Full length article

Non-medical opioid use and sources of opioids among pregnant and non-pregnant reproductive-aged women

Katy B. Kozhimannil [a,*], Amy J. Graves [a], Marian Jarlenski [b], Alene Kennedy-Hendricks [c], Sarah Gollust [a], Colleen L. Barry [c]

[a] Division of Health Policy and Management, University of Minnesota School of Public Health, 420 Delaware St. SE, MMC 729, Minneapolis, MN 55455, United States
[b] Department of Health Policy and Management, University of Pittsburgh Graduate School of Public Health, 130 DeSoto St., A619, Pittsburgh, PA 15261, United States
[c] Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, 624 N. Broadway, Room 311, Baltimore, MD 21205, United States

ARTICLE INFO

ABSTRACT

Background: The morbidity and mortality burden of the US opioid epidemic falls heavily on reproductive-age women. Information on the patterns of and sources for non-medical use of prescription opioids among reproductive age women, including pregnant women, will inform public health and prevention efforts to mitigate the effects of the opioid epidemic. This study characterized non-medical use of prescription opioids among reproductive-age U.S. women, with a focus on pregnancy status.
Methods: We used nationally-representative data from the National Survey of Drug Use and Health (2005–2014) to examine non-medical use (NMU) of prescription opioids in the past 30 days among females ages 18–44 (N = 154,179), distinguishing pregnant women (N = 8069). We used multivariable logistic regression to describe reported sources of opioids, including opioids obtained from a doctor, friend or relative, dealer, or other source.
Results: Nearly 1% of pregnant women and 2.3% of non-pregnant reproductive-age women reported opioid NMU in the past 30 days. Forty-six percent of pregnant women identified a doctor as their source compared with 27.6% of non-pregnant women reporting NMU. Pregnant women reported a friend or relative as their source of opioids less frequently than non-pregnant women (53.8% versus 75.0%), and some pregnant and non-pregnant women acquired opioids from a dealer (14.6% and 10.6%).
Conclusion: Opioid NMU among reproductive-age women is a complex public health challenge affecting a vulnerable population. Pregnant women were more likely than non-pregnant women to list a doctor as their source of opioids for NMU, suggesting the need for targeted policies to address physician prescribing during pregnancy.

© 2017 Published by Elsevier Ireland Ltd.

1. Introduction

The morbidity and mortality burden of the US opioid epidemic falls heavily on reproductive-age women. Between 1999 and 2010, drug overdose deaths related to opioid pain relievers increased five-fold among US women (Mack and Center For Disease Control, 2013). Although on average more men die from drug overdoses than women, including among those treated for opioid use disorders (Evans et al., 2015), the percentage increase in deaths since 1999 is greater among women, and the sex difference in overdose deaths is rapidly disappearing (Mack and Center For Disease Control, 2013). Reproductive-age women are more likely than younger or older women to require emergency care related to opioid misuse and abuse, in part owing to non-medical use of prescription opioid pain relievers (e.g., oxycodone, hydrocodone, fentanyl, morphine) (US Centers for Disesase Control and Prevention, 2016). Non-medical use (NMU) is defined as the "intentional use of a medication without a prescription, in a way other than as prescribed, or for the experience or feeling that it causes (Committee on Health Care for Underserved Women and The American College of Obstetricians and Gynecologists, 2012)."

* Corresponding author.
E-mail addresses: kbk@umn.edu, kbk@umn.edu (K.B. Kozhimannil), agraves@umn.edu (A.J. Graves), marian.jarlenski@pitt.edu (M. Jarlenski), alene@jhu.edu (A. Kennedy-Hendricks), sgollust@umn.edu (S. Gollust), cbarry@jhu.edu (C.L. Barry).

Knowing the source of opioids for NMU is crucial to informing prevention efforts. The majority of persons with recent NMU report obtaining opioids from friends or family, who in turn report obtaining the opioids from medical professionals (Substance Abuse and Mental Health Services Administration, 2014). Indeed, prescribing practices – and policy efforts to address overprescribing – are a focus of broad strategies to combat the opioid epidemic (Dowell et al., 2016). Opioid prescribing has particular relevance as a potential source for NMU among reproductive-age women. A recent study showed that between 2008 and 2012, nearly 40% of reproductive-age female Medicaid beneficiaries and almost 30% of privately-insured reproductive-age women filled at least one opioid prescription annually (Ailes et al., 2012).

Gender-specific research on opioid NMU is needed, owing to the different use patterns and effects among men and women (Evans et al., 2015; Kerridge et al., 2015). One important aspect of understanding women's opioid NMU during reproductive years is the potential for pregnancy, given that almost half (45%) of all US pregnancies are unintended (Finer and Zolna, 2016). Further, the percentage of pregnancies that are unintended is substantially higher among women with opioid use disorders (Heil et al., 2011). Over the last decade, NMU of prescription opioids during pregnancy nearly doubled, mirroring national trends in opioid NMU (Pan and Yi, 2013; Patrick et al., 2015a). This increase in prenatal opioid use poses a significant public health concern, with potential risk for both women and infants. Opioid use during pregnancy is associated with increased risk of newborn withdrawal, known as neonatal abstinence syndrome, and preterm birth, which is the largest contributor to infant mortality (Patrick et al., 2015b). Infants diagnosed with neonatal abstinence syndrome have longer, more complicated birth hospitalizations with clinical signs that range from feeding difficulty to seizures (De'souza, 2015; Creanga et al., 2012; Patrick et al., 2012; Tolia et al., 2015). Women themselves face significant medical and non-medical risks from opioid use during pregnancy, including increased risk of opioid use disorder, which is associated with increased odds of maternal cardiac arrest during delivery and with maternal death (Maeda et al., 2014). Substance use during pregnancy is also associated with broader risks, including intimate partner violence, and parental substance use is associated with involvement with foster care or child protective services (Young et al., 2007).

While pregnant women are an important policy-relevant group because of the risks described above, policy attention must encompass opioid NMU among the broader class of reproductive-age women. In spite of the growing impact of the opioid crisis among women, little of the emergent national attention has focused on addressing opioid use in this group generally, or prior to or during pregnancy specifically. More information on the patterns of and sources for opioid NMU among reproductive age women, including those who are pregnant, will inform public health and prevention efforts to mitigate the effects of the opioid epidemic on women, children and families. The goal of this study was to characterize non-medical prescription opioid use, including sources of opioids, among reproductive-age women in the US, distinguishing women based on pregnancy status.

