40 Tobacco and alcohol use during pregnancy

Beth A. Bailey and Robert J. Sokol

INTRODUCTION

Substance use, including the most common behaviors of smoking and drinking, is a major health issue for women, regardless of age and reproductive or pregnancy status. Health risks to women can be substantial, and during pregnancy, these risks are shared with the developing fetus. Even with the recognition of the adverse impact of these substances on maternal and fetal health, obstetric clinicians, many of us who might be said to have “surgical personalities,” often have difficulty dealing effectively with these “behavioral medicine” issues. Our goal in this concise chapter is to highlight the magnitude of the problems these substances pose during pregnancy and the adverse consequences of the use of these substances on the mother and the offspring, briefly noting some plausible mechanisms for effect. We then turn our attention to the practical issues of how to identify pregnant women who are smoking or consuming alcohol and how to help her make changes in her behavior to benefit both her own health and that of her unborn child.

EPIDEMIOLOGY

Cigarettes

Nationally, approximately 11% to 13% of women report smoking throughout pregnancy (1,2). However, rates of pregnancy smoking vary considerably by region. For example, many Southern states have rates of pregnancy smoking near 20% (2), with rural regions seeing rates from 30% to 40% (3–5).

Smoking during pregnancy can occur in any subpopulation; however, certain women are statistically more likely to smoke while pregnant. Research has revealed that white women are significantly more likely to smoke during pregnancy than their African-American or Hispanic counterparts (1,6). Additionally, women who live in poverty, who have lower levels of education, and who receive Medicaid are more likely to be pregnancy smokers than other women (6–8).

Alcohol

Each year in the United States, approximately half a million pregnant women are thought to drink alcohol (9). This translates into a prevalence rate of nearly 13% and is consistent with the more than 10% of pregnant women who reported current alcohol use as part of the 2002 Behavioral Risk Factor Surveillance Survey (10) and the 15% to 20% identified in a large-scale study conducted more than 15 years ago (11). While estimates vary, anywhere from 2% to 6% of women engage in heavy, frequent, or binge-drinking while pregnant (9,10,12).

Drinking during pregnancy occurs across diverse populations and sociodemographic conditions. However, certain racial groups see higher rates of pregnancy drinking, including African-Americans and American Indians/Alaskan

Natives (13). Additionally, women over the age of 30, those who are unmarried, and those who have lower incomes are also at a statistically increased risk of pregnancy alcohol consumption (14). Finally, smoking and drinking often go hand in hand during pregnancy. Women who smoke more than half a pack of cigarettes per day during pregnancy are more than twice as likely as nonsmokers to consume alcohol (38% vs. 17%) (14).

ETIOLOGY AND PATHOPHYSIOLOGY

Cigarettes

A significant amount of evidence has accumulated documenting the deleterious effects of pregnancy smoking. The potential short- and long-term effects for the mother have been well reported and include significantly increased risk of respiratory, cardiovascular, and cancer-related diseases. The potential for harmful fetal effects is also profound. Tobacco use in pregnancy is associated with significantly increased rates of pregnancy complications and adverse birth outcomes (15). Ectopic pregnancy, placenta previa and abruption, stillbirth, premature rupture of membranes, and intrauterine growth restriction have all been associated with gestational exposure to cigarettes (16–19). For a smoke-exposed fetus that survives to delivery, the increased likelihood of low birth weight and preterm birth is substantial, with risk increasing with the number of cigarettes smoked per day (6,20). Nationally, smoking accounts for 20% to 30% of all low birth weight births (20), and research indicates that infants born to women who smoke are 200 to 300g lighter than those born to nonsmokers (4,21). Smoking in pregnancy also nearly doubles the risk of preterm birth (22,23), producing a significant economic cost through neonatal intensive care unit (NICU) admission and treatment. Indeed, babies born to smokers are twice as likely to be admitted to the NICU as those born to nonsmokers (4). Smoke-exposed newborns have an increased risk for respiratory dysfunction, intraventricular hemorrhage, necrotizing enterocolitis, and retinopathy (15). Finally, an increased likelihood of infant mortality is associated with heavy pregnancy smoking, with exposure accounting for 5% of perinatal deaths (24).

