintenance therapy, BUP is usually started at 2 to 4 mg/day¹⁴ and can be increased by 2 to 4 mg/day. Many clinicians restrict the maximum dose on day 1 to 4 to 8 mg, although higher doses (16 mg) than the usually recommended maximum of 8 mg/day have been proposed^{34,35}; the maximum dose used on day 1 in most studies is 8 mg.³⁶ The typical dosages for maintenance treatment are 8-16 mg/day (FDA dosing limit: 24 mg/day).¹⁴

In Europe, BUP is available in two forms: a tablet with only BUP and one with a combination of BUP and the opioid antagonist naloxone in a 4:1 ratio (ie, BUP 2 mg/naloxone 0.5 mg or BUP 8 mg/naloxone 2 mg). Naloxone has poor sublingual but good parenteral bioavailability; its elimination half-life in plasma is approximately 30 minutes.³⁷ The bioavailability of naloxone after sublingual administration is low enough as to not cause severe withdrawal symptoms in highly opioid-dependent people. However, if a BUP or BUP/naloxone tablet is dissolved and administered intravenously, it precipitates an immediate opioid-withdrawal syndrome. This effect is thought to improve the safety of BUP by reducing its abuse potential. According to guidelines from the American Psychiatric Association (APA),²⁵ the British Association for Psychopharmacology (BAP),²⁷ the WFSBP,¹⁷ a Swedish group,³⁸ and others,²⁶ the BUP/naloxone combination tablet reduces the risk of diversion significantly.²⁵ However, although the combination tablet may reduce intravenous misuse, it probably does not completely eliminate it¹⁵ (for review, see ref 39).

BUP acts as a partial agonist at opioid receptors. It has a ceiling effect for respiratory depression at higher concentrations, which reduces the risk of overdose. Doses above 24 to 32 mg/day do not further increase its respiratory-depressant effect. Furthermore, if BUP metabolism is inhibited, the higher concentrations do not result in the toxicity effects typical of opioids, including respiratory depression.³⁰ If metabolism is induced, BUP's high affinity for μ -opioid receptors may allow it to remain at the opioid receptor even as plasma concentrations decrease. One of the probable advantages of BUP over full opioid agonists is its milder withdrawal syndrome after treatment discontinuation.

Clinical aspects of BUP treatment

Clinical studies that compared MET (mainly in moderate dosages, ie, 50 to 60 mg/day) with BUP (12 to 16 mg/day) generally showed comparable efficacy of the

two drugs and a modestly lower retention rate in BUP-treated patients.^{38,40,41} Optimal doses can be achieved in 2 to 3 days (8 to 16 mg/day to a maximum of 24 mg/day)¹⁴; 16 mg/day of BUP suppresses 80% of the opioid receptor (*Figure 3*).⁴²

Patient preferences and beliefs about opioids are important factors in the treating doctor's decision to use a certain drug. The interesting question about which kind of patient prefers MET and which prefers BUP was addressed in the SUMMIT trial (SUButex vs Methadone MaIntenance Trial), a prospective patient-preference study in 361 opioid-dependent individuals.⁴³ BUP was

