Journal of Health, Medicine and Nursing
ISSN 2422-8419 An International Peer-reviewed Journal
Vol.119, 2025

Systematic Review to assess the efficacy of buprenorphine compared to methadone as an intervention for opiate dependency

S Adams, *BA, MPH, MSc and* S Alhassan, *BA*
Research and Development Division, Ghana Health Service
Post Office Box MB190, Accra-Ghana
Corresponding author: S Adams (sherifdeen.adams@ghs.gov.gh)

ABSTRACT
Objective: To assess the efficacy of buprenorphine compared to methadone as an intervention for opiate dependency.
Data Sources: Electronic databases (MEDLINE, PubMed, PsychARTICLES, ProQuest, ScienceDirect, PsychINFO and Web of Science)
Study Selection: Published studies from 2000-2014 relating to the efficacy of buprenorphine and methadone as maintenance treatments for opioid dependence. These studies included those that looked at retention and relapse rates, had quantitative evidence, and looked at both males and females. Eight out of 20 studies met these inclusion criteria and were included in the systematic review.
Results: The studies looked at efficacy in terms of retention and relapse rates. With regards to retention, three studies found methadone to be more effective than buprenorphine and the other five found no significant differences between the two groups. In terms of relapse measured by urinalysis, four studies found significantly lower positive opiate urine samples in the buprenorphine group and the other four found no significant difference between the two groups. Several problems have been identified with the research studies used. These include no long-term follow-up, potential for participation bias, varied number of participants across studies and the widely varied length of time studies were conducted over.
Conclusion: This systematic review hasn't helped to resolve the conflicting research in this area. It has further been confounded by the inconsistencies of the research methodologies utilised which has created problems in making any meaningful comparisons. This highlights the need for a standardised shared approach to undertaking research in a way that promotes the opportunity for aggregating research data in a meaningful way. The urgency for this is even greater given the imminent introduction of a buprenorphine depot alternative which could potentially add another layer of clinical uncertainty if not resolved.
Keywords: Buprenorphine, Methadone, Intervention, Opiate Dependency, Systematic Review.
DOI: 10.7176/JHMN/119-02
Publication date: January 30th 2025

INTRODUCTION

According to NICE (2008), an opioid can either be a natural derivative of opium or synthetically produced. The opioid heroin has the greatest potential for dependency; however, all have dependency potential to varying degrees and dependency can develop as quickly as 2-10 days of continuous use. Dependency is usually measured by a strong desire to take the substance, regardless of harm to themselves or others, difficulty in controlling use, physiological withdrawal when not using and a build-up of tolerance. The development of dependency and tolerance can build up so quickly and the risks carried by taking opioids include death, overdose, infection and social problems like homelessness and crime.

According to Lo & Stephens (2000), 5.3% of male and 16.6% of female US prisoners met the criteria for current opioid dependence. Given the negative impacts on people's lives, it is vital to understand the best treatment options available. There are two paths available for people with opioid dependency, maintenance therapy or detoxification. Maintenance therapy is usually considered the better option. Its main goal is harm reduction and stabilisation of lifestyle (Ball & Ross, 1991) and is considered more suitable for those who have been addicted for longer periods, inject or have high levels of polydrug use (NICE, 2008). "Opioid-assisted maintenance programs are among the most important strategies in this respect because they are associated with reduced heroin use and reduced HIV risk behaviour" (van den Brink & Haasen, 2006, p. 640).

Two drug treatments available for maintenance therapy are buprenorphine and methadone (Amato et al, 2004). The efficacy of methadone is more widely accepted. There are however some benefits to using buprenorphine over methadone, mainly due to the potential for fatal overdose with methadone which is less likely with buprenorphine due to its partial agonist properties at μ-opioid sites (Amass et al, 1994).