2. Materials and methods

2.1. Data and study population

We used pooled cross-sectional data from 2005 to 2014 from the National Survey of Drug Use and Health (NSDUH). The NSDUH provides population estimates of substance use and health-related behaviors in the U.S. general population. It utilizes multistage area probability sampling methods to select a representative sample of the U.S. civilian, non-institutionalized population aged 12 years or older for participation in the study. All respondents are ensured privacy when answering survey questions in their home, and sensitive questions are asked confidentially via computer with headphones (Substance Abuse and Mental Health Services Administration, 2013). Weighted annual interview response rates ranged between 71.2% and 76.0% during the study period (Substance Abuse and Mental Health Services Administration, 2015). The current study focused on reproductive age women ages 18–44 (N = 154,179; weighted N = 558,385,835). We separately analyzed data for the 8069 (weighted N = 23,064,218) women who reported that they were pregnant at the time of the survey. The sample of pregnant women is a subset of all reproductive age women, but we analyze them separately because opioid NMU may have different effects and implications during pregnancy.

2.2. Variable measurement

We identified past 30-day opioid NMU as responding yes to the survey question "Have you ever, even once, used any type of prescription pain reliever that was not prescribed for you or that you took only for the experience or feeling it caused?" and indicating that the last use of a prescription pain reliever was in the past 30 days. Additional measures of substance use were also defined within the past 30 days, including alcohol, cigarettes, marijuana, tranquilizer or sedative, and other (cocaine, crack, hallucinogen, inhalant, or stimulant). Alcohol use in the past 30 days was categorized as: heavy use (drinking $\geq$5 drinks on $\geq$5days in the past 30 days); binge but not heavy (drinking $\geq$5 drinks on at least 1 day in the past 30 days); past 30 day use but not binge or heavy; and no use in the past 30 days (Ko et al., 2015). Cigarette use in the past 30 days was categorized into $\geq$26 cigarettes per day ($\geq$1.5 packs), 6–25 cigarettes per day (0.5–1 packs), $\leq$5 cigarettes per day (<0.5 pack), and no smoking within the past 30 days.

Survey respondents with past 30-day opioid NMU were asked 10 questions about the sources of these opioids. Respondents could answer affirmatively to each of the 10 questions, and as such, responses are not mutually-exclusive. We categorized affirmative responses to each question into four non-mutually-exclusive indicators of source of opioids for NMU: doctor (from one or more doctors); friend or relative (from friend or relative for free; bought from friend or relative; took from a friend or relative without asking); dealer (bought from a stranger); and other (wrote fake prescription; stole from a doctor's office, clinic, hospital, or pharmacy; bought on the internet; got another way).

In order to measure factors that have a known association with opioid NMU, our multivariable analyses controlled for: (1) sociodemographic factors, such as age, race/ethnicity, education, marital status, health insurance, and family characteristics (King et al., 2014; Stine et al., 2009), (2) health and clinical characteristics, including serious psychological distress (Tetrault et al., 2008; Krans and Patrick, 2016), (3) criminal justice system involvement (Saloner et al., 2016), and (4) other substance use (Ko et al., 2015), as described below. Sociodemographics included age categories (ages 12–25, 26–35, and $\geq$36) and race/ethnicity. Respondents reporting Hispanic ethnicity were categorized as Hispanic and respondents not reporting Hispanic ethnicity were categorized as non-Hispanic Black, non-Hispanic White, and non-Hispanic other. Marital status included married, never married, and widowed, divorced, or separated. Education categories included less than high school, high school graduate, and some post-secondary education or higher. Health insurance categories were private insurance, public insurance (including Medicaid, CHIP, or CHAMPUS), and uninsured. Self-reported health status was reported as excellent, very good, good, and fair or poor. Total family income was categorized as less than $20,000, $20,000–$49,999, $50,000–$74,999, and $\geq$$75,000.

The number of children in the household ages 0–17 was reported as 0, 1, 2, and ≥3. Trimester of pregnancy was included for pregnant respondents. An indicator of serious psychological distress was constructed from the Kessler 6 (K6) scale, a validated scale measuring non-specific psychological distress. We measured serious psychological distress as a dichotomous variable indicated by the highest K6 total score in the past year that exceeded 13 (Kessler et al., 2003). We defined a composite measure of criminal justice system involvement based on arrest at least once in the past year or probation, parole, or supervised release at any point in the past year. Missing values accounted for less than 2% of our sample across all variables.

2.3. Statistical analyses

We described weighted population characteristics and substance use of women in our sample by pregnancy status and by past 30 day opioid NMU. Separately for pregnant and non-pregnant women, we compared those with and without opioid NMU using Pearson chi-square tests.

We investigated associations between the three most frequent sources of opioid NMU – doctor, friend or relative, and dealer – and pregnancy status. We first present univariate results; then models that adjust for: (1) demographic characteristics including age, race, marital status, education, insurance, household income, number of children in household, and year; (2) demographic and health characteristics including self-reported health status and serious psychological distress; (3) demographic and health characteristics and criminal justice system involvement, and (4) fully adjusted models including demographic, health, criminal justice, and substance use variables including past 30 day cigarette, alcohol, marijuana, tranquilizer or sedative, and other drug use. All models were survey-weighted logistic regressions, and separate models were run for each of the three sources.

This study was exempted from review by the University of Minnesota Institutional Review Board. All analyses were conducted using R version 3.3.1.

3. Results

Table 1 presents weighted descriptive characteristics of reproductive-age U.S. women by pregnancy status and, for pregnant and non-pregnant women, comparing those with and without NMU of opioids. Four percent of women reported being pregnant at the time of the survey. Among pregnant women, 0.8% reported opioid NMU in the past 30 days. Compared with pregnant women with no opioid NMU, pregnant women with opioid NMU were younger, more likely to be unmarried, less educated, with lower household incomes, less likely to have private health insurance, in poorer self-reported health, more likely to experience serious psychological distress, and to have recent criminal justice system involvement. Also, pregnant women with opioid NMU were most frequently in their first trimester.

