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Practice Guidance for Buprenorphine for the Treatment of Opioid Use Disorders: Results of an Expert Panel Process

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Abstract

Background—Although numbers of physicians credentialed to prescribe buprenorphine has increased over time, many credentialed physicians may be reluctant to treat individuals with opioid use disorders due to discomfort with prescribing buprenorphine. Though prescribing physicians are required to complete a training course, many have questions about buprenorphine and treatment guidelines have not been updated to reflect clinical experience in recent years. We report on an expert panel process to update and expand buprenorphine guidelines.

Methods—We identified candidate guidelines through expert opinion and a review of the literature and used a modified RAND/UCLA Appropriateness Method to assess the validity of the candidate guidelines. An expert panel completed two rounds of rating, with a meeting to discuss the guidelines between the first and second rating.

Results—Through the rating process, expert panel members rated 90 candidate guideline statements across eight domains, including candidacy for buprenorphine treatment, dosing of buprenorphine, psychosocial counseling, and treatment of co-occurring depression and anxiety. A total of 65 guideline statements (72%) were rated as valid. Expert panel members had agreement

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AUTHOR CONTRIBUTIONS

Drs. Farmer, Flaherty, Lindsay, and Stein and Ms. Williams contributed to all stages of the research, from design to manuscript completion. Dr. Schuster, Ms. Ayers, and Ms. Cilia contributed to the research conception, collection of data, and writing of the manuscript. Drs. Mandell and Gordon contributed to the analysis and interpretation of the results and the writing of the manuscript.

in some areas, such as the treatment of co-occurring mental health problems, but disagreement in others, including the appropriate dosing of buprenorphine given patient complexities.

Conclusions—Through an expert panel process, we developed an updated and expanded set of buprenorphine treatment guidelines; this additional guidance may increase credentialed physicians' comfort with prescribing buprenorphine to patients with opioid use disorders. Future efforts should focus on appropriate dosing guidance and ensuring that guidelines can be adapted to a variety of practice settings.

Keywords

opioid use disorders; buprenorphine; clinical practice guidelines

INTRODUCTION

According to recent estimates, approximately 4.5 million individuals used prescription pain medication for non-medical use in the past month, and 300,000 individuals were regular users of heroin[1] with nearly 2 million meeting diagnostic criteria for an opioid use disorder.[1,2] Unfortunately, the number of people receiving formal treatment for an opioid use disorder are low: only 15% receive treatment and the number receiving opioid agonist treatment is much lower.[3]

Prior to 2002, opioid agonist treatment was only available in licensed methadone treatment programs, where patients face well-known barriers to care including physical distance from such programs, insurance restrictions, complicating co-existing mental disorders, and others.[4] Consequently, fewer than 25% of patients with opioid use disorders have ever received methadone.[5] In 2002, buprenorphine was approved for use in regular office-based treatment settings by physicians who qualify under the Drug Addiction and Treatment Act (DATA 2000).[6] Since buprenorphine's approval, the number of physicians certified to prescribe buprenorphine has continued to increase, with 15,662 physicians certified at the end of 2008, and 23,686 currently.

The availability of an opioid agonist that can be prescribed outside of methadone clinics was welcomed by many addiction experts as an opportunity to increase the number of patients with opioid use disorders receiving opiate agonist treatment,[7] especially among those unable or unwilling to attend methadone clinics.[8,9] While buprenorphine treatment has increased over time, [7,10–13] the number of individuals with opiate use disorders receiving opiate agonist treatment has not increased substantially.[14]

One barrier to buprenorphine treatment may be physician discomfort or uncertainty with prescribing buprenorphine. Before receiving credentials to prescribe buprenorphine, physicians must attend an eight-hour training course on the treatment and management of patients with opioid use disorders. The training course is offered by a number of organizations and is often completed through web-based teaching modules. There are currently no requirements for continuing education related to buprenorphine prescribing, and despite receiving the initial training, many physicians may continue to have questions or feel unprepared to treat this population. Indeed, training itself has not been found to necessarily

increase buprenorphine prescriptions.[15–17] To address a potential need for additional support and education related to buprenorphine prescribing, the Substance Abuse and Mental Health Services Administration/Center for Substance Abuse Treatment (SAMHSA/CSAT) developed the Physician Clinical Support System-Buprenorphine (PCSS-B), which is intended to connect prescribing physicians with experienced mentors and other educational resources, though the extent to which physicians use this resource is unclear.[18]