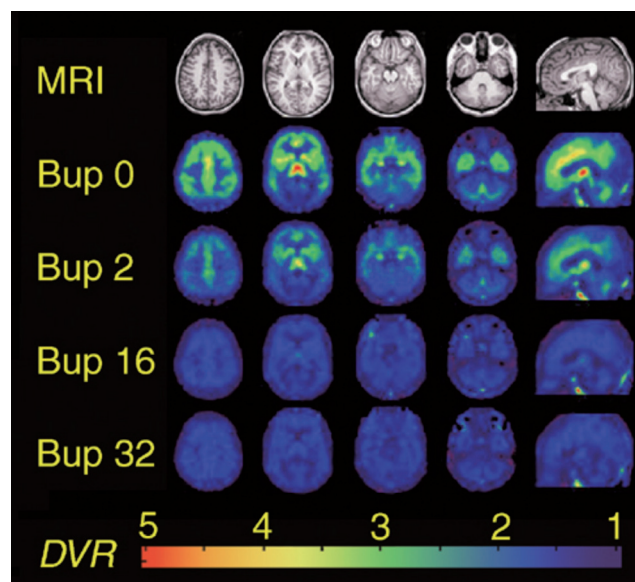


Figure 3. Parametric images of μ -opioid receptor availability from a representative heroin-dependent volunteer during daily maintenance on buprenorphine placebo (row 2 from the top, Bup 0), 2 mg (Bup 2), 16 mg (Bup 16), and 32 mg (Bup 32). Images are scaled so that binding in the occipital cortex, an area devoid of μ -receptors, is equal to 1. Four transverse sections from superior (column 1) to inferior (column 4) and one sagittal section (column 5) are shown, which correspond to T1-weighted anatomical MRI images (row 1). The pseudocolor scale depicts DVR values from 1 to 4. Reproduced from reference 42: Greenwald MK, Johanson CE, Moody DE, et al. Effects of buprenorphine maintenance dose on mu-opioid receptor availability, plasma concentrations, and antagonist blockade in heroin-dependent volunteers. *Group. BUP, buprenorphine; DVR, direct volume rendering; MRI, magnetic resonance imaging.*

Figure reproduced with permission from ref 42: Greenwald MK, Johanson CE, Moody DE, et al. Effects of buprenorphine maintenance dose on mu-opioid receptor availability, plasma concentrations, and antagonist blockade in heroin-dependent volunteers. *Neuropsychopharmacology*. 2003;28(11):2000-2009. © 2003 Nature Publishing Group

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given as a “rapid titration” at flexible doses (BUP: a mean of 6.9 mg at the end of day 1, 9.9 mg at the end of day 2, and 11.3 mg at the end of day 3; MET: 50.7 mg at the end of day 1, 63.8 mg at the end of day 2 and 69.6 mg at the end of day 3). Almost two-thirds of the patients (63%) chose MET, whereas the remaining patients (37%) chose BUP. In line with the common belief of many physicians, MET was chosen by participants whose substance abuse was more severe and who had psychiatric and physical problems. Although the MET group showed a higher retention rate, the likelihood of suppressing illicit opiate use and achieving detoxification was higher among those retained in the BUP group.

The side effects of BUP include respiratory depression, anxiety, sweating, constipation, headache, insomnia, nausea, dizziness, asthenia, and somnolence. BUP has a small risk for liver enzyme elevations or hepatotoxic effects, but less than previously thought.⁴⁴ Unlike MET, BUP lacks both cardiotoxic effects and the risk of arrhythmias.⁴⁵

Studies comparing BUP and MET

Historically, MET has been used more often than BUP in most European countries, with some exceptions (mainly France). The efficacy of opioid maintenance treatment is usually measured by the reduction in opioid use (drug-free urine screens) and the retention/completion rate in treatment. Other important variables are safety (overdose, cardiotoxicity, etc), risk of diversion, reduction in criminality, and improvement of physical disorders and psychosocial functioning.

Studies comparing the effects of MET with BUP have produced mixed results: some show both drugs to be equally effective, whereas others demonstrate a higher retention rate with MET. BUP/naloxone clearly shows better retention than placebo or no treatment⁴⁶ but worse retention than MET. However, only one of the studies in a recent systematic review evaluated retention in periods longer than 12 months.⁴⁶

The results of a large, 24-week randomized multicenter study comparing the effects and treatment retention rates of MET and BUP in 1267 patients⁴⁷ showed a higher retention rate with MET than with BUP (74% vs 46%); retention increased to 80% in the MET group when the maximum dose reached or exceeded 60 mg/day. Remarkably, in the BUP group, the completion rate showed a linear increase and reached a 60% retention rate at 30

to 32 mg/day. Interestingly, in the first 9 weeks, the number of positive opioid urine results among those remaining in treatment was significantly lower in the BUP than in the MET group. A lower dose (BUP <16 mg/day, MET <60 mg/day) was one of several factors associated with dropout. Consequently, the authors discussed that future investigations should use BUP doses above 32 mg/day to increase retention rates. Retention rate was also higher with MET than with BUP in other studies.⁴⁸

A naturalistic long-term study in Germany of patients in opioid maintenance treatment (mean follow-up: 6 years)⁴⁹ showed high overall retention rates in patients (see the section headed “Long-term outcome” below). Most of the patients were still being treated at the end of the study, and retention rates did not differ between MET and BUP.