Among non-pregnant reproductive age women, 2.3% reported opioid NMU in the past 30 days. Compared with non-pregnant reproductive age women with no NMU, non-pregnant women with NMU of opioids were more likely to be non-Hispanic White, to have no children in the household, were younger, less educated, more likely to be unmarried, less likely to have private insurance, and more likely to self-report being in fair/poor health, to have experienced serious psychological distress, and to have recent criminal justice system involvement. Both pregnant and non-pregnant women with opioid NMU had higher rates of past 30 day cigarette smoking, alcohol, marijuana, and other substance use.

Source of opioids among women with NMU by pregnancy status is shown in Fig. 1. A higher share of pregnant women with NMU of opioids reported that their source of opioids was a doctor compared with non-pregnant women with NMU of opioids (46.2% and 27.6%, respectively; p = 0.004). Pregnant women reported a friend or relative as a source less frequently compared with non-pregnant reproductive-age women with NMU of opioids (53.9% and 75.0%, respectively; p = 0.001). Slightly more pregnant women with opioid NMU reported a dealer as a source relative to non-pregnant women, though the difference was not statistically significant (14.6% and 10.6%, respectively; p = 0.44).

Table 2 shows results from multivariable models examining associations between pregnancy status of women with NMU of opioids and opioid source, separately for those reporting that they obtained opioids from doctors, from friends or relatives, and from dealers (Full model results are shown in Supplemental Tables 1–3). In fully adjusted models, pregnant women had nearly twice the odds of getting opioids from a doctor relative to non-pregnant women (aOR 1.82; 95% CI 0.99, 3.37) but had half of the odds of getting opioids from a friend or relative (aOR 0.51; 95% CI 0.25, 1.04). Pregnant women had higher odds of procuring opioids from a dealer relative to non-pregnant women (aOR 1.36; 95% CI 0.53, 3.49; p = 0.53). These differences in source by pregnancy status, which adjust for potential confounders, are measurable, but not statistically significant at p-value <0.05 level (exact p-values are 0.06 and 0.07, respectively), owing in part to small sample sizes in subgroups of pregnant women with opioid NMU sourcing from a doctor (unweighted N = 38, weighted N = 88,720), from a friend or relative (unweighted N = 53, weighted N = 103,401), and from a dealer (unweighted N = 12, weighted N = 28,020).

A variety of other characteristics of women with NMU of opioids were associated with receiving opioids from a doctor. Fig. 2 displays select results for doctor, friend or relative, and dealer models in a forest plot. Full model results are presented in Appendix Tables 1–3 in Supplementary material. Women who were pregnant, non-White, those having government insurance, and using tranquilizers or sedatives in the past 30 days had greater odds of sourcing opioids from a doctor. Younger women, low income women, women with young family members in the household, and those using alcohol and marijuana in the past 30 days had higher odds of procuring opioids from a friend or relative. Younger women and women using marijuana and tranquilizers or sedatives in the past 30 days had higher odds of sourcing opioids from a dealer. Women experiencing serious psychological distress had greater odds of acquiring opioids from all three sources, though these were not statistically significant.

4. Discussion

While the rates of NMU of opioids among reproductive-age women at first glance appear low (at 2.3% and 0.8% among non-pregnant and pregnant women respectively), the public health burden of NMU in this population is quite large. Annually, there are more than 6 million pregnancies each year in the US, occurring among 62 million reproductive-age women (Curtin et al., 2013). Our findings indicate that approximately 1.4 million reproductive-age women (2.3%) and 50,000 pregnant women (0.8%) have recent NMU of opioids. The morbidity and mortality burden of the US opioid epidemic falls heavily on reproductive-age women (Mack and Center For Disease Control, 2013). Additionally, NMU of opioids during pregnancy poses substantial health and social risks to women, infants, and families. Policy efforts to address the public health crisis presented by the opioid epidemic must directly confront the particular needs of reproductive-age and pregnant

Table 1
Characteristics of U.S. women ages 18–44 by pregnancy status and non-medical use of prescription opioids in the past 30 days.