Additional guidance for physicians on the use of buprenorphine is warranted, given common physician questions about dosage, frequency and type of concurrent psychosocial treatment, use in special populations, diversion, co-occurring physical and mental health disorders, and treatment duration.[17,19–23] The most widely available clinical practice guidelines for buprenorphine use are SAMHSA's Treatment Improvement Protocol (TIP 40), were published in 2004,[24] and developed prior to the widespread use of buprenorphine,[25] and subsequent guideline development efforts to develop practice guidelines for buprenorphine have notable limitations. For example, the 2009 SAMHSA Technical Assistance Publication (TAP) 30 guideline for buprenorphine treatment for nurses[26] relied on TIP 40 for substantial amounts of content, while the 2009 Veterans Affairs/Department of Defense (VA/DoD) Clinical Practice Guidelines for Management of Substance Use Disorders[27] addresses the buprenorphine evidence base, but focuses on the management of substance use disorders more generally.[28] The 2010 Vermont Buprenorphine Practice Guidelines[29] were developed to address the use of buprenorphine within a single state system. As a result, the TIP 40 guidelines are still the most comprehensive existing guideline for buprenorphine treatment.

In the years since the TIP 40's publication, substantial clinical experience has accrued through real-world use of buprenorphine. "Best Practices" of buprenorphine prescribing are not well known, and often clinical practice is guided by formulary guidances[30] or insurer mandates.[31] In addition, there are questions about the quality of buprenorphine treatment, such as the adequacy of concurrent behavioral heath care,[32] which updated guidelines could help to address. In this paper we report on the results from an effort to update and expand existing buprenorphine treatment guidelines for prescribing physicians through the use of a formal, non-consensus-based rating methodology that combined expert opinion of actual rural and urban buprenorphine practitioners and clinicians with a comprehensive review of the evidence in the literature of what constitutes good practice for the use of buprenorphine to treat opioid use disorders.

METHODS

Identification of Candidate Guidelines

Existing buprenorphine clinical guidelines were identified through a review of the peer-reviewed literature and nominations from addiction medicine and primary care experts. Clinical practice guidelines from the Substance Abuse and Mental Health Services Administration (SAMHSA), Department of Veterans Affairs, and Department of Defense were identified and included in the review.[24,27]

To elicit buprenorphine treatment related concerns or questions not covered by existing guidelines, we conducted a one-day conference focusing on buprenorphine use with

approximately 60–80 treatment providers, state and county health officials, patient advocates, clinical researchers, and health insurance representatives. Based on the conference discussions of current practices and issues, we identified several areas in which clinical practice and recent research had gone beyond the existing guidelines, particularly around candidacy for treatment, dosing, duration of treatment, and co-occurring mental health and other substance use problems.

To develop a set of candidate guidelines to be included in updated and expanded treatment guidance and to be reviewed and rated by an expert panel, we first compiled all existing guidelines, categorized by phase of treatment (i.e. initiation, dosage, duration, concurrent therapy). From these, we selected candidate guidelines to retain in the new guidance based on the strength of the evidence for each guideline. We next conducted a search of the peer-reviewed literature on the use of buprenorphine and developed a number of new candidate guidelines to address the gaps in treatment guidance identified during the conference.

This work was organized and led by staff from the Community Care Behavioral Health Organization, a non-profit managed behavioral health care company that is part of the UPMC Insurance Division, which also funded the work. The project was reviewed and considered exempt by the University of Pittsburgh IRB.

Expert Consensus Process

The candidate guidelines were assessed using a modified RAND/UCLA Appropriateness Method[32] involving two rounds of expert panel ratings, provided by 10 experts in addiction medicine and primary care. The expert panel members were selected to ensure a variety of clinical and research expertise, as well as diversity of practice setting (e.g. rural/urban). Most panel members were geographically proximal to the study site. Potential expert panelists were nominated based on a literature review (to identify researchers with relevant expertise) and/or were nominated by other known experts in the field. Final expert panel members were selected in concert with the study funder, and all panel members were provided an honorarium for their participation. While the RAND/UCLA Appropriateness Method recommends having 9 expert panel members,[32] we included one additional panel member from a primary care setting to ensure adequate representation across treatment settings. The first guideline rating (Round One) was completed by panel members in advance of an expert panel meeting to discuss the guidelines. Immediately following the expert panel meeting, panelists re-rated the candidate guidelines (Round Two). Individual ratings were kept confidential and each panelist had equal weight in determining the final ratings.

For Round One, panelists were sent a list of candidate guidelines and a rating form. A brief literature review document with a summary of recent research and relevant evidence for each guideline domain was also included. Panelists were prompted to rate the validity of each candidate indicator on a 1–9 point scale, where 1 = definitely not valid, 5 = uncertain or equivocal validity and 9 = definitely valid. Panelists were instructed that a guideline statement should be considered valid if a) adequate scientific evidence or professional consensus exists to support a link between that practice and a health benefit to the patient with opiate dependence; b) a provider with high rates of adherence to that practice would be

considered a higher quality provider; and c) a majority of factors that determine adherence to the practice are under the influence of the provider. Panelists also were given the opportunity to provide comments on each guideline statement with respect to possible changes to the guideline and potential barriers to guideline implementation, as well as to modify or propose new guidelines and submit additional literature or evidence as appropriate.

