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# Current Resources for Evidence-Based Practice, July 2020

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## ABSTRACT

An extensive review of new resources to support the provision of evidence-based care for women and infants. The current column includes a discussion of whether it is ethical not to offer doula care to all women, and commentaries on reviews focused on folic acid and autism spectrum disorder, and timing of influenza vaccination during pregnancy.

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## The Questionable Ethics Behind Lack of Universal Doula Care in the United States

At the end of January, the Centers for Disease Control and Prevention published the U.S. maternal mortality rate for the first time in 13 years (Hoyert & Minino, 2020). The reasons behind the lapse in reporting have been documented (Hoyert & Minino, 2020; MacDorman et al., 2016) and are primarily related to the fact that the United States does not require all states to use the same birth and death certificates. Nonetheless, the newly-published data reveal what many of us had long suspected: the United States has a higher maternal mortality rate than all other high-resource countries (17.4/100,000), and the rate for Black women is much higher (37.1/100,000; Hoyert & Minino, 2020).

In addition to elevated rates of maternal mortality, communities of color in the United States have poorer birth outcomes generally. For instance, women of color bear a disproportionate burden of preterm birth and intrauterine growth restriction (Bryant et al., 2010; Crawford et al., 2017; National Academies of Sciences, Engineering, and Medicine, 2020). We also observe poor birth outcomes in women with low socioeconomic status (Amjad et al., 2019). Based on the work done on fetal origins of adult disease and the microbiome, it is clear that the circumstances surrounding one's birth matter a great deal for later health for the individual and her or his children and grandchildren (Cresci & Bawden, 2015; Fernandez-Twinn et al., 2019;

Yarde et al., 2013). These inequities at birth reinforce the more generalized health inequities shouldered by communities of color in the United States across generations.

Ideally, midwifery care would be a pillar in any strategy designed to reduce inequities in maternal and child health outcomes (Sandall et al., 2016). However, the U.S. midwifery workforce is not currently extensive enough or sufficiently diverse to offer every pregnant woman a midwife in and from her own community, despite decades of robust evidence indicating such an approach could dramatically improve outcomes (Allen et al., 2016; Cheyney et al., 2015; Homer et al., 2014; National Academies of Sciences, Engineering, and Medicine, 2020; Sandall et al., 2016). Furthermore, even if we decided tomorrow to quadruple the midwifery workforce (it is, after all, the year of the Nurse and Midwife; World Health Assembly, 2019), training midwives takes several years and our existing nursing and midwifery schools do not currently have the capacity to sufficiently increase their enrollments (Accreditation Commission for Midwifery Education, 2019).

In the meantime, we could offer doulas to all childbearing families. These traditional health workers can be trained in a matter of weeks, and once in practice they provide the health education, social support, and continuity of care midwives are often unable to provide because they are constrained by hospital policies (Dahlen et al., 2011). Excellent maternal and child outcomes have been associated with the use of

doulas (Bohren et al., 2017), and depending on the particular state in question, reimbursement of \$929–\$1,047 (average \$986) is cost effective because of the vast reductions in preterm and cesarean births (Kozhimannil et al., 2016).

Universal access to doulas during childbirth could be operationalized in practice in a few different ways. First, hospitals could employ doulas as part of their maternity care teams and include their services for all childbearing women as part of the overall care package. As accountability to quality of care has become more prominent since the Affordable Care Act, most hospital administrators are interested in reducing cesarean rates. Doulas would almost certainly help achieve this goal (Bohren et al., 2017). Doula care is a cost-effective, evidence-based solution—the proverbial magic bullet.

The other way doula care could be made more accessible is by enabling individual doulas or multi-doula practices (call doula “hubs” in some states) to bill insurers for services. In practice, this means state Medicaid programs would need to begin to reimburse for doula care; private insurers would likely follow suit. Oregon is one of the few states that has done this via a state Traditional Health Worker Registry. Doulas who meet the training standards set by the state can apply to be on the Registry, after which they can bill for services. Implementation of this system has not been entirely smooth sailing. However, it now seems to be working in at least some areas of the state, since more families from traditionally underrepresented groups can access doula care without cost to themselves.