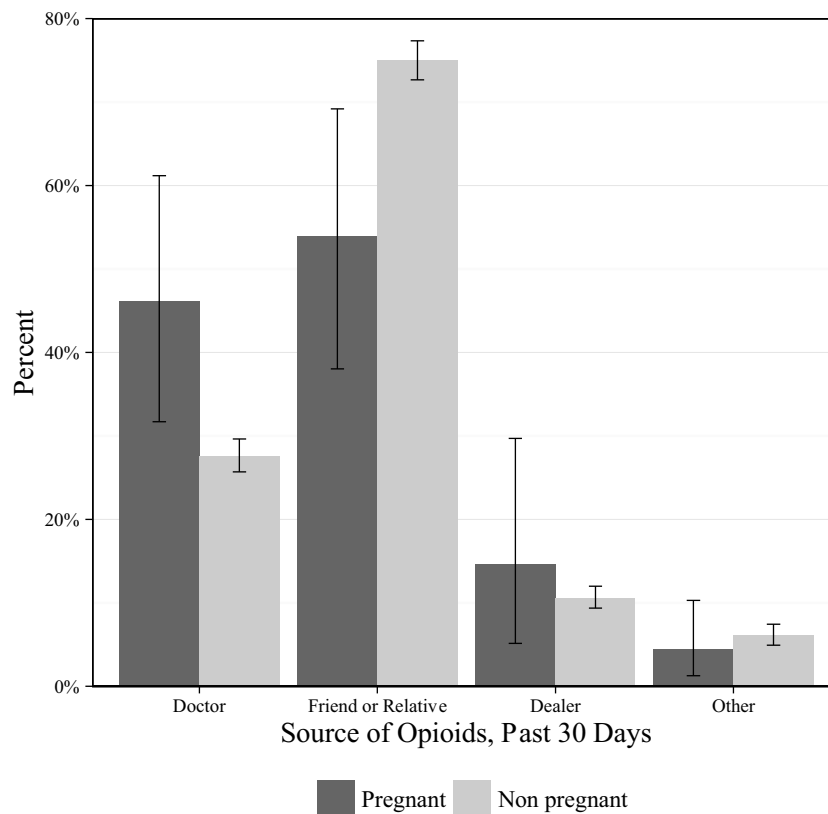| Characteristic	Pregnant Weighted N = 23,064,218 (4.1%)			Non pregnant Weighted N = 535,321,617 (95.9%)		
	Opioid NMU Weighted N = 191,979 (0.8%)	No opioid NMU Weighted N = 22,872,240 (99.2%)	P-value	Opioid NMU Weighted N = 12,557,402 (2.3%)	No opioid NMU Weighted N = 522,764,215 (97.7%)	P-value
Age						
18–25	63.6%	37.8%	0.03	44.2%	29.2%	<0.001
26–35	26.1%	48.9%		30.2%	31.9%	
≥36	10.3%	13.3%		25.6%	39.0%	
Race						
Non-Hispanic Black	22.4%	14.0%	0.39	12.4%	13.9%	<0.001
Non-Hispanic White	52.5%	58.4%		68.7%	59.9%	
Non-Hispanic Other	6.2%	8.2%		4.6%	8.4%	
Hispanic	18.9%	19.3%		14.3%	17.8%	
Marital Status						
Married	26.0%	62.0%	<0.001	25.2%	46.0%	<0.001
Widowed/Divorced/Separated	12.2%	6.3%		14.9%	11.8%	
Never Married	61.8%	31.6%		59.9%	42.3%	
Household Income						
<$20,000	45.6%	23.1%	0.004	29.8%	21.9%	< 0.001
$20,000–$49,999	33.1%	31.5%		36.2%	32.8%	
$50,000–$74,99	10.8%	17.3%		14.9%	17.1%	
≥$75,000	10.5%	28.1%		19.1%	28.2%	
Education						
Less than High School	29.8%	16.4%	0.01	18.3%	12.4%	< 0.001
High School graduate	31.5%	26.8%		32.7%	27.0%	
Some Post-secondary or more	38.7%	56.8%		49.1%	60.6%	
Insurance						
Private	23.1%	54.3%	<0.001	46.8%	62.9%	<0.001
Medicaid/CHIP/CHAMPUS	46.1%	32.6%		22.3%	14.5%	
None	30.8%	13.1%		30.9%	22.6%	
Number of Children in Household						
0	40.7%	34.0%	0.81	47.7%	37.1%	<0.001
1	28.7%	33.2%		21.8%	23.3%	
2	20.4%	20.6%		17.9%	23.8%	
≥3	10.2%	12.2%		12.5%	15.8%	
Self-reported Health Status						
Excellent	12.6%	35.1%	<0.001	13.5%	27.5%	<0.001
Very Good	18.8%	37.7%		36.5%	39.6%	
Good	45.5%	22.0%		34.4%	25.0%	
Fair/Poor	23.0%	5.2%		15.6%	8.0%	
Serious Psychological Distress	52.6%	12.3%	<0.001	44.6%	16.9%	<0.001
Criminal Justice System Involvement	21.3%	4.5%	<0.001	11.7%	3.0%	<0.001
Trimester						
First	46.5%	31.0%	0.05	--	--	--
Second	33.5%	35.6%		--	--	
Third	20.0%	33.4%		--	--	
Cigarettes, Past 30 days						
≤5 cigarettes per day (< 1/2 pack)	30.6%	7.1%	<0.001	23.4%	13.0%	<0.001
6–25 cigarettes per day (1/2 − 1 pack)	26.6%	7.3%		32.8%	12.9%	
≥26 cigarettes per day (≥1/2 packs)	0.1%	0.5%		3.0%	1.1%	
No cigarettes	42.8%	85.1%		40.7%	73.0%	
Alcohol, Past 30 days						
Heavy use	12.6%	0.6%	<0.001	19.9%	5.3%	<0.001
Binge, not heavy	19.5%	2.3%		33.5%	19.8%	
Not binge or heavy	16.2%	6.6%		24.0%	32.7%	
No use	51.8%	90.5%		22.5%	42.3%	
Marijuana, Past 30 days	41.4%	2.9%	<0.001	37.2%	7.0%	<0.001
Tranquilizer or Sedative, Past 30 days	27.4%	0.2%	<0.001	23.7%	0.7%	<0.001
Other (cocaine, crack, hallucinogen, inhalant, stimulant), Past 30 days	14.0%	0.5%	<0.001	19.1%	1.4%	<0.001

Notes: The unweighted number of pregnant women is 8069 and the number of nonpregnant women is 146,110. Among pregnant women, the unweighted number of opioid NMU is 96 and the unweighted number of no opioid NMU is 7973. Among nonpregnant women, the unweighted number of opioid NMU is 4308 and the unweighted number of no opioid NMU is 141,802.

women, who represent a substantial portion of the affected population.

This study's finding that pregnant women have greater odds than non-pregnant women of listing a doctor as the source of their opioids suggests one possible area for intervention. Nearly half of pregnant women in this sample with opioid NMU reported a doctor as the source of opioids, compared with less than a third of non-pregnant women with opioid NMU. Newly updated prescribing guidelines for opioid pain relievers now include information on pregnant women, but attention to all reproductive-age women is important (Dowell et al., 2016). Pregnant women are a subset of all reproductive-age women. Those who continue opioid NMU during pregnancy may have a more severe form of dependency or may have had health conditions, such as chronic pain, that necessitated

Fig. 1. Source of prescription opioids for NMU in the past 30 days among U.S. women age 18–44 by pregnancy status.
Notes: Weighted numbers of each source among pregnant women with opioid NMU are: Doctor: 88,720; Friend or Relative: 103,401; Dealer: 28,020, Other: 8411. Weighted numbers of each source among non-pregnant women with opioid NMU are: Doctor: 3,469,816; Friend or Relative: 9,424,228; Dealer: 1,334,830, Other: 766,478. Unweighted numbers of each source among pregnant women with opioid NMU are: Doctor: 38; Friend or Relative: 53; Dealer: 12; Other: 5. Unweighted numbers of each source among non-pregnant women with opioid NMU are: Doctor: 1135; Friend or Relative: 3320; Dealer: 593, Other: 233