Round One ratings from each expert panel member were compiled and median ratings of validity and agreement for each guideline statement were determined. Guideline statements with a median rating of 7 or higher, and with no more than two ratings outside of the 7–9 range (i.e., agreement), were deemed valid. Guideline statements with a median rating of 3 or lower, and with no more than two ratings outside of the 1–3 range, were deemed invalid. The remaining guideline statements (e.g. those with median ratings in the 4–6 range regardless of agreement, as well as guideline statements with any median rating but without agreement) were considered to have indeterminate validity.

Round One results were used to guide a four-hour expert panel webinar meeting. In preparation for the meeting, panelists were provided with an individualized copy of the proposed guidelines, with the group distribution of Round One ratings overlaid with his or her individual ratings. During the expert panel meeting, each guideline statement with indeterminate validity was discussed, and the meeting moderator guided the discussion to address discordant views and generate revised or new guideline statements accordingly.

Immediately following the expert panel meeting, each panelist re-rated all guideline statements discussed during the meeting, as well as any modified guidelines generated during the meeting (Round Two). The Round Two ratings were analyzed to assess validity and agreement and only those guideline statements with high validity and agreement were retained in the final set of guidelines.

RESULTS

Candidate Guidelines

A total of 90 candidate guideline statements were rated by the expert panel. These guideline statements fell into eight guideline domains related to the use of buprenorphine to treat opioid dependence. Three domains focused on the period prior to buprenorphine initiation, including 1) assessments to determine candidacy for buprenorphine treatment, 2) selection of candidates for buprenorphine treatment, and 3) development of a treatment contract. Three domains focused on buprenorphine prescribing and monitoring, including 1) dosing of buprenorphine, 2) monitoring buprenorphine treatment adherence and effectiveness, and 3) discontinuation of buprenorphine treatment. Two domains focused on concurrent treatment associated with buprenorphine treatment, including psychosocial counseling and treatment of co-occurring mild-to-moderate depression and anxiety.

Round One Ratings

Of the guideline statements rated during Round One, 50 were deemed ‘valid’ by the panel; that is, the median rating was in the 7–9 range and no more than two experts rated the

guideline statement outside that range. The remaining 39 guideline statements were deemed of 'indeterminate validity' and were discussed during the expert panel meeting. None of the guideline statements were rated 'invalid' by the expert panel during the first round of ratings. Certain subgroups of indicators exhibited greater levels of disagreement or uncertainty among the expert panel members, including those having to do with selection of candidates for treatment, dosing and duration of treatment, and concurrent psychosocial counseling.

Expert Panel Discussion

During the expert panel meeting, discussion focused on the 39 guideline statements that had been rated as having indeterminate validity in Round One. The expert panel discussion centered on concerns from panelists about the evidence-base of certain guideline statements, the practicality and feasibility of following the guideline statements, and attention to differences in practice settings and how these may affect providers' ability or willingness to follow the guidelines. Recognizing that buprenorphine is prescribed to a heterogeneous population of individuals in a range of clinical settings, from large sophisticated substance abuse treatment systems to individual psychiatrist and primary care physician offices, panelists emphasized the importance of guideline flexibility and applicability for settings with a wide range of available resources. Panelists also specifically discussed the importance of developing specific resources for prescribers in smaller practices (e.g. how to establish linkages and make referrals, how to conduct a thorough assessment with a small staff) to facilitate good clinical care regardless of the setting. Panelists also emphasized that guidelines should be informative, but not a replacement for clinical judgment about the best approach for an individual. Optimally they would serve as an indicator for when extra efforts should be taken to engage and re-engage individuals in treatment, and not as a rationale for limiting or restricting care.

As a result of the discussion, panelists suggested rewording 19 guideline statements and including an additional 6 guideline statements for the Round Two rating. In general, the rewording of guideline statements resulted in reducing specificity; for example, a guideline statement related to selection of candidates for buprenorphine treatment was changed from "mild to moderate opiate dependence" to "opiate dependence."

Round Two Ratings

Of the 45 guideline statements rated during Round 2 (39 'indeterminate' guideline statements from Round One and 6 new guideline statements generated from the expert panel meeting), 15 were rated as valid, 27 rated as 'indeterminate validity', and 3 were rated as 'invalid'.

Guideline Statements Rated as Valid

Through the rating process, a total of 65 guideline statements were rated as valid, defined as a median score of 7 or greater,[32] with agreement among the panelists. The 65 guideline statements rated as valid are 72% of the 90 initial candidate guidelines, a proportion similar to that found in other studies.[33] Table 1 lists each guideline statement rated as valid, along with the median validity of each statement.