It is not yet clear which of these two implementation methods would be more effective in the U.S. healthcare system. Addressing the systemic racism underpinning centuries of poorer health outcomes for minority families should be our nation's top priority. One way to immediately begin to move the needle on maternal and child health outcomes for communities of color is to provide every childbearing woman who wants one with a socially and linguistically matched doula. As Dr. Christiane Northrup wrote in her iconic book *Women's Bodies, Women's Wisdom*, if doulas were a drug, it would be unethical not to use them (Northrup, 2010).

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## From Cochrane Database of Systematic Reviews (CDSR) Issues 03–04 (2020)

### Systematic Reviews in CDSR: Women's Health

- Ovarian suppression for adjuvant treatment of hormone receptor-positive early breast cancer
- Health education interventions to promote early presentation and referral for women with symptoms of endometrial cancer
- Green tea (*Camellia sinensis*) for the prevention of cancer

### Systematic Reviews in CDSR: Fertility, Contraception, and ART

- Self-administered versus provider-administered medical abortion
- Intra-uterine insemination for unexplained subfertility

### Systematic Reviews in CDSR: Pregnancy and Birth

- Death audits and reviews for reducing maternal, perinatal and child mortality
- Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

### Systematic Reviews in CDSR: Infant Health and Breastfeeding

- Zinc supplementation for the promotion of growth and prevention of infections in infants less than six months of age
- Early versus late parenteral nutrition for critically ill term and late preterm infants
- Non-invasive respiratory support for the management of transient tachypnea of the newborn

- Enteral lactoferrin supplementation for prevention of sepsis and necrotizing enterocolitis in preterm infants
- Diaphragm-triggered non-invasive respiratory support in preterm infants
- Normal saline (0.9% sodium chloride) versus heparin intermittent flushing for the prevention of occlusion in long-term central venous catheters in infants and children
- Postnatal corticosteroids for transient tachypnoea of the newborn

### Systematic Reviews in CDSR: Nursing Education and Practice

- Health workers' perceptions and experiences of using mHealth technologies to deliver primary healthcare services: A qualitative evidence synthesis

### Systematic Reviews in CDSR: SARS-CoV-2

- Quarantine alone or in combination with other public health measures to control COVID-19: A rapid review
- Hand cleaning with ash for reducing the spread of viral and bacterial infections: A rapid review
- Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare staff

## Evidence-Based Reviews From Other Sources

### Recent Evidence-Based Reviews: Women's Health

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- Featured Review:** Guo, B.-Q., Li, H.-B., Zhai, D.-S., & Ding, S.-B. (2019). Association of maternal prenatal folic acid intake with subsequent risk of autism spectrum disorder in children: A systematic review and meta-analysis. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 94, 109650. <https://doi.org/10.1016/j.pnpbp.2019.109650>

In this meta-analysis, Guo et al. (2019) pooled data from eight observational studies, including a total of 840,776 children of whom 7127 were diagnosed with autism spectrum disorder (ASD). The exposure of interest was folic acid, which, in addition to reducing neural tube defects (Werler et al., 1993), appears to be associated with other beneficial pregnancy outcomes, including childhood neurodevelopment (Hua et al., 2016; McNulty et al., 2019). Numerous researchers have therefore postulated folic acid might also be associated with ASD.

Guo et al. (2019), however, found no association between folic acid and ASD; the pooled estimate from studies reporting odds ratios was 0.91 (95% CI, 0.73–1.13), and the pooled estimate from studies reporting hazard ratios was 0.66 (0.38–1.17). They concluded, “This study does not provide support for the association between maternal FA [folic acid] intake during the prenatal period and the reduced risk of ASD in children.... More investigation is needed” (Guo et al., 2019, p. 12).