Table 2
Associations between sources of opioids and pregnancy status of women ages 18–44 with non-medical use of opioids in the past 30 days.
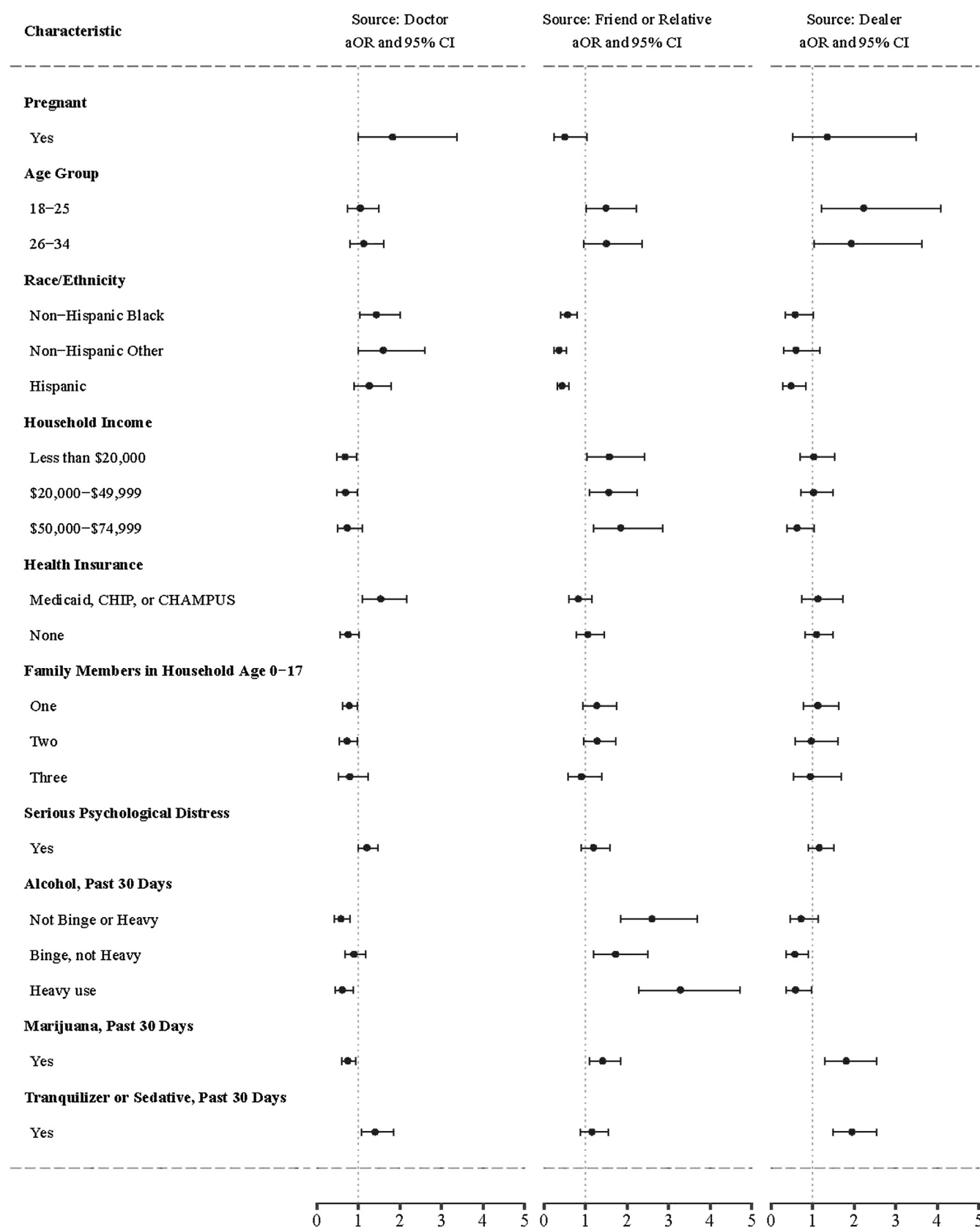
	Unadjusted		Adjusted (1)		Adjusted (2)		Adjusted (3)		Adjusted (4)	
	OR (95% CI)	P-value	aOR (95% CI)	P-value	aOR (95% CI)	P-value	aOR (95% CI)	P-value	aOR (95% CI)	P-value
Source: Doctor Pregnancy Status Pregnant (vs. not pregnant)	2.25 (1.28, 3.95)	0.006	1.96 (1.10, 3.49)	0.03	1.94 (1.09, 3.45)	0.03	1.96 (1.09, 3.53)	0.03	1.82 (0.99, 3.37)	0.06
Source: Friend or Relative Pregnancy Status Pregnant (vs. not pregnant)	0.39 (0.21, 0.71)	0.003	0.44 (0.23, 0.83)	0.01	0.43 (0.22, 0.82)	0.01	0.44 (0.23, 0.85)	0.02	0.51 (0.25, 1.04)	0.07
Source: Dealer Pregnancy Status Pregnant (vs. not pregnant)	1.44 (0.57, 3.62)	0.44	1.34 (0.48, 3.73)	0.58	1.32 (0.48, 3.62)	0.60	1.32 (0.47, 3.73)	0.60	1.36 (0.53, 3.49)	0.53

Notes: Adjusted (1) models include demographic characteristics age, race, marital status, household income, education, insurance, number of children in household, self-reported health status, and year. Adjusted (2) models additionally include serious psychological distress. Adjusted (3) models additionally include criminal justice system involvement. Adjusted (4) models additionally include use of the following substances: cigarettes, alcohol, tranquilizer or sedative, and other illicit drugs. Full multivariable model results are presented in Appendix 1.

prescription opioid medications at point in time prior to the use becoming nonmedical. As such, physician-prescribed opioids as a source for opioid NMU during pregnancy may have originated prior to pregnancy.

Efforts to limit access to opioids for NMU require a multi-faceted approach. Public health detailing, a model using one-on-one educational visits (Kattan et al., 2016), could include tailored information for clinicians that care for reproductive-age and pregnant women. Physician-based systems, such as prescription drug monitoring programs, which have been associated with decreases in opioid-associated adverse outcomes (Patrick et al., 2016), may also hold promise for mitigating the effects of opioid NMU among preg-

nant women. Given evidence that abrupt discontinuation of opioid use can pose severe risks to the woman and fetus, efforts to curtail prescribing to pregnant women believed to be using opioids non-medically must be combined with concerted efforts to initiate addiction treatment. Opioid maintenance therapy (with methadone or buprenorphine) is the standard of care for pregnant women with opioid use disorder (Hall et al., 2016), and may improve the likelihood that families remain cohesive in cases involving the child welfare system (ACOGA Committee on Health Care for Underserved Women and American Society of Addiction Medicine, 2012). Given that rates of opioid prescribing are higher among pregnant Medicaid beneficiaries compared with privately-

Fig. 2. Forest plot charting adjusted odds of reporting a doctor, friend or relative, or dealer as the source of opioids by the characteristics of reproductive-age women using opioids non-medically.

insured pregnant women (Desai et al., 2014), developing guidelines and targeting physician interventions to community health centers and other settings relying heavily on Medicaid reimbursement are worth considering. More broadly, our findings highlight the relative socioeconomic disadvantage of women with opioid NMU, emphasizing the need for efforts around prescribing to account for the complex interplay of risk factors that affect both the source of opioids and the consequences of opioid NMU.