Other studies also emphasize the relevance of dose. In fixed-dose studies, BUP is less effective at lower doses than at higher ones.¹⁶ A meta-analysis of 21 randomized clinical studies also (indicated that the retention rate is better at a higher dose (16 to 32 mg/day) than at a lower one (<16 mg/day).⁵⁰ The question of dosing was also studied by Jacobs et al.⁵¹ A total of 740 patients were started on BUP at a flexible dose. Outcomes were better in patients who received higher BUP doses in the induction phase (first 7 days) and were significantly better in participants receiving ≥ 16 mg/day on day 28 than in those receiving <16 mg/day.

Future trends – BUP depot/implant

The development of novel opioids and opioid formulations is one goal to fight the current opioid crisis, especially in the US.⁵² In May 2016, a 6-month buprenorphine subdermal implant (Probuphine) was approved in the US for the maintenance treatment of opioid dependence in people who showed sustained, prolonged clinical stability at doses of no more than 8 mg/day sublingual BUP. First studies⁵³⁻⁵⁵ indicate that the BUP implant shows noninferiority or equal effects to sublingual BUP. A depot of long-acting implant formulations may lower the risk of diversion and facilitate the clinical management of otherwise stable opioid-dependent patients. This formulation is not yet available in Europe. Recent data on a weekly BUP depot preparation, CAM2038 (24 mg and 32 mg), indicate that it is safely tolerated and produces immediate and sustained opioid blockade and opioid withdrawal suppression.⁵⁶

Drug interactions with BUP

BUP can interact with other drugs as a result of altered pharmacokinetics or pharmacodynamic interactions. The former are related to inhibition or induction of hepatic cytochrome P450 (CYP) enzymes and effects on glucuronidation, drug transporter function (P-glycoprotein), and drug absorption^{57,58}; other possible mechanisms, eg, changes in blood-brain-barrier permeability, remain hypothetical. The latter include the additive effects of two drugs that have similar actions.

Pharmacokinetic interactions

These interactions are more complex than pharmacodynamic ones. Most drugs are metabolized in the liver and interactions of a drug with BUP may change the rate of metabolism of either drug and subsequently alter plasma concentrations, among other things. Inhibitors of the CYP enzymes may cause increases in plasma drug concentrations, with associated risks of toxicity or overdose. Drugs that induce synthesis of CYP enzymes may lead to reduced drug efficacy or withdrawal.

BUP is generally believed to have fewer interactions than MET, for both pharmacokinetic and pharmacodynamic reasons.⁵⁹ After BUP is absorbed sublingually, CYP3A4 and to a lesser extent CYP2C8 convert and *N*-dealkylate it to the active metabolite norbuprenorphine. Subsequently, both BUP and norbuprenorphine are metabolized further by uridine diphosphate glucuronosyltransferases (UGTs), mostly UGT 1A3 but also 2B6 and 1A1.⁶⁰ BUP does not significantly induce or inhibit P450 enzymes (and neither does MET), but it may compete with drugs that are metabolized by the same pathways. BUP is a weak inhibitor of CYP3A4.

Although inhibitors of CYP3A4 may result in increased BUP concentrations in plasma, BUP's effect as a partial agonist may reduce the chance of opioid toxicity and overdose. Nevertheless, clinicians are recommended to monitor patients for side effects, including sedation or complications, such as liver toxicity, and monitoring is indicated if inhibitors of BUP metabolism are coadministered. Inducers of CYP3A4 may increase BUP metabolism, thus decreasing plasma concentrations and perhaps leading to opioid withdrawal; withdrawal is unlikely, however, because of the ceiling effect and half-life of BUP at the opioid receptor. Furthermore, the active metabolite norbuprenorphine may also

prevent opioid withdrawal. In vitro studies have shown an inhibitory effect of BUP and norbuprenorphine on the CYP2D6 system, but this effect is not relevant in humans. Norbuprenorphine is also of relevance for BUP toxicity, including respiratory depression.