**Comment:** I agree Guo et al.'s (2019) results are compatible with no association between folic acid supplementation and ASD. However, I disagree with their conclusion that more investigations are necessary. It is possible a beneficial effect of folic acid would be observed with more careful assessment of the exposure. Not all of the studies included in this meta-analysis assessed folic acid during the pre-conception period. Perhaps nuancing exactly when the supplements were taken would allow a more precise estimate of any association with ASD.

However, it is fairly clear from looking at Figure 1 in Guo et al.'s (2019) article that folic acid is not harmful, at least in terms of ASD. Given the current recommendations concerning folic acid for women of childbearing age, I would argue it does not matter whether folic acid might also prevent ASD. Folic acid is known to prevent neural tube defects, and on the basis of that knowledge, we supplement our food supply and encourage women to take folic acid before and during pregnancy. This clinical message would not change if folic acid also prevents ASD. Thus, in my opinion, we do not need more studies on this topic. Completed studies combine to indicate no association, and, even if there was one, we would not change practice.

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**Featured Review:** Cuningham, W., Geard, N., Fielding, J. E., Braat, S., Madhi, S. A., Nunes, M. C., ... Moss, R. (2019). Optimal timing of influenza vaccine during pregnancy: A systematic review and meta-analysis. *Influenza and Other*

*Respiratory Viruses*, *13*(5), 438–452. <https://doi.org/10.1111/irv.12649>

In this meta-analysis, Cuningham et al. (2019) summarized the results from 16 studies on timing of influenza vaccine during pregnancy, spanning eight countries and eight influenza seasons. The studies varied in design, and researchers compared immunologic responses of women vaccinated in the first, second, or third trimesters; none included confirmed or suspected influenza illness as an outcome. The authors of the meta-analysis concluded third trimester inoculation induces a greater immune response.

**Comment:** I do not think this conclusion is supported by the data. Based on data displayed in the meta-analysis (specifically, Figures 1–3), there does not appear to be a clinically-relevant difference in immune response for women vaccinated in the third trimester compared to the other trimesters (Cuningham et al., 2019). Indeed, there does not seem to be much of a difference at all. Furthermore, realistically, in clinical practice during flu season, we would vaccinate women when we see them, regardless of gestational age. If a woman presented in January for antenatal care at 14 weeks gestation, she would be sent for a flu shot if she had not already had one that season. Likewise it would not be ethical to tell a 20-week pregnant woman in October that she must wait until December to get vaccinated because that would be her third trimester.

Cuningham et al. (2019) make a legitimate attempt to adjust for seasonality, but this is nearly impossible to tease out given the nature of the data and durations of pregnancies and flu seasons. I also find it problematic that none of the researchers in the included studies looked at the actual end-point: influenza infection. Immune response is at best a proxy for this, and proxy (surrogate) outcomes are always suspect (Alonso et al., 2015; Bovbjerg et al., 2019; Buyse et al., 2016; Gomella & Oliver Sartor, 2014; Patel et al., 2016; Schievink et al., 2014). Given that pregnancy is known to induce alterations in one's immune system (Blackburn, 2003), how valid it is to compare antibody titers across trimesters?

Finally, I would like to raise a related idea: immortal time bias (Hutcheon & Savitz, 2016). This epidemiological concept must always be considered when studying pregnancy, particularly when pre-term birth (or gestational age more generally) is



the outcome. Immortal time bias can arise when you have a one-time exposure and a time-variant outcome. For instance, if we did a study on whether flu vaccines during pregnancy were associated with preterm birth, we would run into trouble because women who gave birth preterm had a shorter window during which they could have been exposed to having a flu shot. Thus, we could easily find influenza vaccination is protective because fewer women who gave birth preterm had one. However, it is not that the vaccine itself actually reduces the preterm risk; rather, women who remained pregnant then had another several weeks during which they might have gotten the flu shot. Studying flu vaccination during pregnancy is then made even more complex because of seasonality. Bottom line: all of us should get flu shots, including pregnant women.

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