Prenatal exposure to cigarettes has also been shown to have long-term developmental consequences. Physical health effects well into childhood include growth restriction, abnormal neuromotor tone, increases in respiratory infections, asthma, otitis media, and obesity (25–30). Long-term effects on cognitive development, including learning problems and delayed academic achievement, have also been reported (31–33). Finally, prenatal exposure to cigarettes has been implicated in significantly increased rates of behavioral and mental health problems, including attention deficit hyperactivity disorder, conduct disorders,

depressive and anxiety disorders, criminal behavior, and substance use, abuse, and dependence (34–44).

While not yet completely understood, the mechanisms by which maternal smoking leads to fetal harm and longer term developmental problems have been explored in both animal and human models. The most often cited compounds in cigarettes known to cause harm to the fetus are nicotine, carbon monoxide, and cyanide. Cyanide has been shown, in multiple studies, to be harmful to rapidly dividing cells (45). Carbon monoxide combines with hemoglobin to produce carboxyhemoglobin thus lowering blood oxygen tension and likely contributing to fetal hypoxia (46). In addition, nicotine and carbon monoxide both reduce placental blood flow, impacting fetal growth. A recent study suggested that maternal smoking leads to decreased concentrations of fetal insulin, insulin-like growth factor (IGF), and IGF binding protein, which all may be involved in the pathway by which prenatal cigarette exposure impacts development (47). Thus, both hypoxia and chemicals responsible for growth may be responsible for cell death, structural alterations, and consequent delayed development when prenatal cigarette exposure occurs. Still other studies have focused on the potential impact of nicotine on the developing nervous and neurochemical systems (48). Fetal exposure to smoking, and nicotine in particular, has been proposed to impact serotonin uptake, changes in dopaminergic systems, and changes in DNA and RNA synthesis in the brain during critical developmental periods (49,50). Any one of these potential pathways could impact both structural and functional development, leading to the negative outcomes that have been observed in children exposed to smoking during gestation (51). However, further study is needed.

Alcohol

It has been four decades since the characteristics of children born to women who consumed alcohol during pregnancy were described in the medical literature (52). The term “fetal alcohol syndrome” (FAS) describes children with prenatal alcohol exposure and resultant growth restriction, central nervous system/neurodevelopmental delays, and facial malformations. In addition to typical or classic FAS, terms such as “alcohol-related neurodevelopmental disorder” and “fetal alcohol spectrum disorder” characterize a range of problems associated with prenatal alcohol exposure (53). Research has clearly documented the adverse outcomes associated with alcohol exposure during gestation. Full FAS is characterized by prenatal and postnatal growth deficiency, including reduced overall height and microcephaly, and being born small for gestational age with little catch-up seen into childhood; specific facial dysmorphology including long smooth philtrum, thin upper lip, midfacial hypoplasia, small eyes, and inner epicanthal folds; and central nervous system and neurodevelopmental abnormalities including decreased cognitive abilities (52,53).

Even in the absence of diagnosable FAS, alcohol consumption during pregnancy increases the risk of poor outcomes in children. Prenatal alcohol consumption is a strong predictor of low birth weight. Early studies clearly identified a link between even moderate consumption and low birth weight (54), and recent large-scale studies have reported strong associations between exposure and birth weight (55). Consuming one or more drinks

per day was associated with a fivefold increase in the likelihood of a low-birth weight delivery (56), while three or more drinks per week were associated with a nearly 150-g reduction in birth weight (57). Recent evidence suggests that some of the lowered birth weight associated with pregnancy alcohol consumption is accounted for by an increased risk of preterm birth. One or more drinks per day have been found to more than double the risk of preterm birth (56). Even lesser levels of consumption have been linked to 10-fold or more increases in the risk of extreme preterm birth (prior to 32 weeks of gestation) (58). Mild prematurity was also linked to pregnancy alcohol consumption, particularly in women over the age of 30 (58).