DISCUSSION

Buprenorphine can play an important role in increasing the use of effective treatment for opioid use disorders, and updated treatment guidance for prescribing physicians has the potential of facilitating greater use of buprenorphine by addressing existing clinical challenges or uncertainty among clinicians regarding its use in actual clinical practice.[19,22] The goal of this current work was to develop updated guidance for clinicians using buprenorphine to treat individuals with opioid use disorders, drawing upon expert opinion and clinical experience obtained through the increasing use of buprenorphine.

We found a substantial amount of consensus among the expert panel in a number of the domain areas, including the nature and extent of assessments conducted prior to prescribing buprenorphine, the approach to and necessity of treating comorbid mental health disorders, and the importance and content of treatment contracts (or agreements) that should be agreed to prior to initiating buprenorphine treatment. The panel's consensus in these areas is consistent with the empirical literature, which has documented the high prevalence of comorbid mental health disorders among individuals with opioid dependence,[34–37] and the need for adequate assessments prior to initiating buprenorphine to prevent complications.[38,39] Such consensus regarding the importance of such activities is encouraging, as it can also contribute to the development of clinical pathways and other tools, which can increase access while improving the appropriateness, safety and outcomes of the implementation of such processes in healthcare settings.[40]

However, in domains concerned primarily with the prescribing of buprenorphine, such as dosing, monitoring, and duration, a lack of consensus was much more common. During discussion of the candidate guidelines in these areas, panel members frequently observed that dosing, monitoring, and duration of buprenorphine treatment decisions are influenced by a wide range of nuanced clinical and contextual factors, such as the availability of social support, stability of housing and employment, and concerns about diversion,[20,41] making a consensus in these areas much more challenging to achieve. Panelists also disagreed about whether patients with previous buprenorphine treatment attempts would be good candidates for treatment, with panel members noting the diverse factors associated with treatment attempts. Such factors have challenged efforts to increase the use of medication algorithms or pathways in outpatient or community settings for other disorders,[42–44] and reflect the complexity in many clinical decisions regarding the appropriate and effective use of medications. Yet, at a time when uncertainty regarding how best to use proven medications such as buprenorphine may be one of the factors constraining more widespread uptake, there is a need for continued research to better inform the decisions of physicians serving socially complex and heterogeneous patient populations.

Panelists noted that the utility of treatment guidelines depends in part on their flexibility in regards to treatment setting. Given the variety in provider settings, guidelines should strive to be widely applicable and offer specific suggestions to fit smaller providers (e.g. how to establish linkages and make referrals, how to conduct a thorough assessment with a small staff) to ensure high-quality clinical care regardless of the setting. This is consistent with recent research that has found that uptake of clinical practice guidelines can be improved

with modifications to allow adaptation of the guidelines relative to resource availability and other practice setting factors.[45,46] While such adaptation was outside the scope of the current project, future efforts should consider how to adapt buprenorphine treatment guidelines to accommodate the diverse practice settings and resource availability among credentialed providers.

There are several limitations to this study. First, all of the expert panelists were primarily located in one region of the country. Other studies have described geographical variation in the treatment of opiate dependence;[14,47,48] experts practicing in other areas of the country may have different perspectives and opinions on buprenorphine treatment than those who participated in this study. Second, while we conducted a literature review to identify recent research on the use of buprenorphine, we did not conduct a systematic literature review to identify best buprenorphine treatment practices. Rather, we primarily relied on clinical expertise to draft new guideline statements and the expert panel to come to consensus. In doing so, we may have omitted important aspects of treatment that should be included in future efforts to develop additional treatment guidelines for buprenorphine. In particular, these guidelines do not address issues related to diversion and illegal use, which have become important considerations in buprenorphine treatment.[49,50] The guidelines also do not address buprenorphine induction location, in particular the extent to which induction could or should occur at home.[51] Finally, we note that the level of research evidence to support many of the guideline statements is weak. Buprenorphine treatment for opioid use disorders, especially in office-based settings, is a relatively recent treatment advance, and the empirical base supporting the effectiveness of treatment approaches is still evolving. Much additional research is warranted to determine the clinical utility of the processes described in these guidelines for improving individual outcomes.

Conclusion

In this study, we used an expert consensus process to update clinical practice guidelines for the use of buprenorphine to treat opiate use disorders. As noted above, one reason for a lower than anticipated uptake in the use of buprenorphine may be related to physicians' discomfort or uncertainty about prescribing and monitoring individuals on this medication. These updated guidelines provide an additional resource to physicians currently prescribing or considering prescribing buprenorphine and may serve to inform future efforts to develop and disseminate clinical practice guidelines for buprenorphine treatment. While the expert panel process revealed areas of disagreement – for example, there was no consensus on setting a maximum daily dose of buprenorphine – there was considerable consensus around other aspects of treatment, namely around identifying appropriate candidates for treatment, developing a treatment contract, and providing concurrent mental health treatment for patients with complex needs.

