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Opioid Agonist Treatment for Patients With Dependence on Prescription Opioids

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Abstract
Clinical Question Are different opioid agonist treatments (eg, methadone vs buprenorphine) associated with differences in efficacy for treating prescription opioid dependence, and is long-term maintenance of opioid agonist treatment associated with differences in efficacy compared with opioid taper or psychological treatments alone? Bottom Line For patients who are dependent on prescription opioids, long-term maintenance of opioid agonists is associated with less prescription opioid use and better adherence to medication and psychological therapies for opioid dependence compared with opioid taper or psychological treatments alone. Methadone maintenance was not associated with differences in therapeutic efficacy compared with buprenorphine maintenance treatment. Evidence quality was low to moderate.

Keywords
prescription, dependence, opioids, opioid, treatment, agonist, patients

Disciplines
Education | Social and Behavioral Sciences

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Introduction
The United States is experiencing an opioid overdose epidemic, with recent increases in prescription opioid-related mortality.1,2 Opioid agonist treatment is recommended for treating prescription opioid dependence by the US Centers for Disease Control and Prevention.3 This Clinical Evidence Synopsis summarizes findings from a Cochrane review that aimed to summarize current evidence for the treatment of prescription opioid dependence using opioid agonist treatments.4

Summary of Findings
Methadone vs Buprenorphine
Three studies compared methadone with buprenorphine (Table). No difference was found in the mean number of days of opioid use (assessed during final 30 days of the intervention, 1.51 days [SD, 4.97 days] for methadone vs 2.92 days [SD, 6.38 days] for buprenorphine; mean difference, −1.41 [95% CI, −3.37 to 0.55]; P = .16), opioid use as measured by opioid-positive urine drug screening (27 of 79 participants [34.2%] for methadone vs 51 of 117 participants [43.6%] for buprenorphine; risk ratio [RR], 0.81 [95% CI, 0.56 to 1.18]; P = .28), and self-reported opioid use (11 of 66 participants [16.7%] for methadone vs 34 of 89 participants [38.2%] for buprenorphine; RR, 0.37 [95% CI, 0.08 to 1.63]; P = .19). No between-group difference was found in treatment adherence for methadone (Table).

Buprenorphine Maintenance vs Opioid Taper
Three studies compared buprenorphine maintenance with opioid taper or psychological treatment only. No between-group difference was found for mean days of opioid use during past 7 days or 30 days (standardized mean difference, −0.31 [95% CI, −0.66 to 0.04]; P = .08). Buprenorphine maintenance treatment was associated with reduced opioid use as determined by urine opioid-positive drug screening (39 of 97 participants [40.2%] vs 67 of 109 participants [61.5%] for buprenorphine; risk ratio [RR], 0.63 [95% CI, 0.43 to 0.91]; P = .02) and reduced opioid use by self-report (37 of 100 participants [37.0%] vs 62 of 104 participants [59.6%] with opioid taper; RR, 0.54 [95% CI, 0.31 to 0.93]; P = .003). Buprenorphine maintenance therapy was associated with greater treatment adherence (83 of 110 participants [75.5%] vs 36 of 137 participants [26.3%] with opioid taper; RR, 0.33 [95% CI, 0.23 to 0.47]; P < .001).

Discussion
No difference was found in treatment outcomes between methadone and buprenorphine maintenance therapy in prescription opioid dependence treatment. Maintenance treatment was associated with better substance use and treatment adherence outcomes compared with shorter-term treatments. Updated searches (conducted in August 2016) identified no additional eligible trials.
Limitations
Most studies were conducted in the United States. No studies used a double-blind method, and all studies had relatively small sample sizes (53–204 participants). Due to the overall low to moderate quality of the evidence and sample sizes, it is possible further research may change these conclusions.

Comparison of Findings With Current Practice Guidelines
The US Center for Substance Abuse Treatment guidelines and A Guideline for the Clinical Management of Opioid Addiction suggest that long-term treatment is preferable to withdrawal treatment alone, consistent with the findings of this review. The American Society of Addiction Medicine guidelines concluded that evidence supports methadone and buprenorphine maintenance, consistent with the results of this review, and that treatment setting (supervised dosing in a drug treatment clinic vs treatment provided in a physician’s office) is important when taking into account patient preference and safety considerations.

Areas in Need of Future Study
Further research should include examining the treatment of concurrent chronic pain and opioid dependence and comparing outcomes for psychological treatment and taper. Inclusion of validated pain measures in future studies will facilitate a better understanding of pain as it relates to treatment of opioid addiction. See JAMA opioid microsite (http://sites.jamanetwork.com/opioids/) for further clinical information such as differences between methadone and buprenorphine induction.

Table. Opioid Agonist Treatments for Prescription Opioid Dependence

<table>
<thead>
<tr>
<th>Primary Outcomes</th>
<th>No. of Studies</th>
<th>Range, wk</th>
<th>Treatment Duration</th>
<th>Total Follow-up</th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illicit opioid use during final 30 d of the intervention</td>
<td>1</td>
<td>24</td>
<td>32</td>
<td>1.51 (4.97)</td>
<td>53</td>
<td>2.92 (6.38)</td>
</tr>
<tr>
<td>Opioid-positive urine drug screening at treatment completion</td>
<td>2</td>
<td>24 to 26</td>
<td>26 to 32</td>
<td>27</td>
<td>79</td>
<td>51</td>
</tr>
<tr>
<td>Self-reported substance use at end of treatment</td>
<td>3</td>
<td>24 to 26</td>
<td>26 to 32</td>
<td>11</td>
<td>66</td>
<td>34</td>
</tr>
<tr>
<td>Adherence</td>
<td>3</td>
<td>24 to 26</td>
<td>24 to 32</td>
<td>121</td>
<td>162</td>
<td>125</td>
</tr>
</tbody>
</table>

**Studies That Compared Methadone With Buprenorphine**

<table>
<thead>
<tr>
<th>Primary Outcomes</th>
<th>No. of Studies</th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illicit opioid use</td>
<td>2</td>
<td>100</td>
<td>62</td>
</tr>
<tr>
<td>Opioid-positive urine drug screening at treatment completion</td>
<td>3</td>
<td>97</td>
<td>67</td>
</tr>
<tr>
<td>Self-reported opioid use at end of treatment</td>
<td>3</td>
<td>100</td>
<td>62</td>
</tr>
<tr>
<td>Adherence</td>
<td>3</td>
<td>110</td>
<td>36</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary Outcomes</th>
<th>No. of Studies</th>
<th>Buprenorphine</th>
<th>Opioid Taper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illicit opioid use</td>
<td>2</td>
<td>69</td>
<td>64</td>
</tr>
<tr>
<td>Opioid-positive urine drug screening at treatment completion</td>
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<td>97</td>
<td>109</td>
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<td>100</td>
<td>104</td>
</tr>
<tr>
<td>Adherence</td>
<td>3</td>
<td>83</td>
<td>137</td>
</tr>
</tbody>
</table>

**Abbreviations:** GRADE, Grading of Recommendations, Assessment, Development and Evaluations; NA, not available.

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