Fully three-fourths of non-pregnant women reported a friend or relative as source, while over half of pregnant women (almost as many who reported doctor) reported a friend or relative as source. Prior studies describe unused pain medications (including post-surgical medications) as a potential source that may be accessed by friends or relatives for opioid NMU (Bartels et al., 2016; Kennedy-Hendricks et al., 2016a). Disposal of opioids at designated collection sites may hold promise as a policy strategy to address this source (Maughan et al., 2016). Also, a small but substantial portion of reproductive-age women (pregnant and not pregnant) reported that drug dealers were the source of opioids for NMU, emphasizing the importance of ongoing efforts to reduce illegal sales of prescription opioids, but attention should be paid to whether tailored strategies to reduce dealer sourcing for pregnant or reproductive-age women would be warranted.

When neonatal abstinence syndrome is discussed in policy initiatives, the focus is frequently on treatment of infants, not on reproductive-age or pregnant women (De'souza, 2015; Krans and Patrick, 2016). Further complicating efforts to ensure opioid use disorder treatment for pregnant women are punitive laws that criminalize addiction in the case of pregnancy (Kennedy-Hendricks et al., 2016b; Terplan et al., 2015a; Roberts and Pies, 2011; Guttmacher Institute, 2016). Public health and clinical efforts to promote screening for substance use before and during pregnancy may allow for greater detection, but care must be taken to ensure that such programs take account of the broader policy environment, including the criminalization of substance use during pregnancy. The state of Tennessee, for example, implemented statewide surveillance for neonatal abstinence syndrome, starting in 2013 (Warren et al., 2013). This system has dramatically increased detection rates, but has done so in a context where state law – until 2016 – allowed for criminal prosecution of a pregnant woman for fetal endangerment. Tennessee's example is instructive and highlights the importance of screening and detection practices that do not discourage prenatal care seeking (Roberts and Pies, 2011).

Opioid NMU among reproductive-age women affects individuals and families at a crucial point in the lifecourse, and efforts to mitigate the health and social impacts of opioid NMU in this population ought to focus on screening and treatment efforts that occur at multiple time points during women's reproductive lives: during, prior to, or outside the context of pregnancy. The need for woman-centered treatment for substance abuse has greatly outpaced availability (Terplan et al., 2015b), and to be effective, future policy efforts should ensure attention to the particular needs of reproductive-age and pregnant women in prevention and treatment efforts.

4.1. Limitations

While this study presents national estimates of opioid NMU and source of opioids among reproductive-age women in the US, there are several important limitations of the data used in this analysis. First, although self-report is considered a reliable measure for pregnancy status (Overbeek et al., 2013), it is possible that respondents may have misreported or been unaware of their pregnancy status. Opioid NMU and other substance use may be under-reported generally and among pregnant individuals, owing

to both recall bias and social desirability bias (McQueen et al., 2015), but NSDUH undertakes considerable efforts to diminish the potential effects of such biases (Substance Abuse and Mental Health Services Administration, 2014). Repeat cross-sections of NSDUH data from 2005 to 2014 were pooled to increase the analytic sample size, but longitudinal assessment was not possible and there were substantial shifts in awareness of the risks of addiction associated with prescription opioid use among both clinicians and the general public over this time period.

5. Conclusions

Opioid NMU has health, social and cost consequences for reproductive-age women, and potential impacts are heightened during pregnancy, when a fetus may also be affected. Opioid NMU among reproductive-age women is a complex public health challenge affecting a vulnerable population. While friends and relatives were the most common source of opioids among reproductive-age women overall, pregnant women were more likely than non-pregnant women to list a doctor as the source of their opioids, suggesting the need for targeted policy efforts to address opioid access and NMU during pregnancy and over the reproductive years. Efforts to address opioid use disorders should build on existing systems for substance use identification and treatment and recognize the myriad needs of women at highest risk of poor outcomes associated with substance use generally and during pregnancy.

Conflict of interest

None.

Contributors

K. Kozhimannil conceived the study, acquired the data, supervised the analysis, and drafted portions of the manuscript. A. Graves conducted the analysis, contributed to data presentation, and drafted portions of the manuscript. M. Jarlenski, A. Kennedy-Hendricks, S. Gollust, and C. Barry contributed to the conception and design of the study, the analysis and interpretation of the results, data presentation, and public health and policy implications. All authors reviewed the results, revised the article for important intellectual content, and approved the final version.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.drugalcdep.2017.01.003.

References

ACOG Committee on Health Care for Underserved Women and American Society of Addiction Medicine, 2012. ACOG committee opinion No. 524: opioid abuse, dependence, and addiction in pregnancy. Obstet. Gynecol. 119, 1070–1076, http://dx.doi.org/10.1097/AOG.0b013e318256496e.

Ailes, E.C., Dawson, A.L., Lind, J.N., Gilboa, S.M., Frey, M.T., Broussard, C.S., Honein, M.A., 2012. Centers for Disease Control and Preventon, 2015. Opioid prescription claims among women of reproductive age–United States, 2008–2012. MMWR 64, 37–41 (Accessed 24 August 2016) http://www.ncbi.nlm.nih.gov/pubmed/25611168.

Bartels, K., Mayes, L.M., Dingmann, C., Bullard, K.J., Hopfer, C.J., Binswanger, I.A., 2016. Opioid use and storage patterns by patients after hospital discharge following surgery. PLoS One 11, e0147972, http://dx.doi.org/10.1371/journal.pone.0147972.

Committee on Health Care for Underserved Women and The American College of Obstetricians and Gynecologists, 2012. Committee opinion No. 538: nonmedical use of prescription drugs. Obstet. Gynecol. 120, 977–982, http://dx.doi.org/10.1097/AOG.0b013e3182723b5a.