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References

1. Substance Abuse and Mental Health Services Administration, U.S. Department of Health and Human Services. . Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings. Rockville, MD: SAMHSA; 2013.
2. American Psychiatric Association APADSMTF. . Diagnostic and statistical manual of mental disorders: DSM-5. Washington, D.C: American Psychiatric Association; 2013.
3. Becker WC, Fiellin DA, Merrill JO, et al. Opioid use disorder in the United States: insurance status and treatment access. Drug Alcohol Depend. Apr 1; 2008 94(1–3):207–213. [PubMed: 18222051]
4. Oliva EM, Maisel NC, Gordon AJ, et al. Barriers to use of pharmacotherapy for addiction disorders and how to overcome them. Current Psychiatry Reports. 2011; 13(5):374–391. [PubMed: 21773951]
5. American Methadone Treatment Association. . Methadone maintenance program and patient census in the US. New York: American Methadone Treatment Association; 1998.
6. Arfken CL, Johanson CE, di Menza S, et al. Expanding treatment capacity for opioid dependence with office-based treatment with buprenorphine: National surveys of physicians. J Subst Abuse Treat. Sep; 2010 39(2):96–104. [PubMed: 20598829]
7. Ducharme LJ, Abraham AJ. State policy influence on the early diffusion of buprenorphine in community treatment programs. Subst Abuse Treat Prev Policy. 2008; 3:17. [PubMed: 18570665]
8. O'Connor PG, Oliveto AH, Shi JM, et al. A randomized trial of buprenorphine maintenance for heroin dependence in a primary care clinic for substance users versus a methadone clinic. Am J Med. Aug; 1998 105(2):100–105. [PubMed: 9727815]
9. Sullivan LE, Chawarski M, O'Connor PG, et al. The practice of office-based buprenorphine treatment of opioid dependence: is it associated with new patients entering into treatment? Drug Alcohol Depend. Jul; 2005 79(1):113–116. [PubMed: 15943950]
10. Gordon AJ, Fiellin DA, Friedmann PD, et al. Update in addiction medicine for the primary care clinician. J Gen Intern Med. Dec; 2008 23(12):2112–2116. [PubMed: 18830761]
11. Gordon AJ, Trafton JA, Saxon AJ, et al. Implementation of buprenorphine in the Veterans Health Administration: results of the first 3 years. Drug Alcohol Depend. Oct 8; 2007 90(2–3):292–296. [PubMed: 17493771]
12. Ling W, Jacobs P, Hillhouse M, et al. From research to the real world: buprenorphine in the decade of the Clinical Trials Network. J Subst Abuse Treat. Jun; 2010 38(Suppl 1):S53–60. [PubMed: 20307796]
13. Roman PM, Abraham AJ, Knudsen HK. Using medication-assisted treatment for substance use disorders: evidence of barriers and facilitators of implementation. Addict Behav. Jun; 2011 36(6): 584–589. [PubMed: 21377275]
14. Stein BD, Gordon AJ, Sorbero M, et al. The impact of buprenorphine on treatment of opioid dependence in a Medicaid population: recent service utilization trends in the use of buprenorphine and methadone. Drug Alcohol Depend. Jun 1; 2012 123(1–3):72–78. [PubMed: 22093488]
15. Gordon AJ, Liberto J, Granda S, et al. Outcomes of DATA 2000 certification trainings for the provision of buprenorphine treatment in the Veterans Health Administration. Am J Addict. Nov-Dec;2008 17(6):459–462. [PubMed: 19034736]
16. Gordon AJ, Liberto J, Granda S, et al. Physician training is never a failure. American Journal on Addictions. 2009; 18(4):337–338.

