EDITORIAL

Cannabis Use in Pregnancy
A Tale of 2 Concerns

Michael Silverstein, MD, MPH; Elizabeth A. Howell, MD, MPH; Barry Zuckerman, MD

In an article in *JAMA*, Corsi and colleagues[1] present the results of a retrospective cohort study of 661 617 women designed to assess associations between maternal cannabis use during pregnancy and adverse obstetrical and birth outcomes. In a matched analysis designed to control for confounding, the investigators compared 5639 self-reported cannabis users with 92 873 nonusers and found elevated rates of preterm birth (defined as gestational age <37 weeks) among those who reported cannabis use. Specifically, the rates of preterm birth in the matched cohort were 10.2% vs 7.2% (risk difference, 2.98% [95% CI, 2.63%-3.34%]; relative risk, 1.41 [95% CI, 1.36-1.47]). While similar risks were observed for small-for-gestational-age birth and placental abruption, there appeared to be a small protective association between cannabis use and preeclampsia and gestational diabetes. In another article in *JAMA*, Volkow and colleagues[2] report findings on cannabis use among 4400 pregnant women and 133 900 nonpregnant women aged 12 to 44 years who participated in the National Survey on Drug Use and Health from 2002 to 2017. The authors documented an increase in the adjusted prevalence of cannabis use during pregnancy from 3.4% in 2002 to 7.0% in 2017—almost of all which appeared to be explained by nonmedical use.[2]

Related articles pages 145 and 167

These 2 studies send a straightforward message: cannabis use in pregnancy is likely unsafe; with an increasing prevalence of use (presumably related to growing social acceptability and legalization in many states), its potential for harm may represent a public health problem. This message is based on the sound, if imperfect, epidemiology of these 2 studies and is heightened by a misperception that marijuana is safe, as evidenced by its direct marketing to pregnant women for morning sickness despite accumulating evidence of harm.[3] However, there is an additional series of equally legitimate concerns, rooted more in history than epidemiology. These historical concerns relate to past and ongoing discourses on alcohol use in pregnancy and to the cocaine "epidemic that wasn't"[4] of the 1980s. Both of these histories, although imperfect comparators with the emerging data on cannabis, illustrate points that provide important context to the 2 present studies published in *JAMA*.

First, there are issues involving the epidemiology. Randomized designs are impractical for studying risks and harms, and observational studies are prone to unmeasured confounding.[5] In this respect, the study by Corsi and colleagues[1] is no different from any other cohort study; it is, however, further limited by use of registry data, derived primarily from clinical encounters, to assess cannabis exposure. Although the investigators performed some internal validity checks on their measurement of exposure, clinical data in the field of substance use tend to lack validation (and thus are prone to misclassification error), particularly when unaccompanied by biological markers.[6] Compounding this limitation is the inability to glean from the data the timing of cannabis exposure or a dose-response relationship between exposure and outcomes, both of which represent fundamental epidemiologic principles to support causality.[5] There was also no assessment of birth weight, which tends to be measured more accurately than gestational age. Despite these limitations, the study is consistent with previous studies that have assessed the association between cannabis use in pregnancy and birth outcomes[7,8] and provides important, population-based data.

Second, the historical context requires consideration. What has been learned from the debates about alcohol and cocaine use in pregnancy? Although it is accepted that heavy alcohol drinking during pregnancy poses an unacceptable risk to the developing fetus, the effect of moderate alcohol consumption continues to be controversial.[9] On one side of this argument, those who interpret the data using a strict, by-the-numbers approach conclude that there is only minimal evidence that moderate alcohol consumption poses a demonstrable risk.[10] On the other side of the argument are those who interpret the data more broadly to conclude that without an empirically proven safe level of exposure, abstinence is the only reasonable advice the medical community can give to pregnant women.[11]

One lesson of the current alcohol debate—which is often couched in terms of women's ability to enjoy wine with dinner and thus assumes the perception of an issue that predominantly affects the privileged—is that 2 reasonable perspectives can be applied to the same body of literature and reach opposing, nonstigmatizing conclusions. In other words, the issue is not the data but the values that individuals bring to the data and to whom the data are thought to be most relevant. Extrapolating this logic to the data Corsi et al[1] present on cannabis, some might choose to focus on the reported 41% increased relative risk of preterm birth as unacceptably high; others might choose to focus on the 2.98% absolute risk difference to be such that cannabis-related relaxation or improvement in morning sickness may not be worth abstaining from this drug.

