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SYSTEMATIC UNDERFUNDING OF RESEARCH AND DEVELOPMENT IN MATERNAL AND PERINATAL HEALTH

Several recent publications point to evidence of systematic underfunding of research and development in maternal and perinatal health. This gross underrepresentation on research budgets persists worldwide despite the push for greater focus on health improvements for mothers and babies in public health goals from major national and international organizations, including the United Nations Millennium Development Goals and Healthy People 2010.

Fisk and Atun¹ conducted a systematic review of funding for maternal and perinatal clinical research in the United Kingdom, the European Union, the United States, Canada, Australia, India, and South Africa, looking at both governmental and philanthropic funding. They report that although maternal and perinatal conditions are the single largest contributor by category to the global disease burden, the proportion of total spending allocated to maternal and perinatal research in the countries studied ranged from <1% to 4% of all health research funding.

These findings are mirrored in the same authors' earlier analysis of funding by the global pharmaceutical industry for research and development of new drugs for use in pregnancy.² Here, the authors found that despite the fact that three-quarters of the world's >500,000 maternal deaths are attributable to preventable or treatable conditions, only 1 new class of drug licensed in the last 20 years was primarily for obstetric use, and only 17 drugs were under active development for maternal health indications at the time of their assessment.

Lyerly, Little, and Faden³ point out that in the United States, two-thirds of women take 4 to 5 medications during pregnancy, and of the more than 4 million pregnancies each year in this country, 1% are complicated by hypertension or diabetes, and >10% by psychiatric illness. Virtually all medications taken during pregnancy are prescribed "off-label," i.e., without approval by the US Food and Drug Administration for use in pregnancy. This means that there are no data on their safety or efficacy or information to guide dosing regimens in pregnancy. The Institute of Medicine 1994 report, *Women and Health Research: Ethical and Legal Implications of Including Women in Clinical Studies*, strongly recommended clinical

research to advance the medical management of diseases of pregnancy and conditions that threaten the outcomes of pregnancy.⁴ However, 15 years after the release of that report, the health and safety of pregnant women and their infants remain poorly addressed and sorely neglected on the health research agenda. The recent heightened focus on comparative effectiveness research presents an opportunity to address some of the established research gaps relating to maternal and newborn health.

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FROM COCHRANE DATABASE OF SYSTEMATIC REVIEWS (CDSR), ISSUE 2, 2009

New Systematic Reviews

- Early amniotomy and early oxytocin for prevention of, or therapy for, delay in the first stage of spontaneous labour compared with routine care
- Effect of administration of antihelminthics for soil transmitted helminths during pregnancy
- Effects of restricted caffeine intake by mother on fetal, neonatal and pregnancy outcomes
- Herbal preparations for uterine fibroids
- Maternal positions and mobility during first stage labour
- Metformin treatment before and during IVF or ICSI in women with polycystic ovary syndrome
- Music during caesarean section under regional anaesthesia for improving maternal and infant outcomes
- Outpatient versus inpatient induction of labour for improving birth outcomes
- Psychological and/or educational interventions for reducing alcohol consumption in pregnant women and women planning pregnancy

- Transcutaneous electric nerve stimulation (TENS) for pain relief in labour

Updated Systematic Reviews

- Antibiotics for prelabour rupture of membranes at or near term
- Early postnatal discharge from hospital for healthy mothers and term infants
- Elective caesarean section versus expectant management for delivery of the small baby
- Gowning by attendants and visitors in newborn nurseries for prevention of neonatal morbidity and mortality
- Hormonal versus non-hormonal contraceptives in women with diabetes mellitus type 1 and 2
- Immersion in water in labour and birth
- Oral contraceptive pill for primary dysmenorrhoea
- Oral contraceptives for functional ovarian cysts
- Prenatal administration of progesterone for preventing preterm birth in women considered to be at risk of preterm birth
- Steroidal contraceptives: effect on bone fractures in women

Cochrane Reviews are available by subscription to *The Cochrane Library*, and review abstracts are available without charge. See <http://www.thecochranelibrary.com>

FROM DATABASE OF ABSTRACTS OF REVIEWS OF EFFECTS (DARE)

Recent Abstract Entries Assessing Quality of Systematic Reviews

- Acupuncture for pelvic and back pain in pregnancy: A systematic review
- Behavioural counseling to prevent sexually transmitted infections
- Optimal frequency of imiquimod (Aldara) 5% cream for the treatment of external genital warts in immunocompetent adults: A meta-analysis
- Perinatal mortality and other severe adverse pregnancy outcomes associated with treatment of cervical intraepithelial neoplasia: Meta-analysis
- Postoperative urinary incontinence after total abdominal hysterectomy or supracervical hysterectomy: A metaanalysis
- Self-help smoking cessation interventions in pregnancy: A systematic review and meta-analysis
- Therapeutic management, delivery, and postpartum risk assessment and screening in gestational diabetes
- The role of exercise in preventing and treating gestational diabetes: A comprehensive review and recommendations for future research
- Universal newborn hearing screening: Systematic review to update the 2001 U.S. preventive services task force recommendation

DARE abstracts are available without charge from www.york.ac.uk/inst/crd/crddatabases.htm#DARE

EVIDENCE-BASED REVIEWS FROM OTHER SOURCES

Featured review: Poobalan AS, Aucott LS, Gurung T, Smith WC, Bhattacharya S. Obesity as an independent risk factor for elective and emergency caesarean delivery in nulliparous women—Systematic review and meta-analysis of cohort studies. Obes Rev 2009;10:28–35.