However, partial agonism is considered to limit its therapeutic efficacy as maximal doses are equivalent to approximately 70 mg of methadone, whereas optimal doses of methadone are around 100 mg with some people needing up to 140 mg per day (Kakko et al, 2007). Other advantages of buprenorphine are it has anti-depressant properties and is less dysphoric than methadone (Paetzold et al, 2000). Buprenorphine also has the added advantage of blocking the effects of exogenous opioids and in turn, reducing illicit opioid use (Walsh et al, 1995) and cravings (Fudala et al, 2003).

It is accepted that people dependent on opiates should have readily accessible and supervised maintenance therapy. One barrier that has been identified that prevents people from entering treatment is stigma, attached to the label of 'drug addict' and associated with attendance to clinics exclusive to the treatment of drug misuse. Buprenorphine already has the benefit of long dose duration, allowing for 2-3 days between administrations, compared to methadone which is required daily (Brady, 2007).

A depot formulation of buprenorphine has been developed which can last for 6 months (Ling, 2012). Although not currently widely prescribed as yet, it is possible that this long-term alternative to methadone could further reduce abuse potential and the stigma of frequent attendance necessary for daily prescription of methadone. Historically clinicians have tended to support methadone as the first line of treatment, based on studies which have evidenced methadone having the greatest likelihood of success. Given that methadone is also a cheaper alternative (Wesson & Smith, 2010) this is unlikely to change without clearer research evidence challenging the status quo.

Therefore, this present review is set to identify further research needs in this area and update existing reviews with recently published buprenorphine compared to methadone as an intervention for opiate dependency. This systematic review aimed to identify and review studies comparing the relative efficacy of buprenorphine and methadone as maintenance treatments for opiate dependence.

METHOD

The following electronic databases were used to search for and identify relevant papers for inclusion in the review: MEDLINE, PubMed, PsychARTICLES, ProQuest, ScienceDirect, PsychINFO and Web of Science. An initial search using the key words "opiate dependence" AND "efficacy of buprenorphine" AND "methadone" and a period of 2000-2014 were used as the search strategy. MEDLINE yielded 6 hits, PubMed- 105, PsychARTICLES-66, ProQuest- 367, ScienceDirect-11, PsychINFO- 57 and Web of Science-92. Another search using the same databases was carried out using the key words; "buprenorphine versus methadone" AND "opiate dependence" using the same date range of 2004-2014. MEDLINE yielded 2 hits, ProQuest- 353, PsychARTICLES-58, PsychINFO-37, PubMed-75, ScienceDirect-2 and Web of Science-61.

Search Selection

From the above, 20 journals were retrieved for a more detailed evaluation. A large number were excluded from the systematic review because they:

- were not related to both buprenorphine and methadone,
- focussed on pain relief/management,
- focussed on HIV and needle sharing,
- focussed on pregnant women,
- were duplicated,
- the full article was unavailable online.

The 20 journals were initially subjected to more in-depth consideration based on the following inclusion criteria:

- Studies specifically comparing buprenorphine to methadone
- Studies specifically looking at opiate dependency
- Studies looking specifically at retention and relapse rates
- Studies published during the previous 10 years; 2000-2014

- Studies that used trials and had quantitative evidence of the results
- Studies that looked at both females and males

Subsequently, 12 of these studies were excluded from the systematic review as they did not meet all elements of the inclusion criteria (see Table 1 for excluded studies).

Table 1: Characteristics of the 12 studies excluded from the systematic review

Study	Reason for Exclusion
Wesson, D.R. & Smith, D.E. (2010).	Review, no primary data is available
Ling, W. et al., (2013)	Review, no primary data available
Cropsey, K. L. et al (2011).	Only looked at females
Whelan, P.J. & Remski, K. (2012).	Review article, no primary data
Kakko, J. et al (2003).	No methadone comparator just used buprenorphine and a placebo
Cozzolino, E. et al (2006).	Replaced methadone with buprenorphine, no comparison
Seifert, J. et al (2005).	Combined both buprenorphine and methadone with carbamazepin
Ponizovsky, A.M. et al (2007)	Looking specifically at the quality of life
Giacomuzzi, S.M. et al (2002)	Looking at quality of life
Marsch, L.A. et al (2005)	Comparing to LAAM
Agar, M. et al (2001)	Qualitative, no quantifiable data
Ahmadi, J. (2003).	Just looked at the males