The study by Corsi and colleagues[1] could also be interpreted through a slightly different lens. Perhaps it represents part of an emerging story of an in utero substance exposure that is neither highly prevalent nor extremely rare, an outcome that is consequential more on a population than individual level, and an association between exposure and outcome that is moderate in both its magnitude and degree of

certainty. Unlike the "wine with dinner" debate, the dialogue on cannabis use is likely to be relevant to many sectors of society and may end up focusing on young people, especially those of color, among whom use is markedly increasing.[12] In these respects, a comparison with certain aspects of the history of cocaine use in pregnancy may be instructive.

In 1985, the first "scientific" observation of the relationship between in utero cocaine exposure and neonatal outcomes was published.[13] Even by the standards of its day, this study (and many that followed) were fundamentally flawed. Yet, they provided "evidence" for those in the medical community and lay press to publicly exaggerate risks of cocaine in pregnancy and to attribute (both implicitly and explicitly) lifelong disability to a large cohort of primarily minority children,[14] for whom subsequent research demonstrated similar outcomes to unexposed children raised in similar environments.[15] Perhaps worse, this exaggerated risk amplified judgment and stereotype, leading to the enduring racist social constructs of the "cocaine mother" and "crack baby"[16] and to criminalization of substance use among pregnant women. Regrettably, the exaggerated dialogue on cocaine did little to shed light on the sequelae of urban poverty and legacy of racism in the United States.

It is possible to argue that the comparisons of cannabis vs alcohol and cocaine are not entirely fair. Cocaine in particular is biologically more destructive than cannabis, universally illegal in the United States, and without health benefit. Furthermore, the dialogue on cocaine was defined by exaggeration; so far, the dialogue on cannabis has largely been defined by a false perception of safety. While these are fair criticisms, some historic lessons of both alcohol and cocaine apply: it is impossible to separate data from the values that individuals bring to those data, no group is immune to the judgment of others, and women and minority groups (particularly pregnant women of color) tend to bear the greatest burden of many of these judgments.

While an obvious reaction to these new data on in utero cannabis exposure is that more research is necessary, more epidemiology is unlikely to completely resolve the complex issue of potentially safe moderate use or to completely remove the tendency to imbue data interpretation with implicit biases about groups of people. Perhaps the best reflection that can be offered is a reprise of that offered by Mayes et al[17] in 1992. This commentary acknowledged the potential harms of prenatal cocaine exposure, dispassionately delineated the methodologic problems with the state of the literature at the time, and expressed concern that premature conclusions attributing irremediable damage in children to exposure to a single substance (isolated from the broader social milieu) were, in and of themselves, harmful. This harm, the commentary argued, accrued by way of permanently lowered expectations and by a discourse that focused on judgment and attribution as opposed to prevention and positive intervention.[15]

The current data reported by Corsi et al[1] and Volkow et al[2] should spark genuine concern about the association of cannabis use in pregnancy with preterm birth. However, there should be additional concern about whether such findings may ripple through society and re-create some of the mistakes of the past.

ARTICLE INFORMATION

Author Affiliations: Department of Pediatrics, Boston Medical Center, School of Medicine, Boston University, Boston, Massachusetts (Silverstein, Zuckerman); Grayken Center for Addiction, Boston Medical Center, Boston, Massachusetts (Silverstein); Department of Obstetrics and Gynecology, Mount Sinai School of Medicine, New York, New York (Howell).

Corresponding Author: Michael Silverstein, MD, MPH, Department of Pediatrics, Boston Medical Center, 88 E Newton St, Vose 3, Boston, MA 02118 (michael.silverstein@bmc.org).