Pharmacodynamic interactions

BUP shows pharmacodynamic interactions primarily with other depressants of the central nervous system, including alcohol, opioids, and psychotropic drugs. The toxicological and forensic literature is clear: BUP-related deaths are almost exclusively associated with co-consumption of other psychotropic agents or drugs.

Safety issues

A scholarly review on 58 prospective studies of samples with opioid dependence⁶¹ showed high mortality rates (all-cause mortality: 2.09/100 person years [PY]) but confirmed that, overall, maintenance treatment significantly lowers rates compared with untreated heroin dependence (1% to 3% deaths/year). The review found that most patients died from overdose and that risk was higher in males and during out-of-treatment periods.

Opioid-related deaths, especially from prescription opioids, such as fentanyl, have risen sharply in the US in particular.⁶² It is generally accepted that overdoses related to consumption solely of BUP are rare⁶³⁻⁶⁵ and that the risk for BUP-treated patients is lower than for MET-treated patients. The lower risk for respiratory depression in BUP-treated people must be balanced against the risk for other side effects, patients' preferences, and the somewhat lower retention rate found in some trials comparing BUP with MET.²²

Many medications, including full opioid agonists, such as MET, may cause prolongation of the rate-corrected QT (QTc) interval in the electrocardiogram (ECG), arrhythmias, and torsades de pointes and may carry a risk of sudden cardiac death.⁶⁶ BUP appears to be safer in this respect (see above).

Long-term outcome

A large naturalistic, nationally representative, prospective follow-up study conducted in Germany examined the 6-year outcome in opioid-dependent patients on maintenance treatment (N=2694); it consisted of three

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phases (baseline, 1 year, 5 to 7 years) and evaluated a nationwide representative sample of clinicians and the opioid-dependent patients in their care. The study found an annual mortality rate of about 1.9% for both MET- and BUP-treated patients.⁴⁹ Mortality rates were 1.2% (n=28/2284) after 1 year and 5.7% (n=131/2284) after 6 years. Rates did not differ between males and females.¹⁸ The most frequent causes of death were physical disorders (n=57, 36.6%; eg, human immunodeficiency virus (HIV)/AIDS [n=14], cancer [n=6], cardiovascular events [n=6; n=5 (0.3%) in the MET group and n=1 (0.2%) in the BUP group, not significant]), drug overdose (28.3%, eg, heroin, benzodiazepines, cocaine; n=6/37 for polyintoxication including the substitution drug) and suicide (16%). Fatal overdose of MET or BUP alone was almost never the sole cause of death (n=2, 1.5%), and interactions of MET or BUP with other drugs were also quite rare (n=6, 6.1%). The majority of patients who died were not receiving maintenance treatment (n=73, 55.7%) in the weeks before their death, either because the physician had decided to stop treatment or because the patient had stopped visiting the physician. In line with this finding is that overdose rates seemed to be higher for those who died outside treatment. Among the 58 patients (44.3%) who died while receiving maintenance treatment, 52/1690 treated with MET at baseline were receiving MET and 6/578 treated with BUP at baseline were receiving BUP. Thus, the mortality risk was significantly lower in the BUP patients than in the MET patients. Overall retention rate was similar for both medications over time.