17. Gordon AJ, Kavanagh G, Krumm M, et al. Facilitators and barriers in implementing buprenorphine in the Veterans Health Administration. Psychology of addictive behaviors: journal of the Society of Psychologists in Addictive Behaviors. Jun; 2011 25(2):215–224. [PubMed: 21480679]
18. Egan JE, Casadonte P, Gartenmann T, et al. The Physician Clinical Support System-Buprenorphine (PCSS-B): a novel project to expand/improve buprenorphine treatment. Journal of general internal medicine. Sep; 2010 25(9):936–941. [PubMed: 20458550]
19. Cunningham CO, Kunins HV, Roose RJ, et al. Barriers to obtaining waivers to prescribe buprenorphine for opioid addiction treatment among HIV physicians. Journal of general internal medicine. Sep; 2007 22(9):1325–1329. [PubMed: 17619934]
20. Hutchinson E, Catlin M, Andrilla CH, et al. Barriers to primary care physicians prescribing buprenorphine. Annals of family medicine. Mar-Apr;2014 12(2):128–133. [PubMed: 24615308]
21. Lofwall MR, Wunsch MJ, Nuzzo PA, et al. Efficacy of continuing medical education to reduce the risk of buprenorphine diversion. Journal of substance abuse treatment. Oct; 2011 41(3):321–329. [PubMed: 21664789]
22. Netherland J, Botsko M, Egan JE, et al. Factors affecting willingness to provide buprenorphine treatment. Journal of substance abuse treatment. Apr; 2009 36(3):244–251. [PubMed: 18715741]
23. Suzuki J, Connery HS, Ellison TV, et al. Preliminary survey of office-based opioid treatment practices and attitudes among psychiatrists never receiving buprenorphine training to those who received training during residency. The American journal on addictions/American Academy of Psychiatrists in Alcoholism and Addictions. Jul 25.2014
24. Center for Substance Abuse Treatment. Clinical guidelines for the use of buprenorphine treatment of opioid addiction. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2004.
25. McNicholas, L. Personal communication to Bradley D Stein. 2011.
26. Center for Substance Abuse Treatment. Buprenorphine: A guide for nurses. Washington, DC: Substance Abuse and Mental Health Services Administration; 2009. DHHS Pub. No. (SMA) 09-4376
27. Department of Veteran's Affairs. VA/DoD clinical practice guideline for management of substance use disorders. Washington, DC: U.S. Department of Defense; 2009.
28. Affairs USDoV. VA/DoD clinical practice guideline for management of substance use disorder (SUD). Department of Defense; 2009.
29. Vermont Department of Health Division of Alcohol and Drug Abuse Programs (VDH/ADAP), Office of Vermont Health Access (OVHA) . Vermont buprenorphine practice guidelines. Morrisville, VT: 2010.
30. Goodman, F.; Gordon, A.; Kivlahan, D., et al. Criteria for use of buprenophine/naloxone and Buprenorphine sublingual tablets: VHA Pharmacy Benefits Management Strategic Healthcare Group and Medical Advisory Panel. Dept of Veterans Affairs; 2007.
31. Stein BD, Sorbero MJ, Goswami U, et al. Impact of a private health insurance mandate on public sector autism service use in Pennsylvania. Journal of the American Academy of Child and Adolescent Psychiatry. Aug; 2012 51(8):771–779. [PubMed: 22840548]
32. Shuster, J. Community Care Behavioral Health Organization, Personal Communication. 2011.
33. Fitch K, Bernstein SJ, Aguilar MD, et al. The RAND/UCLA appropriateness method user's manual. 2001 DTIC Document.
34. McGory ML, Shekelle PG, Ko CY. Development of quality indicators for patients undergoing colorectal cancer surgery. Journal of the National Cancer Institute. Nov 15; 2006 98(22):1623–1633. [PubMed: 17105985]
35. Grant BF, Stinson FS, Dawson DA, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry. Aug; 2004 61(8):807–816. [PubMed: 15289279]
36. Kessler RC, Nelson CB, McGonagle KA, et al. The epidemiology of co-occurring addictive and mental disorders: implications for prevention and service utilization. Am J Orthopsychiatry. Jan; 1996 66(1):17–31. [PubMed: 8720638]