RESULTS

Table 2: Main characteristics of the studies included in the systematic review

Study Ref	Study	Methods and Design	Participants	Intervention	Outcome	Notes
(1)	Pani, P.P. et al (2000)	Multicenter randomized controlled double-blind study Patients were assigned to MMT (n= 34) or BMT (n= 38) for 6 months	72 opioid-dependent patients recruited from 9 drug treatment units were randomly assigned to either BMT 8 mg/ day or MMT 60 mg/day Inclusion;	The intervention lasted 8 months and the patient received an oral solution of MMT or placebo and a sublingual administration of either BMT or placebo	There was no significant difference with urinalysis, 60.4% with BMT and 65.5% with MMT. A non-significant trend in favor of MMT was	Other outcome measures were craving, self-reported use of heroin, psychosocial adjustment and psychopathy Patients who dropped out of BMT had a higher level of psychopathological

			diagnosis of opioid dependence recognized by DSM IV criteria, dependent for at least 2 years, aged 18-40, remain on location for the entirety of the study. Exclusion; any serious medical condition, alcohol or hypnotic-sedative dependence, using antiepileptics, disulfiram or neuroleptics, pregnant or had doubts about staying in the programme	All doses were administered under the supervision of a nurse. Patients were also involved in a weekly counselling session	observed in retention rates (T= -0.53: P=0.60) Patients also improved in terms of psychosocial adjustment and global functioning.	symptoms and a lower level of psychosocial functioning. No long-term follow-up Thanks to Reckitt & Coman
(2)	Petitjean, S. et al, (2001).	58 patients seeking treatment for opioid dependence were recruited in three outpatient facilities and randomly assigned to substitution with BMT (n=27) or MMT (n=31) Randomized, double-blind 6-week trial using a flexible dosing procedure.	58 participants were recruited and randomly assigned to either BMT (n=27) or MMT (n=31) Patients were excluded if they missed 3 consecutive days of medication or for medical reasons.	To maintain double-blind conditions, all the subjects first received an oral liquid formulation or either a placebo or MMT and BMT 2 mg or 8mg or placebo. They received their medication in a flexible treatment schedule during the first 3 weeks of treatment. All	The retention rate was significantly better in the MMT-maintained group (90 vs 56%; P<0.001). Subjects completing the study in both treatment groups had similar proportions of opioid-positive urine samples (BMT 62%, MMT 59%) Mean heroin craving scores	One subject requested discharge for personal reasons, one was excluded for missing 3 clinic visits, 2 made a request for a BMT detoxification and 8 reported withdrawals and switched to MMT. Patients in BMT reported more serious headaches and more sedation in the MMT group. No long-term follow-up Thanks to Reckitt & Colman

				participants were also required to participate in a 1-hour weekly counselling session.	decreased significantly over time (P= 0.035 and P<0.001)	
(3)	Mattick, R.P. et al (2003)	Randomized double-blind study Buprenorphine (BMT) (n=200) Methadone (MMT) (n=205)	405 opioid-dependent patients recruited from three MMT clinics in Australia Eligibility; diagnosis of opioid dependence measured by DSM IV criteria, 18 years or older, within commuting distance of the clinic, mentally competent to give consent Exclusion; pregnant or nursing women, suffered an acute medical condition, using anticonvulsant medication, in opioid replacement treatment, unable to attend the clinic daily, in a study of BMT previously, currently in another clinical trial.	Patients received BMT or MMT using a flexible dosage regime over 13 weeks During weeks 1-6 patients were dosed daily. From weeks 7-13 BMT patients received double their week 6 dose on alternate days Self-report questionnaires were administered to assess drug use, alcohol consumption, adverse and serious events and withdrawal symptoms	No significant differences in retention rates at 13 weeks. There were no significant between groups differences in morphine-positive urines or self-reported heroin or other illicit drug use.	11 of the patients failed to return to the clinic for a dose and were not included in the trial BMT retained approx 10% less patients than MMT Self-reported drug use, psychological functioning, HIV risk behavior, general health and subjective outcomes were secondary ratings Thanks to Reckitt Beckinser
(4)	Gerra et al, (2004).	Observational non-randomized study	144 participants were recruited from patients participating in	All patients were evaluated for 12 weeks after the beginning	Retention rates in BMT and MMT groups at 12 weeks were	No missed doses and missed clinic visits were reported for both MMT and BMT.