In comparison with findings of an earlier meta-analysis,⁶¹ in the 6-year follow-up study, the mean crude annual mortality rate of about 1.0% was comparably low. In contrast with the findings of the meta-analysis, however, in the 6-year follow-up study, the most frequent cause of death was physical illness, followed by fatal overdose or intoxication with multiple substances. BUP and MET were rarely (1.5%) involved in premature death. Suicide (16%) was another frequent cause of death, but accidents or other violent causes were uncommon (4.6%). Of interest is that the annual mortality rate decreased only modestly over time; it was highest in the first year, but thereafter the decrease was not as large as might have been expected. This finding is in line with other long-term studies that also found a continued high rate of mortality in opioid-dependent patients.⁶⁷

As mentioned above, in the 6-year follow-up study, just over half of patients who died were no longer receiving maintenance treatment at the time of their death. As in earlier studies,⁶ discontinuation for any reason and not being in treatment were key predictors of death. This study also confirmed the well-known predictors of death identified in earlier studies with shorter follow-up periods,⁶¹ eg, unemployment, greater age, longer use of opioids, and comorbid mental or physical disorders.

The lower premature death rate at the 6-year follow-up in patients treated with BUP was remarkable,¹⁸ and BUP was shown to be a significant predictor for survival. This finding is consistent with other studies, in particular with French and German forensic autopsy data that indicate a low mortality risk for BUP.^{68,69} Cornish et al⁷⁰ examined the risk of death in a large cohort of patients and found a crude mortality rate of 0.7/100 PY in patients receiving treatment and of 1.3/100 PY in patients out of treatment. Unlike in the German 6-year follow-up study, mortality risk was twice as high in men and higher during the first 2 weeks of treatment.⁷⁰ Outcome and mortality may differ because of differences in the samples studied or because severely affected patients were allocated to the MET group, which may be indicated by a higher rate of comorbid psychiatric diagnoses at baseline.⁷¹

Retention is essential for treatment outcome. Overall, the dropout rate for drug therapies is high. Gossop and Marsden⁷² estimated the dropout rate to be about 40%, but some authors report significantly higher rates. Gossop and Marsden⁷² also reported optimistic abstinence rates of 51% at 6 months after discharge from inpatient treatment. However, most international studies have shown much lower abstinence rates of 20% to a maximum of 30% in the long term. Large studies were presented by Simpson and Sells^{73,74} and Hubbard et al⁷⁵ as part of the Treatment Outcome Prospective Study, a 5-year follow-up study. Depending on the definition used in the study, in the first year of treatment often 30% to 50% of the patients were drug free.

Psychotherapy in BUP-maintained patients

What kind of psychosocial therapies work in opioid maintenance therapy? In particular, motivational interviewing and contingency management are important evidence-based forms. These forms of psychotherapy

have the highest level of evidence and have also been investigated in opioid dependence. Several studies found positive results for cognitive behavioral therapy (CBT), which is also generally used as the basis for dependence-specific forms of psychotherapy. Long-term studies^{73,74} and meta-analyses have evaluated the efficacy of psychosocial therapies. Of particular importance is the meta-analysis by Dutra et al⁷⁶—who found that contingency management, relapse prevention, general CBT, and treatments combining CBT and contingency management have moderate effect sizes—and several Cochrane analyses⁷⁷ on the efficacy of psychosocial therapies in combination with substitution treatment. The APA guidelines²⁵ emphasize among other things that after inpatient treatment, continued treatment as an outpatient is important for drug-dependent patients. A comprehensive meta-analysis on the treatment of opioid dependence was also published by Berglund et al.⁷⁸ This meta-analysis examined 24 methodologically sound studies and found that, overall, the psychotherapies showed moderately large effect sizes in comparison with the control groups. Purely supportive therapies are probably ineffective.

The number of available studies on psychosocial interventions in conjunction with opioid maintenance treatment is much more limited.^{79,80} Two Cochrane analyses have been published,^{81,82} but most of the studies were conducted on MET maintenance. Again, CBT and contingency management have the best evidence. Three studies examined the efficacy of CBT patients in BUP treatment,⁸³⁻⁸⁵ with mixed results. In their systematic review on the available relevant studies, Dugosh et al⁷⁹ concluded that the evidence for efficacy of psychosocial interventions in BUP treatment is less robust than for MET. Retention and completion rates and opioid use in general improved in some of the studies. A recent study comparing CBT, contingency management, and the combination of both with no additional treatment in BUP-treated patients did not find any differences between groups.⁸⁴ The optimal psychosocial support for BUP-treated people remains a challenging topic of research.