Published Online: June 18, 2019. doi:10.1001/jama.2019.8860

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank Kari Hironaka, MD, MPH (Atrius Health, Boston, Massachusetts); Caroline Kistin, MD, MSc; Scott Hadland, MD, MPH (Department of Pediatrics, Boston University School of Medicine; Boston Medical Center, Boston, Massachusetts); and Shambie Singer, JD, for their thoughtful input on the Editorial. They did not receive compensation.

REFERENCES

1. Corsi DJ, Walsh L, Weiss D, et al. Association between self-reported prenatal cannabis use and maternal, perinatal, and neonatal outcomes [published June 18, 2019]. *JAMA*. doi:10.1001/jama.2019.8734.

2. Volkow ND, Han B, Compton WM, McCance-Katz EF. Self-reported medical and nonmedical cannabis use among pregnant women in the United States [published June 18, 2019]. *JAMA*. doi:10.1001/jama.2019.7982

3. Volkow ND, Compton WM, Wargo EM. The risks of marijuana use during pregnancy. *JAMA*. 2017;317(2):129-130. doi:10.1001/jama.2016.18612

4. Okie S. The Epidemic That Wasn't. *New York Times*. https://www.nytimes.com/2009/01/27/health/27coca.html.Published January 26, 2019. Accessed June 10, 2019.

5. Koepsell TD, Weiss NS. *Epidemiologic Methods*. New York, NY: Oxford University Press; 2003.

6. Young-Wolff KC, Tucker LY, Alexeeff S, et al. Trends in self-reported and biochemically tested marijuana use among pregnant females in California from 2009-2016. *JAMA*. 2017;318(24):2490-2491. doi:10.1001/jama.2017.17225

7. Hingson R, Alpert JJ, Day N, et al. Effects of maternal drinking and marijuana use on fetal growth and development. *Pediatrics*. 1982;70(4):539-546.

8. Zuckerman B, Frank DA, Hingson R, et al. Effects of maternal marijuana and cocaine use on fetal growth. *N Engl J Med*. 1989;320(12):762-768. doi:10.1056/NEJM198903233201203

9. Widdicombe L. Parenting by the numbers. *The New Yorker*. https://www.newyorker.com/magazine/2019/06/03/parenting-by-the-numbers. Published May 27, 2019. Accessed June 10, 2019.

10. Oster E. *Expecting Better: Why the Conventional Pregnancy Wisdom Is Wrong—and What you Really Need to Know*. New York, NY: Penguin Books; 2018.

11. American College of Obstetricians and Gynecologists. Committee on Health Care for Underserved Women. Committee opinion No. 496: at-risk drinking and alcohol dependence: obstetric and gynecologic implications. *Obstet Gynecol*. 2011;118(2, pt 1):383-388.

12. Kann L, McManus T, Harris WA, et al. Youth risk behavior surveillance—United States, 2017. *MMWR Surveill Summ*. 2018;67(8):1-114. doi:10.15585/mmwr.ss6708a1

13. Chasnoff IJ, Burns WJ, Schnoll SH, Burns KA. Cocaine use in pregnancy. *N Engl J Med*. 1985;313(11):666-669. doi:10.1056/NEJM198509123131105

14. Hopkins E. Childhood's end: what life is like for crack babies. *Rolling Stone*. https://www.rollingstone.com/culture/culture-news/childhoods-end-what-life-is-like-for-crack-babies-188557/. Published October 18, 1990. Accessed June 10, 2019.

15. Frank DA, Augustyn M, Knight WG, Pell T, Zuckerman B. Growth, development, and behavior in early childhood following prenatal cocaine exposure: a systematic review. *JAMA*. 2001;285(12):1613-1625. doi:10.1001/jama.285.12.1613

16. Le V. The crack mother: an enduring social construct with political usefulness. *Anthropology*. Stanford University. https://anthropology.stanford.edu/sites/g/files/sbiybj9346/f/context2016-final_0.pdf. Published spring 2016. Accessed June 10, 2019.

17. Mayes LC, Granger RH, Bornstein MH, Zuckerman B. The problem of prenatal cocaine exposure: a rush to judgment. *JAMA*. 1992;267(3):406-408. doi:10.1001/jama.1992.03480030084043