		Patients were assigned to MMT (n=78) or BMT (n=76)	the Parma Addiction Service Program. No exclusion criteria The only eligibility was for patients who had to enter into MMT or BMT maintenance during the 12 months of 2002.	of the opioid substitution therapy. MMT and BMT were administered daily in the outpatient centre 36% of MMT and 39% of BMT were permitted to take home doses three times a week. Treatment was integrated with psychosocial support, including weekly individual counselling and money vouchers for all the patients. Patients with significant psychiatric co-morbidity were also referred to a weekly meeting with the psychiatrist and possible psychotropic medication.	respectively 59.2% and 61.5% with no significant difference. Positive urine testing was similar between BMT and MMT at week 4 and week 12 and positive samples at week 4 were 40.8% and 38.4% and at week 12 44.7% and 46.2% respectively. BMT displayed a significantly lower rate of positive urines for morphine metabolites (25%) as an expression of heroin use than those treated with MMT (32.1%)	No long term follows up Higher doses in both treatments were more effective than low in reducing illicit opioid use.
(5)	Soyka, M. et al, (2008)	This was a 6 month, randomized, flexible-dose study comparing the efficacy of MMT (n=76) and BMT (n=64)	140 participants, who were admitted for treatment of opioid dependence to one of six outpatient clinics in Bavaria were included.	Participants were randomly recruited to either BMT or MMT. All patients also received standardized psychosocial intervention	Overall retention rate of 51% and no significant differences between treatment groups. MMT= 55.3% BMT 48.4% Substance use	Three patients changed from MMT to BMT and eight from BMT to MMT. Predictors of outcome were length of continuous opioid use and age at onset of opioid use, although only sig

			Inclusion criteria were opioid dependence, a history of heroin abuse and minimum age of 18 years. Exclusion criteria; acute psychosis, regular substitution treatment, regular psychosocial treatment in the month before treatment		decreased significantly over time in both groups and was non-significantly lower in BMT.	in the BMT group.
(6)	Pinto, H. Et al, (2010)	Non randomized multi-site trial MMT (n= 227) BMT (n=134) Treatment occurred according to usual clinical practice and was not influenced by participation in the trial.	555 clients recruited from three sites within a community drug service in Norfolk presented for maintenance treatment, of whom 105 were excluded and 44 were not approached due to logistical difficulties covering three sites. Inclusion; new opiate dependent patients, not prescribed either study drug for the preceding month, requesting maintenance treatment (and for whom was appropriate)	Most patients received medication under supervision on most days either in the clinic or a community pharmacy. Take-home doses were introduced on an individual basis Prescriptions for stable subjects were transferred to primary care. Subjects were also seen individually by key workers, initially weekly and then at a frequency negotiated with the patient.	Those prescribed MMT were twice as likely to be retained (hazard ratio for retention was 2.08 and 95% confidence interval [CI]=1.49-2.94 for MMT vx BMT) Those retained on BMT were more likely to suppress illicit opioid use (odds ratio= 2.136, 95% CI=1.509-3.027, p<.001) and achieve detoxification.	Two patients died during the trial, both in the MMT group. 28% of those choosing BMT stated they would have not accessed treatment with MMT. No long term follows up Patients were discharged from the trial if they failed to take their prescription for more than 7 days or were discharged from the service.
(7)	McKeganey, N. et al, (2013)	Participants were randomly drawn from	109 participants, either	Patients attended a structured	A total of 51% had not used heroin	When only data provided by patients who had

