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Newest Evidence to Guide the Care of Neonates With Neonatal Abstinence Syndrome and Their Mothers

Use of opioids among pregnant women has increased rapidly over the past 15 years, often leaving health care providers unprepared to care for affected women and their neonates (Martin, Longinaker, & Terplan, 2015). Currently, 4% of NICU admissions across the United States are attributed to neonatal abstinence syndrome (NAS), an increase from 0.7% of NICU admissions in 2004 (Tolia et al., 2015). In some areas of the United States, more than 20% of all neonates admitted to the NICU experienced drug withdrawal from in utero opioid exposure. In two new reviews, reviewers provide much-needed guidance and examine the evidence on the best care for pregnant women addicted to opioids (Terplan et al., 2018) and their neonates (MacMillan et al., 2018).

Since the 1970s, the American College of Obstetricians and Gynecologists and other professional organizations have endorsed opioid agonist therapy for women with opioid use disorders during pregnancy (American College of Obstetricians and Gynecologists, 2017; American Society of Addiction Medicine, 2018). Methadone, the leading form of opioid agonist therapy in the United States, has been standard treatment for pregnant women with opioid addiction for the past 40 years based on studies from the 1970s. At that time, researchers found that women who received methadone as part of a comprehensive addiction and prenatal care program had similar birth outcomes as women without substance use disorders (Strauss, Andresko, Stryker, Wardell, & Dunkel, 1974). By contrast, detoxification from opioids (withdrawal) during pregnancy was associated

with increased stress for the women and fetus (Zuspan, Gumpel, Mejia-Zelaya, Madden, & Davis, 1975). Research in this area has not progressed over the past decades. As a result, many contemporary providers are newly interested in a strategy of detoxification during pregnancy as a possible means to prevent neonatal abstinence syndrome (NAS) caused by maternal use of opioids or opioid agonist therapy (Terplan et al., 2018). As the epidemic of opioid-addicted pregnant women has risen over the past few years, so has interest in maternal detoxification.

Terplan and colleagues recently performed a systematic review of the evidence on maternal and neonatal outcomes of opioid detoxification versus opioid agonist therapy during pregnancy (Terplan et al., 2018). Fifteen studies ($N = 1,997$ women, of whom 1,126 underwent detoxification) published between 1975 and 2016 were included in this review. All of these studies were observational, and most were retrospective; thus, study quality was rated as fair to poor. Detoxification treatment ranged from comprehensive inpatient or residential treatment programs to forced withdrawal of women in prison systems. Most women comprising the samples in the included studies underwent withdrawal during their second or third trimesters. Some women were weaned off opioids gradually using methadone or buprenorphine, while others quit cold turkey. The authors found that opioid detoxification during pregnancy compared to ongoing opioid agonist therapy was not associated with increased rates of fetal loss (14/1,126 fetal deaths [1.2%] in detoxification group vs. 17/871 deaths [2.0%] in comparison group). However, rates of detoxification completion varied greatly across studies (9–100%), as did rates of opioid use relapse among women undergoing detoxification. For these reasons, there was a high loss to follow-up of women included in most of the studies. In addition, because there were no standard guidelines on supportive psychosocial services for women with opioid use disorders during pregnancy, the

113 existence and quality of these services varied
114 greatly among included studies. There was also
115 evidence of harm related to opioid detoxification
116 during pregnancy. In one study, two women who
117 successfully detoxified during pregnancy went on
118 to overdose at 2 and 6 weeks postpartum.
119 Weighing all of the evidence, the reviewers rec-
120 ommended that providers promote maintenance
121 pharmacotherapy over detoxification for women
122 with opioid use disorders during pregnancy.
123

124 When exposed to opioids in utero, neonates
125 manifest opioid withdrawal, with symptoms of
126 increased muscle tone, tremors, sweating, vom-
127 iting, and diarrhea that manifest between 24 and
128 96 hours following birth. Most newborns with NAS
129 are cared for in NICUs, where they receive
130 pharmacologic therapies that are titrated and
131 tracked using standardized scoring systems to
132 quantify NAS symptoms. However, evidence
133 suggests that opioid-exposed neonates treated
134 in NICUs experience more severe withdrawal
135 symptoms, have longer lengths of hospital stay,
136 and require increased pharmacotherapy
137 compared to neonates who room-in with their
138 mothers (Abrahams et al., 2007; Newman et al.,
139 2015).
140

141 MacMillan and colleagues conducted a sys-
142 tematic review and meta-analysis to compare
143 rooming-in versus NICU care of neonates
144 affected by NAS (MacMillan et al., 2018). They
145 included six studies ($N = 549$ neonates) and
146 examined the neonates' need for pharmaco-
147 therapy, length of hospital stay for the neonate,
148 inpatient cost, adverse events, and readmission
149 rates by place of NAS treatment. Neonates who
150 roomed-in with their mothers during NAS treat-
151 ment had reduced use of pharmacotherapy (risk
152 ratio [RR] 0.37; 95% confidence interval [CI]
153 [0.19–0.71]) and stayed in the hospital for about
154 10 fewer days (–10.41 days; 95% CI [–16.84 to –
155 3.98 days]) compared to neonates who received
156 NAS treatment in a NICU. The reviewers also
157 found evidence that rooming-in was associated
158 with lower inpatient costs and higher rates of
159 breastfeeding, although these outcomes were
160 not included in meta-analyses. Importantly,
161 rooming-in was not associated with increased
162 rates of hospital readmission or adverse events
163 compared to NICU care for neonates with NAS.
164

165 Opioid use disorders during pregnancy are
166 no longer rare and affect women regardless of
167 socioeconomic factors, race/ethnicity, and ge-
168 ography. Women's health providers require

169 better evidence to help guide their care of
170 women and their neonates in situations of opioid
171 use during pregnancy from prospective studies
172 to compare different combinations of pharma-
173 cotherapy and psychosocial support services
174 for women. Providers should work in teams with
175 their local hospital systems and mental health
176 facilities to develop evidence-based protocols to
177 screen for opioid use disorders during preg-
178 nancy and support women and their families
179 who are affected. Finally, the United States
180 desperately needs better medical insurance
181 coverage and comprehensive services for
182 women, neonates, and others affected by opioid
183 use disorders.
184

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