37. Kessler RC, Nelson CB, McGonagle KA, et al. Comorbidity of DSM-III-R major depressive disorder in the general population: results from the US National Comorbidity Survey. Br J Psychiatry Suppl. Jun.1996 (30):17–30. [PubMed: 8864145]
38. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. JAMA. Nov 21; 1990 264(19):2511–2518. [PubMed: 2232018]
39. Kraus ML, Alford DP, Kotz MM, et al. Statement of the American Society Of Addiction Medicine Consensus Panel on the use of buprenorphine in office-based treatment of opioid addiction. Journal of addiction medicine. Dec; 2011 5(4):254–263. [PubMed: 22042215]
40. Nielsen S, Dietze P, Lee N, et al. Concurrent buprenorphine and benzodiazepines use and self-reported opioid toxicity in opioid substitution treatment. Addiction. Apr; 2007 102(4):616–622. [PubMed: 17286641]
41. Rotter T, Kinsman L, James E, et al. The effects of clinical pathways on professional practice, patient outcomes, length of stay, and hospital costs: Cochrane systematic review and meta-analysis. Evaluation & the health professions. Mar; 2012 35(1):3–27. [PubMed: 21613244]
42. Schuman-Olivier Z, Connery H, Griffin ML, et al. Clinician beliefs and attitudes about buprenorphine/naloxone diversion. The American journal on addictions/American Academy of Psychiatrists in Alcoholism and Addictions. Nov-Dec;2013 22(6):574–580. [PubMed: 24131165]
43. Crabtree BL, Dostrow VG, Evans CJ, et al. Outcome assessment of an antipsychotic drug algorithm: effects of the Mississippi State Hospital algorithm project. Psychiatric services. Aug; 2011 62(8):963–965. [PubMed: 21807839]
44. Miller AL, Crismon ML, Rush AJ, et al. The Texas Medication Algorithm Project. Schizophrenia Bulletin. 2004; 30(3):627–647. [PubMed: 15631256]
45. Stevens J, Kelleher KJ, Wang W, et al. Use of psychotropic medication guidelines at child-serving community mental health centers as assessed by clinic directors. Community mental health journal. Jun; 2011 47(3):361–363. [PubMed: 20878547]
46. Gagliardi AR, Brouwers MC, Palda VA, et al. How can we improve guideline use? A conceptual framework of implementability. Implement Sci. 2011; 6(1):26. [PubMed: 21426574]
47. Shekelle P, Woolf S, Grimshaw JM, et al. Developing clinical practice guidelines: reviewing, reporting, and publishing guidelines; updating guidelines; and the emerging issues of enhancing guideline implementability and accounting for comorbid conditions in guideline development. Implementation Science. 2012; 7(1):62. [PubMed: 22762242]
48. Fiellin DA. The first three years of buprenorphine in the United States: experience to date and future directions. J Addict Med. Jun; 2007 1(2):62–67. [PubMed: 21768936]
49. Koch AL, Arfken CL, Schuster CR. Characteristics of U.S. substance abuse treatment facilities adopting buprenorphine in its initial stage of availability. Drug Alcohol Depend. Jul 27; 2006 83(3):274–278. [PubMed: 16413146]
50. Maxwell JC. Diversion and Abuse of Buprenorphine: A Brief Assessment of Emerging Indicators. 2006
51. Yokell MA, Zaller ND, Green TC, et al. Buprenorphine and buprenorphine/naloxone diversion, misuse, and illicit use: an international review. Curr Drug Abuse Rev. Mar; 2011 4(1):28–41. [PubMed: 21466501]
52. Sohler NL, Li X, Kunins HV, et al. Home-versus office-based buprenorphine inductions for opioid-dependent patients. Journal of substance abuse treatment. 2010; 38(2):153–159. [PubMed: 19801178]

Table 1

Guideline statements rated as valid for the treatment of opioid dependence with buprenorphine with median score ≥7.0 and without disagreement among panelists during the first or second rounds of ratings

Domain	Median rating (range)
1. Conduct assessments to determine candidacy for treatment	
1.1. Determine opiod use disorder by DSM-5 standards	9.0 (8–9)
1.2. Assess psychiatric history with attention to current compliance with medication	8.0 (3–9)
1.3. Assess medical history with attention paid to liver and cardiac status, medications, and seizures	8.0 (7–9)
1.4. Assess pregnancy status	9.0 (3–9)
1.5. Assess psychosocial supports – employment, family, housing, 12-step involvement	8.0 (5–9)
1.6. Assess substance use history and current substance use	9.0 (8–9)
1.7. Assess treatment history – previous treatment episodes with buprenorphine, methadone	8.5 (5–9)
1.8. Assess for current opioid agonist treatment by conducting a witnessed urine screen (methadone, buprenorphine, benzodiazepines)	9.0 (5–9)
1.9. Assess withdrawal status	9.0 (6–9)
1.10. Assess addiction severity	8.0 (7–9)
1.11. Assess potential treatment needs in relation to the physician's ability to accommodate them (intensive monitoring, interactions with legal system, employers, others)	8.0 (4–9)
1.12 Assess pain	8.0 (6–9)
2. *Patients who meet the following criteria are considered to be good candidates for treatment:*	
2.1. Have current opioid dependence	9.0 (3–9)
2.2. If currently on methadone, are unable/unwilling to receive treatment from a methadone clinic	8.0 (7–9)
2.3. Have adequate psychosocial support	8.0 (1–9)
2.4. Do not have co-occurring mental disorder or co-occurring disorder is stable	8.0 (1–9)
2.5. Are not suicidal	8.5 (4–9)
2.6. May be pregnant	8.0 (8–9)
2.7. Are expected to be reasonably compliant with treatment	8.0 (5–9)
2.8. Are not dependent on CNS depressants, including benzodiazepines and alcohol	8.0 (1–9)
2.9. Are interested in treatment	8.0 (3–9)
3. Prior to initiation of treatment, patients should complete and sign a treatment contract containing, at a minimum, the following components:	
3.1. Discussion of voluntary participation in treatment	9.0 (7–9)
3.2. Agreement to notify prescribing physician if they are or plan to become pregnant	9.0 (8–9)
3.3. Discussion of the use of other medications	9.0 (7–9)
3.4. Discussion of the use of alcohol and illicit drugs	8.5 (4–9)
3.5. Agreement to use medications only as prescribed	9.0 (7–9)
3.6. Agreement to attend scheduled appointments	8.0 (6–9)
3.7. Compliance with required pill counts and drug tests	9.0 (7–9)
3.8. Attendance at counseling and other referrals	9.0 (7–9)
3.9. Consequences for attending appointments under the influence	8.0 (3–9)
3.10. Policies for recovery and relapse	7.5 (3–9)