		lists of individuals who had been prescribed either MMT (n=56) or BMT (n=53) for 6 months in Glasgow and Fife. All patients received their prescriptions for MMT or BMT from community-based retail pharmacies.	prescribed to MMT or BMT All patients had received a diagnosis of opiate dependence within the past 12 months and had been using MMT or BMT for maintenance for 6 months.	interview on two occasions. At study intake- 6 months and at 8 months post intake Interviews were conducted at local health centers or the patient's houses. Data was collected on demographic variables, drug use history, treatment motivation and self rated physical and mental health. Current heroin use was defined as any heroin use in the past 90 days prior to the study intake assessment.	within the past 90 days, 37.7% of MMT and 71.4% of BMT. There was no significant difference in the retention rates from the 8 month follow up with 62.3% of MMT and 67.9% of BMT returning. In the BMT group, number of days heroin use reduced from 38.64 at intake to 8.50 at 8 month follow up. Compared to MMT with 37.40 at intake to 24.15 at follow up.	90-day point abstinence from heroin use at study intake and who provided follow-up data were included, the rates of 90-day point prevalence abstinence at 8-month follow up were similarly and statistically equivalent for both medication groups. BMT- (87.5%) and MMT (100%) Small sample size No follow up Thanks to Reckitt Benckiser
(8)	Hser, Y. et al (2013).	A multi- site randomized trial. BMT (n= 740) MMT (n=529). Compensation was provided in accordance with local site policies	A total of 1269 patients recruited from nine federally licensed opioid treatment programmes across the United States	Participants remained on the study medication for 24 weeks, and were tapered off medication over <8 weeks or referred for ongoing clinical treatment, with study completion by week 32. Daily observed medication administration except when take home	Treatment completion rate was 74% for MMT versus 46% for BMT (P<0.01); MMT increased to 80% when the max dosage reached or exceeded 60 mg per day. BMT completion rate increased linearly with higher doses, reaching 60% with doses of	Two females were excluded who became pregnant Lower medication dose, younger age, Hispanic and use of opioids, amphetamine, cannabinoids or cocaine were associated with dropout from the trial No long-term follow-up Males in BMT group were less likely to dropout

				medications were permitted Weekly urine assessments and 4 weekly self reported questionnaires	30-32 mg/ day. Positive opioid urine results were significantly lower [odds ratio (OR)=0.63, 95% confidence interval (CI)-0.52-0.76, P<0.001] among BMT relative to MMT in the first 9 weeks of treatment	Those with higher BMT dose were 1.04 times more likely to drop out than those with lower MMT dose Thanks to Reckitt Benckiser

DISCUSSION

This systematic review sought to assess the efficacy of buprenorphine compared to methadone as interventions for opiate dependency. Eight studies were selected to evaluate this, with a total number of participants (n=2703). All of these studies equate efficacy with two specific factors, i.e. retention and relapse rates, as measured by completion of the study and urinalysis respectively[1]. The systematic review appears to support previous research indicating that both forms of treatment are viable options for opiate dependence maintenance therapy. There is not a particularly clear difference between the two as far as retention and relapse are concerned.

In terms of which drug is more effective in relation to retention rates the one area of agreement is that none of the studies found buprenorphine to be more effective than methadone. Further, out of the eight studies, three showed methadone to have significantly better retention rates compared to buprenorphine (Hser et al, 2013; Pinto et al, 2010; Petitjean et al, 2001). The remaining five studies found no significant differences between the methadone or buprenorphine treatment conditions in relation to retention rates. It should be noted that Hser et al (2013) had the largest sample size (n=1269) amongst all the studies reviewed which has greater power by reducing sampling error. This adds further weight to the view that methadone is associated with a higher level of retention in the treatment of people with opiate dependence, but without further research this cannot be confirmed.

As far as which drug was more effective to relapse, as established through urinalysis, no studies found methadone to be more effective than buprenorphine. In addition, four of the studies found non-significance between group results in terms of relapse measured by urinalysis (Mattick et al, 2003; Soyka et al, 2008; Pettijean et al, 2001; Pani et al, 2000). The remaining four studies found buprenorphine to have significantly lower opioid-positive urine samples at the end of the study. This suggests buprenorphine to be more, or at least as, effective in preventing relapse in opioid use.