Creanga, A., Sabel, J.C., Ko, J.Y., Wasserman, C.R., Shapiro-Mendoza, C.K., Taylor, P., Barfield, W., Cawthon, L., Paulozzi, L.J., 2012. Maternal drug use and its effect

on neonates: a population-based study in Washington State. Obstet. Gynecol. 119, 924–933, http://dx.doi.org/10.1097/AOG.0b013e31824ea276.

Curtin, S.C., Abma, J.C., Ventura, S.J., Henshaw, S.K., 2013. Pregnancy rates for U.S. women continue to drop. NCHS Data Brief 136, 1–8 http://www.ncbi.nlm.nih.gov/pubmed/24314113.

De'souza, V., 2015. Prenatal Drug Use and Newborn Health: Federal Efforts Need Better Planning and Coordination GAO-15-203. Government Accountability Office, Washington, D.C.

Desai, R.J., Hernandez-Diaz, S., Bateman, B.T., Huybrechts, K.F., 2014. Increase in prescription opioid use during pregnancy among medicaid-enrolled women. Obstet. Gynecol. 123, 997–1002, http://dx.doi.org/10.1097/AOG.0000000000000208.

Dowell, D., Haegerich, T.M., Chou, R., 2016. CDC guideline for prescribing opioids for chronic pain-United States, 2016. JAMA 315, 1624–1645, http://dx.doi.org/10.1001/jama.2016.1464.

Evans, E., Kelleghan, A., Li, L., Min, J., Huang, D., Urada, D., Hser, Y., Nosyk, B., 2015. Gender differences in mortality among treated opioid dependent patients. Drug Alcohol Depend. 155, 228–235, http://dx.doi.org/10.1016/j.drugalcdep.2015.07.010.

Finer, L.B., Zolna, M.R., 2016. Declines in unintended pregnancy in the United States, 2008–2011. N. Engl. J. Med. 374, 843–852, http://dx.doi.org/10.1056/NEJMsa1506575.

Guttmacher Institute, 2016. State Policies In Brief: Substance Abuse During Pregnancy. Washington, DC (Accessed 24 August 2016) https://www.guttmacher.org/sites/default/files/pdfs/spibs/spib_SADP.pdf.

Hall, M.T., Wilfong, J., Huebner, R.A., Posze, L., Willauer, T., 2016. Medication-assisted treatment improves child permanency outcomes for opioid-using families in the child welfare system. J. Subst. Abuse Treat. 71, 63–67, http://dx.doi.org/10.1016/j.jsat.2016.09.006.

Heil, S.H., Jones, H.E., Arria, A., Kaltenbach, K., Coyle, M., Fischer, G., Stine, S., Selby, P., Martin, P.R., 2011. Unintended pregnancy in opioid-abusing women. J. Subst. Abuse Treat. 40, 199–202, http://dx.doi.org/10.1016/j.jsat.2010.08.011.

Kattan, J.A., Tuazon, E., Paone, D., Dowell, D., Vo, L., Starrels, J.L., Jones, C.M., Kunins, H.V., 2016. Public health detailing—a successful strategy to promote judicious opioid analgesic prescribing. Am. J. Public Health 106, 1430–1438, http://dx.doi.org/10.2105/AJPH.2016.303274.

Kennedy-Hendricks, A., Gielen, A., McDonald, E., McGinty, E.E., Shields, W., Barry, C.L., 2016a. Medication sharing, storage, and disposal practices for opioid medications among us adults. JAMA Intern. Med. 6, 1027, http://dx.doi.org/10.1001/jamainternmed.2016.2543.

Kennedy-Hendricks, A., McGinty, E.E., Barry, C.L., 2016b. Effects of competing narratives on public perceptions of opioid pain reliever addiction during pregnancy. J. Health Polit. Policy Law 41, 873–916, http://dx.doi.org/10.1215/03616878-3632230.

Kerridge, B.T., Saha, T.D., Chou, S.P., Zhang, H., Jung, J., Ruan, W.J., Smith, S.M., Huang, B., Hasin, D.S., 2015. Gender and nonmedical prescription opioid use and DSM-5 nonmedical prescription opioid use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions − III. Drug Alcohol Depend. 156, 47–56, http://dx.doi.org/10.1016/j.drugalcdep.2015.08.026.

Kessler, R.C., Barker, P.R., Colpe, L.J., Epstein, J.F., Gfroerer, J.C., Hiripi, E., Howes, M.J., Normand, S.L., Manderscheid, R.W., Walters, E.E., Zaslavsky, A.M., 2003. Screening for serious mental illness in the general population. Arch. Gen. Psychiatry 60, 184–189 (Accessed 24 August 2016) http://www.ncbi.nlm.nih.gov/pubmed/12578436.

King, N.B., Fraser, V., Boikos, C., Richardson, R., Harper, S., 2014. Determinants of increased opioid-related mortality in the United States and Canada, 1990–2013: a systematic review. Anesthesiology 311, 367–370, http://dx.doi.org/10.3109/00952990.2015.1047502.

Ko, J.Y., Farr, S.L., Tong, V.T., Creanga, A.A., Callaghan, W.M., 2015. Prevalence and patterns of marijuana use among pregnant and nonpregnant women of reproductive age. Am. J. Obstet. Gynecol. 213 (201), e1–e201, http://dx.doi.org/10.1016/j.ajog.2015.03.021.

Krans, E.E., Patrick, S.W., 2016. Opioid use disorder in pregnancy: health policy and practice in the midst of an epidemic. Obstet. Gynecol. 128, 4–10, http://dx.doi.org/10.1097/AOG.1.0000000000001446.

Mack, K.A., Centers for Disease Control and Prevention (CDC), 2013. Centers for disease control and prevention (CDC), 2013. drug-induced deaths − United States, 1999–2010. MMWR, 161–163 (Accessed 24 August 2016) http://www.ncbi.nlm.nih.gov/pubmed/24264508.

Maeda, A., Bateman, B.T., Clancy, C.R., Creanga, A., Leffert, L.R., 2014. Opioid abuse and dependence during pregnancy: temporal trends and obstetrical outcomes. Anesthesiology 121, 1158–1165, http://dx.doi.org/10.1097/ALN.1;0000000000000472.