Many clinicians—and authorities—consider adequate psychosocial treatment to be mandatory in patients in opioid maintenance treatment, despite the limited success rates. For many patients, rapid induction of treatment may be crucial to reduce the overdose risk. Interestingly, a recent pilot study examined the effects of “interim” BUP treatment in reducing illicit opi-

oid use among 50 people on waiting lists for entry into treatment⁸⁶ and found that illicit opioid use was significantly less in patients on interim BUP than in those on the waiting list.

Outlook

Although psychosocial treatments are effective in opioid dependence,⁷⁶ opioid maintenance treatment is a well-established first-line approach^{16,87} and is recommended by numerous treatment guidelines.^{17,25-28} Patients out of treatment have a much higher mortality rate than those in maintenance treatment.⁸⁸

A significant number of treatment studies have been performed in opioid dependence, including some long-term studies in opioid-dependent individuals^{67,89} and some short- to mid-term clinical experimental studies.^{16,87} Most studies indicate that opioid-dependent patients with and without maintenance therapy have a high risk for inpatient treatments and detoxification.⁹⁰ A 15-year follow-up of an Israeli sample ($N=613$)⁶ found that patients staying longer in treatment had a lower mortality rate. This finding is also supported by many other clinical studies.

	Level of evidence
Possible advantages	
Better safety, less respiratory depression	Strong
Better suppression of illicit opioid use	Some; inconclusive
Less sedation, better social functioning	Some; inconclusive
Easier progress to detoxification	None
Less risk of diversion (BUP/naloxone combination)	Some
Fewer pharmacological interactions	Modest
Less cardiotoxicity	Some
Less alcohol use	Some; inconclusive
Antidepressant effect ⁹¹	Some
Less sweating	Some
Possible disadvantages	
Can precipitate withdrawal at induction	Strong
Unpleasant taste	Some
Lower retention rate	Some

Table 1. Possible advantages of buprenorphine over full opioid agonists. BUP, buprenorphine

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In conclusion, BUP and BUP/naloxone are safe and effective for treating opioid dependence. In addition to MET and BUP, the BUP/naloxone combination is a first-line treatment option. The combination drug may have some advantages and disadvantages compared with MET and BUP (*Table I*). The novel BUP implant may be an interesting alternative for otherwise more stable patients. □

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Actualización del tratamiento de la dependencia a opioides con buprenorfina

La primera elección para el tratamiento de la dependencia a opioides es la terapia de mantenimiento con opioides. Tanto la metadona (MET), agonista opioide total, como la buprenorfina (BUP), un agonista parcial, están autorizados para el tratamiento de la dependencia a opioides. La BUP se diferencia significativamente de la MET en su farmacología, los efectos indeseables y la seguridad. Por ejemplo, el riesgo de depresión respiratoria es menor con BUP que con MET. El riesgo del uso recreativo y de la inyección de BUP se ha reducido al tenerla disponible también en forma de comprimidos que contienen el antagonista opioide naloxona. Esta revisión resume los efectos clínicos de la BUP y analiza posibles factores que puedan sustentar decisiones en relación con el uso de BUP o MET en personas dependientes de opioides.

Actualisation du traitement de la dépendance aux opioïdes par la buprénorphine

Le traitement d'entretien aux opioïdes est l'approche de première ligne dans la dépendance à ces substances. La méthadone (MET), agoniste complet des opioïdes, et la buprénorphine (BUP), agoniste partiel, sont autorisés tous les deux pour le traitement de la dépendance aux opioïdes. La pharmacologie, les effets secondaires et les problèmes de sécurité d'emploi de la BUP sont très différents de celle de la MET. Par exemple, le risque de dépression respiratoire est plus faible qu'avec la MET. Le risque de détournement et d'injection de la BUP a été réduit en la présentant aussi sous forme de comprimés contenant de la naloxone, un antagoniste des opioïdes. Cet article résume les effets cliniques de la BUP et s'intéresse aux facteurs susceptibles d'influer sur la décision d'utiliser la BUP ou la MET chez les personnes dépendantes aux opioïdes.