Although relapse and retention rates are appropriate measures of efficacy to drug dependency, they should not be considered the only measures and their exclusive use imposes a limited view of what efficacy amounts to. For instance, two studies that were not included in the systematic review were Ponizovsky et al (2007) and Giacomuzzi et al (2002). Both of these had a primary focus on quality-of-life measures. These were excluded because no other studies of this nature were returned in the search process. According to Giacomuzzi et al (2002), quality of life is an important measure in not only assessing the benefits of particular health programmes but also in helping to predict patient suitability for a particular treatment.

None of the studies were subjected to long-term follow up so the information provided regarding relapse is subject generally to a limited period. These studies do not indicate what happened to people who dropped out of the trial or what happened to those following the completion of the study. In addition, there is a large variation in the length of studies which ranged from 6 weeks (Petitjean et al, 2001) to 60 weeks (McKeganey et al, 2013), the mean being 23.38 weeks. This presents difficulties in making meaningful comparisons within the data set which is inconsistent in its relapse results measured by urinalysis.

There are several limitations in comparing studies that don't use standardized measures. The sample sizes used within the eight studies differ greatly, as do the length of time the studies were carried out. Only three are double-blind (Mattick et al, 2003; Petitjean et al, 2001; Pani et al, 2000) and in one study the patients chose which treatment option they wanted (Pinto et al, 2010). Some patients were also allowed to take their medication home with them (Pinto et al, 2010). In contrast, the most controlled trial was carried out with the participants living in the clinic for six months (Pani et al, 2000).

One methodological flaw that exists in all eight of the studies was no long-term follow-up took place. This would have particular implications in considering issues to do with relapse. Participation bias may have also occurred within these studies as all participants were recruited from clinics or in one case a pharmacy so would have already been potentially committed to treatment, excluding the wider population of drug users not engaged in a treatment programme.

According to Petitjean et al (2001) buprenorphine in tablet formation is only 75%-80% as effective as the liquid form. Six of the studies specify having used the tablet form and two have not included this information. This does raise an issue that potentially like for like is not being compared in relation to buprenorphine. It is also interesting to note that five of the eight studies were funded or part funded by Reckitt Benckiser, formerly Reckitt Colman, who manufacture Subutex, Suboxone and Temgesic, the tablet forms of buprenorphine. This raise concerns that the funding is provided by an organization that has a vested commercial interest in the research outcomes.

Buprenorphine has the added advantage of being an 'office-based' treatment, providing easier non-stigmatizing access to the treatment of opiate dependence. However, there is a danger of seeing the issues solely within a medical model. This risks not addressing the wider social context of how drug dependency is formed and maintained. The phrase 'maintenance therapy' speaks volumes! Undoubtedly the physiological aspects need to be addressed but this alone will not address the likely wider impacts of drug dependency on an individual's life, e.g. insecure housing, unemployment, fragmented relationships and poor engagement with education. To address these requires a multi-disciplinary approach. In research terms, this requires a much broader definition of efficacy and how it is measured.

In terms of future research, the development of the buprenorphine depot which lasts for periods of up to 6 months at a time has the potential to further reduce stigma, abuse potential, and criminal activity of selling buprenorphine or opiate substitutes on the street. Whether these benefits are achieved will only be demonstrated through subsequent research.

CONCLUSION

Eight (8) studies were included in this systematic review to assess the efficacy of buprenorphine compared to methadone as an intervention for opiate dependency. All were randomised controlled trials. Out of the eight studies, three showed methadone to have significantly better retention rates compared to buprenorphine. The remaining five studies found no significant differences between the methadone or buprenorphine treatment conditions in relation to retention rates. This highlights the need for a standardised shared approach to undertaking research in a way that promotes the opportunity for aggregating research data in a meaningful way. The urgency for this is even greater given the imminent introduction of a buprenorphine depot alternative which could potentially add another layer of clinical uncertainty if not resolved.