Maughan, B.C., Hersh, E.V., Shofer, F.S., Wanner, K.J., Archer, E., Carrasco, L.R., Rhodes, K.V., 2016. Unused opioid analgesics and drug disposal following

outpatient dental surgery: a randomized controlled trial. Drug Alcohol Depend. 168, 328–334, http://dx.doi.org/10.1016/j.drugalcdep.2016.08.016.

McQueen, K.A., Murphy-Oikonen, J., Desaulniers, L., 2015. Maternal substance use and neonatal abstinence syndrome: a descriptive study. Matern. Child Health J. 19, 1756–1765, http://dx.doi.org/10.1007/s10995-015-1689-y.

Overbeek, A., van den Berg, M.H., Hukkelhoven, C.W., Kremer, L.C., van den Heuvel-Eibrink, M.M., Tissing, W.J., Loonen, J.J., Versluys, A.B., Bresters, D., Kaspers, G.J., Lambalk, C.B., van Leeuwen, F.E., van Dulmen-den Broeder, E., DCOG LATER/VEVO Study Group, 2013. Validity of self-reported data on pregnancies for childhood cancer survivors: a comparison with data from a nationwide population-based registry. Hum. Reprod. 28, 819–827, http://dx.doi.org/10.1093/humrep/des405.

Pan, I.J., Yi, H.Y., 2013. Prevalence of hospitalized live births affected by alcohol and drugs and parturient women diagnosed with substance abuse at liveborn delivery: united States, 1999–2008. Matern. Child Health J. 17, 667–676, http://dx.doi.org/10.1007/s10995-012-1046-3.

Patrick, S.W., Schumacher, R.E., Benneyworth, B.D., Krans, E.E., McAllister, J.M., Davis, M.M., 2012. Neonatal abstinence syndrome and associated health care expenditures, United States, 2000–2009. JAMA 307, 1934–1940, http://dx.doi.org/10.1001/jama.2012.3951.

Patrick, S.W., Davis, M.M., Lehman, C.U., Cooper, W.O., 2015a. Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009–2012. J. Perinatol. 35, 667, http://dx.doi.org/10.1038/jp.2015.63.

Patrick, S.W., Dudley, J., Martin, P.R., Harrell, F.E., Warren, M.D., Hartmann, K.E., Ely, E.W., Grijalva, C.G., Cooper, W.O., 2015b. Prescription opioid epidemic and infant outcomes. Pediatrics 135, 842–850, http://dx.doi.org/10.1542/peds.2014-3299.

Patrick, S.W., Fry, C.E., Jones, T.F., Buntin, M.B., 2016. Implementation of prescription drug monitoring programs associated with reductions in opioid-related death rates. Health Aff. (Millwood) 35, 1324–1332, http://dx.doi.org/10.1377/hlthaff.2015.1496.

Roberts, S.C.M., Pies, C., 2011. Complex calculations: how drug use during pregnancy becomes a barrier to prenatal care. Matern. Child Health J. 15, 333–341, http://dx.doi.org/10.1007/s10995-010-0594-7.

Saloner, B., Bandara, S.N., McGinty, E.E., Barry, C.L., 2016. Justice-involved adults with substance use disorders: coverage increased but rates of treatment did not in 2014. Health Aff. (Millwood) 35, 1058–1066, http://dx.doi.org/10.1377/hlthaff.2016.0005.

Stine, S.M., Heil, S.H., Kaltenbach, K., Martin, P.R., Coyle, M.G., Fischer, G., Arria, A.M., Selby, P., Jones, H.E., 2009. Characteristics of opioid-using pregnant women who accept or refuse participation in a clinical trial: screening results from the MOTHER Study. Am. J. Drug Alcohol Abuse 35, 429–433, http://dx.doi.org/10.3109/00952990903374080.

Substance Abuse and Mental Health Services Administration, 2013. 2014 National Survey on Drug Use and Heath: Field Interviewer Manual. Rockville, MD. http://www.samhsa.gov/data/sites/default/files/NSDUHmrbFImanual2014_opt.pdf.

Substance Abuse and Mental Health Services Administration, 2014. Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings NSDUH Series H-41. HHS Publication No. (SMA), pp. 11–4658.

Substance Abuse and Mental Health Services Administration, 2015. 2014 National Survey on Drug Use and Health: Methodological Summary and Definitions Rockville, MD. http://www.samhsa.gov/data/sites/default/files/NSDUH-MethodSummDefs2014/NSDUH-MethodSummDefs2014.htm#b3-1.

Terplan, M., Kennedy-Hendricks, A., Chisolm, M.S., 2015a. Prenatal substance use: exploring assumptions of maternal unfitness. Subst. Abuse 9 (Suppl. 2), 1–4, http://dx.doi.org/10.4137/SART.S23328.

Terplan, M., Longinaker, N., Appel, L., 2015b. Women-centered drug treatment services and need in the United States, 2002–2009. Am. J. Public Health 105, e50–e54, http://dx.doi.org/10.2105/ajph.2015.302821.

Tetrault, J.M., Desai, R.A., Becker, W.C., Fiellin, D.A., Concato, J., Sullivan, L.E., 2008. Gender and non-medical use of prescription opioids: results from a national US survey. Addiction 103, 258–268, http://dx.doi.org/10.1111/j.1360-0443.2007.02056.x.

Tolia, V.N., Patrick, S.W., Bennett, M.M., Muthy, K., Sousa, J., Smith, B., Clark, R.H., Spitzer, A.R., 2015. Increasing incidence of the neonatal abstinence syndrome in U.S. neonatal ICUs. N. Engl. J. Med. 372, 2118–2126, http://dx.doi.org/10.1056/NEJMsa1500439.

US Centers for Disease Control and Prevention. Prescription Painkiller Overdoses | VitalSigns. https://www.cdc.gov/vitalsigns/prescriptionpainkilleroverdoses/index.html. Accessed 20 December 2016.

Warren, M.D., Miller, A.M., Traylor, J., Bauer, A., Patrick, S.W., 2013. Implementation of a statewide surveillance system for neonatal abstinence syndrome ? Tennessee. MMWR 64, 125–128 (Accessed 21 March 2016) http://www.ncbi.nlm.nih.gov/pubmed/25674995.

Young, N.K., Boles, S.M., Otero, C., 2007. Parental substance use disorders and child maltreatment: overlap, gaps, and opportunities. Child Maltreat. 12, 137–149, http://dx.doi.org/10.1177/1077559507300322.