Domain	Median rating (range)
3.11. Consequences for diversion	9.0 (8–9)
3.12. Instructions on safe storage of medication	9.0 (8–9)
4. Administer appropriate dosing of buprenorphine during induction, stabilization, and maintenance phases	
4.1. Induction: Ensure that patient is experiencing objective signs of withdrawal.	8.5 (7–9)
4.2: Induction: Day two maximum dose between 8–16 mg	8.0 (1–9)
4.3: Induction after methadone: Induction for patients coming off methadone should be managed by experienced physicians only.	8.0 (7–9)
4.4: Induction after methadone: monitor for withdrawal symptoms. If not observed within 24+ hours after last methadone treatment, wait prior to initiation.	8.0 (4–9)
4.5: Stabilization: Adjust dose (as needed) in no more than 2–4 mg increments/week.	8.0 (2–9)
4.6: Stabilization: Daily dose has been established when patient is not using illicit opioids, withdrawal symptoms are not present, and the patient is not experiencing cravings.	8.0 (7–9)
4.7: Maintenance: After a period of time that varies with each patient but should reflect compliance with treatment, a prescription for 30 days may be written.	8.0 (7–9)
5. Provide or refer to concurrent psychosocial treatment	
5.1: Patients receiving buprenorphine should receive simultaneous psychosocial counseling.	9.0 (3–9)
5.2: Physicians should establish linkages with a variety of psychosocial supports and be able to refer to qualified providers.	9.0 (7–9)
5.3 Patients starting buprenorphine should receive an evidence-based psychosocial treatment.	8.0 (7–9)
5.4: Patients should receive weekly psychosocial therapy appointments during the stabilization phase.	8.0 (1–9)
5.5 Early in treatment, patients should be contacted if the physician is aware they are noncompliant with psychosocial therapy.	8.0 (7–9)
5.6 During the maintenance phase, psychosocial therapy can be less frequent than during stabilization.	8.0 (5–9)
6. Monitor treatment adherence and effectiveness	
6.1: During induction and stabilization phases, conduct weekly urine screens to detect alcohol and other drugs of abuse and the presence of the buprenorphine metabolite.	8.0 (1–9)
6.2: During the maintenance phase, conduct biweekly or monthly urine screens to detect alcohol and other drugs of abuse and the presence of the buprenorphine metabolite.	8.0 (1–9)
7. Discontinue treatment only when the following conditions are met:	
7.1: Before discontinuing buprenorphine, patients must express a desire to discontinue.	9.0 (7–9)
7.2: Before discontinuing buprenorphine, patients must have stable housing and income.	7.5 (1–9)
7.3: Before discontinuing buprenorphine, patients must have adequate psychosocial support.	8.0 (4–9)
7.4: Conditions for termination and contingencies for treatment should be outlined in the treatment agreement.	9.0 (8–9)
8. Provide adequate assessment and treatment for patients with co-occurring depression and/or anxiety	
8.1: Screen for depression and anxiety.	8.5 (7–9)
8.2: Assess previous history of mental disorders and treatment, focusing on temporal relationship of symptoms to substance use and response to previous treatment.	8.5 (7–9)
8.3: Assess type, quantity, frequency, and time of last use of illicit substances or prescribed psychotropic drugs.	9.0 (7–9)
8.4: Assess family history of mental disorders.	8.0 (6–9)
8.5: Assess severity of depression/anxiety.	9.0 (7–9)
8.6: Reassess symptoms of depression and anxiety with regularity	9.0 (7–9)
8.7: Refer to specialized behavioral health care if patient fails to respond to treatment provided by prescribing physician.	9.0 (8–9)

Domain	Median rating (range)
8.8: Refer to concurrent evidence-based psychosocial treatment, such as Cognitive Behavioral Therapy, Motivational Interviewing, Relapse Prevention, Contingency Management, or supportive therapy.	8.5 (3–9)
8.9: Refer to Twelve-Step Facilitation, such as Dual Recovery Anonymous.	8.5 (2–9)
8.10: Once stabilized, if a patient continues to present symptoms of depression and anxiety, consider prescribing medications with low potential for abuse, such as SSRIs or tricyclic antidepressants.	8.0 (5–9)
8.11: Consider alternatives to benzodiazepines.	9.0 (8–9)
8.11a: Patients should be strongly advised against self-medicating with benzodiazepines.	9.0 (8–9)
8.11b: If a patient has a prescription for benzodiazepines at the outset of treatment, use caution taking him or her off of the benzodiazepines and do not discontinue abruptly.	9.0 (7–9)
8.12: Integrate treatment for opiate dependence and depression/anxiety to the greatest degree possible, as on-site integrated care is associated with better outcomes than referrals off-site.	9.0 (1–9)