DECLARATIONS

Ethics Approval and consent to participate

There is no ethical approval for this study as it is a systematic review. The results will be submitted to peer-reviewed journals for publication and presented at conferences.

Competing interests

The author declares that he has no competing interests.

Funding
This work received no funding support.

Consent for publication
Not applicable

Availability of data and materials
Upon request

Authors' contributions
SA conceived the study and drafted and reviewed the manuscript. SA also extracted data from the included studies.

REFERENCES

1. Agar, M., Bourois, P., French, J. & Murdoch, O. (2001). Buprenorphine: "Field Trials" of a New Drug. Qualitative Health Research. Sage. Retrieved from http://qhr.sagepub.com/content/11/1/69 on 14.03.14.
2. Ahmadi, J. (2003). Methadone versus buprenorphine maintenance for the treatment of heroin-dependent outpatients. Journal of Substance Abuse Treatment. 24, 217-220.
3. Amass, L., Bickel, W.K., Higgins, S.T. & Hughes, J.R. (1994). A preliminary investigation of outcome following gradual or rapid buprenorphine detoxification. Journal of Addictive Disorders. 13, 33-45.
4. Amato, L., Davoli, M., Ferri, M., Gowling, L. & Perucci, C.A. (2004). Effectiveness of systematic reviews. Drug and Alcohol Dependency. 73, 219-226.
5. Ball, J.C. & Ross, A. (1991). The Effectiveness of Methadone Maintenance Treatment Patients, Programs and Outcomes. Springer: New York.
6. Brady, K.T. (2007). Medical Treatment of Opiate Dependence: Expanding Treatment Options. The American Journal of Psychiatry. 164 (5): 702-704.
7. Cropsey, K.L., Lane, P.S., Hale, G.J., Jackson, D.O., Clark, B.C., Ingersoll, K.S., Islam, M.A. & Stitzer, M.L. (2011). Results of a pilot randomized controlled trial of buprenorphine for opioid-dependent women in the criminal justice system. Drug and Alcohol Dependence. 119, 172-178.
8. Cozzolino, E., Guglielmino, L., Vigezzi, P., Marzorati, P., Silenzio, R., De Chiara, M., Corrado, F. & Cocchi, L. (2006). Buprenorphine Treatment: A Three-Year Prospective Study in Opioid-Addicted Patients of a Public Out-Patient Addiction Center in Milan. The American Journal on Addictions. 15, 246-251.
9. Gerra, G., Borella, F., Zaimovic, A., Moi, G., Bussandri, M., Bubici, C. & Bertacca, S. (2004). Buprenorphine versus methadone for opioid dependence predictor variables for treatment outcomes. Drug and Alcohol Dependence. 75, 37-45.
10. Giacomuzzi, S.M., Ertl, R.M., Kemmler, G., Rossler, H., Hinterhuber, H. & Kurz, M. (2003). Buprenorphine versus methadone maintenance treatment in an ambulant setting: a health-related quality of life assessment. Addiction. 98, 693-702.
11. Gossop, M., Stewart, D., Browne, N. & Marsden, J. (2002). Factors associated with abstinence, lapse or relapse to heroin use after residential treatment: protective effect of coping responses. Addiction. 97, 1259-1267.
12. Hser, Y-I., Saxon, A.J., Huang, D., Hasson, A., Thomas, C., Hillhouse, M., Jacobs, P., Teruya, C., McLaughlin, P., Wiest, K., Cohen, A. & Ling, W. (2013). Treatment retention among patients randomized to buprenorphine/naloxone compared to methadone in a multi-site trial. Addiction. 109, 79-87.
13. Kakko, J., Svanborg, K.D., Kreek, M.J. & Hellig, M. (2003). 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomized, placebo-controlled trial. The LANCET. 361, 662-668.
14. Lo, C.C. & Stephens, R.C. (2000). Drugs and prisoners: treatment needs on entering prison. Journal of Drug and Alcohol Abuse. 26, 229-245.
15. Ling, W. (2012). Buprenorphine implant for opioid addiction. Pain Management. 2(4): 345-350.
16. Ling, W., Mooney, L. & Torrington, M. (2013). Buprenorphine for opioid addiction. Neuropsychiatry. 3(5): 535-543.
17. Marsch, L.A., Stephens, A.C., Mudric, T., Strain, E.C., Bigelow, G.E. & Johnson, R.E. (2005). Predictors of Outcome in LAAM, Buprenorphine, and Methadone Treatment for Opioid Dependence. Experimental and Clinical Psychopharmacology. 13 (4): 293-302.
18. Mattick, R.P., Ali, R., White, J.M., O'Brien, S., Wolk, S. & Danz, C. (2003). Buprenorphine versus methadone maintenance therapy: a randomized double-blind trial with 405 opioid-dependent patients. Addiction. 98, 441-452.