A meta-analysis examined the influence of body weight on birth modality, clarifying the association between obesity and both elective and emergency cesarean section in nulliparous women, independent of related comorbidities, such as diabetes and hypertension. Eleven cohort studies published between 1996 and 2007, reporting data from 209,193 women, were included. All were all rated high quality. Raw data were converted into crude odds ratios with 95% confidence intervals, which were then pooled through meta-analysis, adjusting for potentially confounding comorbidities. When compared to women of normal body mass index, overweight women were 47% more likely to deliver by cesarean section, while obese women were more than twice as likely and morbidly obese women were more than 3 times as likely to have a cesarean birth. In subgroup analysis, odds of emergency cesarean were slightly higher than odds of elective cesarean in each weight category, in comparison with normal weight women.

Comment: Obesity in the United States has soared over the last 10 years, with only 1 state (Colorado) reporting a population rate under 20% in 2007, according to data from the Centers for Disease Control and Prevention. Pervasive cultural bias may lower expectations of health professionals and women themselves for obese women's ability to have a successful vaginal birth and could contribute to higher cesarean rates in this population. Yet, paradoxically, the surgical risk of anesthesia complications and infection is significantly higher in obese women. While research on weight restriction in pregnancy is needed, this study supports the value of identifying and implementing effective interventions to help women achieve a normal body mass index in the preconception period.

Featured review: Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: A systematic review and meta-analysis. JAMA 2009;301:636–50.

The authors conducted a systematic review and separate meta-analysis of observational studies reporting data on body mass index and congenital anomalies. Thirty-nine studies were included in the systematic review, and pooled analysis from 18 of those was presented in the accompanying meta-analysis. Overweight and obesity were defined according to World Health Organization criteria as body mass index (BMI) >25 and BMI >30, respectively. Fetuses of women who were obese at onset of pregnancy had

a significantly elevated risk of neural tube defects, cardiovascular anomalies, cleft lip and palate, anorectal atresia, hydrocephaly, and limb reduction defects. Increased risk for overweight women did not reach significance for any of the anomalies studied; differences in weight categorization across studies and small numbers of cases of certain anomalies may have influenced these outcomes, and further research is warranted.

Comment: While the increase in absolute risk of a congenital anomaly associated with obesity is small for any individual woman (on average, 0.55 per 1000 births), with a third of American women over age 15 reportedly obese in 2004, the population risk is significant. Congenital anomalies account for 20% of all infant deaths in the United States, and contribute to long-term morbidity. As childbearing women are highly motivated to make health improvements that benefit their offspring, pre- and inter-conceptual messages should include information for obese women on the presumed benefits for their babies of pre-pregnancy weight loss.

Featured reviews: (1) Maruthur NM, Bolen SD, Brancati FL, Clark JM. The association of obesity and cervical cancer screening: A systematic review and meta-analysis. *Obesity* 2009;17:375–81. (2) Maruthur NM, Bolen S, Brancati FL, Clark JM. Obesity and mammography. *J Gen Intern Med* 2009;24:665–77.

Two meta-analyses addressed the influence of obesity on rates of screening for cervical and breast cancer, and assessed differential effects for black and white women. Included studies were conducted in the United States using nationally representative samples, and World Health Organization body mass index (BMI) categories (normal = 18.5–24.9; overweight = 25–29.9; class I obesity = 30–34.9; class II obesity = 35–39.9; class III obesity >40). Odds of reported Papanicolaou screening in the last 1 to 3 years were 10%, 20%, 25%, and 40% lower for overweight, class I, class II, and class III obese women, respectively, than for those of normal weight. Odds of reported mammography in the last 2 years were 20% lower for class III obese women compared to women of normal BMI. In stratified analysis by race, these results held for white women, but no statistically significant difference in rates of screening by BMI was observed for black women in any overweight category, compared to those of normal weight.

Comment: Hormonal effects of obesity may contribute to the pathogenesis of cervical and postmenopausal breast cancer. While screening rates for black and white women are comparable, black women experience higher mortality from breast and cervical cancer than their white counterparts. The prevalence of overweight and obesity is higher in black women than in white women in all BMI categories. The authors highlight racial differences in body image as a potential reason for the disparate rates of preventive screening. Cultural pressure to comply with idealized standards of beauty is detrimental to all women. Given the

increasing prevalence of obesity among women, special efforts should be made to ensure regular screening for breast and cervical cancer for women at higher than normal BMI.

Recent Evidence-Based Reviews

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