19. McKeganey, N., Russell, C. & Cockayne, L. (2013). Medically assisted recovery from opiate dependence within the context of the UK drug strategy: Methadone and Suboxone (buprenorphine-naloxone) patients compared. Journal of Substance Abuse Treatment. 44, 97-102.
20. NICE (2008). Opioid dependence summary. Clinical Knowledge Summary. Accessed from http://cks.nice.org.uk/opioid-dependence#!topicsummary on 02.04.14
21. Paetzold, W., Eronat, V., Seifert, J., Holze, I., Emrich, H.M. & Schneider, U. (2000). Detoxification of poly-substance abusers with buprenorphine. Effects on affect, anxiety and withdrawal symptoms. Nervenartz. 71: 722-729.
22. Pani, P.P., Maremmani, I., Pirastu, R., Tagliamonte, A. & Gessa, G.L. (2000). Buprenorphine: a controlled clinical trial in the treatment of opioid dependence. Drug and Alcohol Dependence. 60, 39-50.
23. Petitjean, S., Stohler, R., Deglon, J., Livoti, S., Waldvogel, D., Uehlinger, C. & Ladewig, D. (2001). Double-blind randomized trial of buprenorphine and methadone in opiate dependence. Drug and Alcohol Dependence. 62, 97-104.
24. Pinto, H., Maskrey, V., Swift, L., Rumball, D., Wagle, A. & Holland, R. (2010). The SUMMIT Trial: A filed comparison of buprenorphine versus methadone maintenance treatment. Journal of Substance Abuse Treatment. 39, 340-352.
25. Ponizovsky, A.M. & Grinshpoon, A. (2007). Quality of Life Among Heroin Users on Burepnorphine versus Methadone Maintenance. The American Journal of Drug and Alcohol Abuse. 33, 631-642.
26. Seifert, J., Metzner, C., Paetzold, W., Borsutzky, M., Ohlmeier, M., Passie, T., Hauser, U., Becker, H., Wiese, B., Emrich, M. & Schneider, U. (2005). Mood and affect during detoxification of opiate addicts: a comparison of buprenorphine versus methadone. Addiction Biology. 10, 157-164.
27. Soyka, M., Zingg, C., Koller, G. & Kuefner, H. (2008). Retention rate and substance use in methadone and buprenorphine maintenance therapy and predictors of outcome: results from a randomized study. International Journal of Neuropsychopharmacology. 11, 641-653.
28. Walsh, S.L., Preston, K.L., Bigelow, G.E. & Stitzer, M.L. (1995). Acute administration of buprenorphine in humans: partial agonist and blockade effects. Journal of Pharmacology and Experimental Therapeutics. 274 (1): 361-372.
29. Wesson, D.R. & Smith, D.E. (2010). Buprenorphine in the Treatment of Opiate Dependence. Journal of Psychoactive Drugs. 42 (2): 161-175.
30. van den Brink, W & Haasen, C. (2006). Evidenced-Based Treatment of Opioid-Dependent Patients. Canadian Journal of Psychiatry. 51 (10): 635-646.