The link between prenatal alcohol exposure and low birth weight and preterm birth is of significant consequence as these are leading causes of neonatal morbidity and mortality in the United States and the strongest biologic predictors of immediate and long-term developmental outcomes (59). In addition to the pathway through birth weight and gestational age, gestational alcohol exposure, even in the absence of full FAS, appears to independently impact a multitude of outcomes into childhood. Continued growth restriction, delays in gross and fine motor development, and impairments in visual motor integration have all been reported (30,60–62). Decreases in overall cognitive performance and general intelligence quotient scores have been associated with even moderate levels of prenatal alcohol exposure (63), in addition to specific deficits including slowed mental processing (64), delayed language and reading abilities (65,66), and increased learning problems (63). Studies have shown that children with prenatal alcohol exposure have problems with organizing and maintaining attention, and with impulsivity (67). Behavioral problems, including hyperactivity and delinquent behavior, have also been reported (68,69). Finally, long-term studies have described associations between prenatal alcohol exposure and many specific psychiatric disorders (70).

The mechanism by which prenatal exposure to alcohol leads to adverse pregnancy, newborn, and longer term developmental outcomes is not yet thoroughly understood. As has been recently reviewed, neuroimaging studies have shown overall and region-specific surface area and volumetric reductions, structural alterations, and white and gray matter density abnormalities (71). These alterations could all be involved in the physical and neurobehavioral effects of exposure. In addition, both animal and human studies have suggested that exposure to alcohol during gestation may cause hypothalamic–pituitary–adrenal (HPA) axis hyperactivity, thereby leading to significant adverse cognitive and behavioral outcomes (72). Furthermore, animal models have shown alcohol intake to decrease blood flow to the placenta, impacting cell growth and death (73). Finally, alcohol consumption increases the production of prostaglandins during pregnancy (74), resulting in decreased cell division (75). Any one, or a combination of these processes, could explain the mechanism by which prenatal alcohol exposure impacts development and outcomes, but further study is clearly needed.

DIAGNOSIS

Cigarettes

In a 2000 bulletin (updated in 2005), the American College of Obstetricians and Gynecologists (ACOG) recommended

screening all pregnant women for smoking (76). Recent reports suggest that prenatal care providers vary widely in rates of screening all pregnant patients for smoking. For example, one study found that 98% of Ohio obstetricians reported asking all patients about smoking (77), while another study found that only 28% of obstetricians in rural southern Appalachia reported always asking (78). Reasons providers have given for failure to screen for pregnancy smoking have included lack of time, other issues taking priority, lack of confidence in skills, lack of referral sources, and beliefs that attempts to intervene will not be successful (77,78).

The most common method of determining smoking status during pregnancy has been via self-report, either by oral or written questioning. Self-report data have the advantage of being inexpensive and easy to collect, with responses immediately available (79), and a handful of studies involving pregnant women have suggested that self-reported smoking status is accurate (80,81). Others have suggested, however, that self-report of smoking status during pregnancy is unreliable and results in significant misclassification and underestimation of prevalence rates (82). An examination of the numerous studies that have investigated the association between self-report of pregnancy smoking status and biochemical verification has revealed false denial or deception rates as low as 1% and as high as 35%. A recent review of this literature concluded that measuring smoking status during pregnancy by self-report alone significantly underestimates smoking rates and misclassifies a significant proportion of women (79).

Several factors likely contribute to inaccuracies in self-report of smoking status during pregnancy, including faulty recall and intentional deception (79). As greater attention is given to the health effects of smoking, both in general and during pregnancy, and as efforts to regulate and reduce smoking increase, smoking becomes stigmatized and individuals are sensitized to socially desirable forms of behavior (83). As this occurs, it is likely that concealment of smoking during pregnancy in particular may increase (84). Multiple studies have shown that many factors may help reduce false denial of smoking among pregnant women, including appropriate wording, timing, and setting of inquiries of smoking status (85,86). For example, we know that the use of a structured multiple choice format in a private confidential setting may increase disclosure (87). Indeed, studies have shown that use of a five-response choice question (Box 1) increases disclosure over asking “Do you smoke?” by 40% (87).

Given the drawbacks of self-report, determination of pregnancy smoking status in both clinical and research settings often relies on biochemical assessment. Cotinine, a major metabolite of nicotine, is a commonly used biomarker of exposure to tobacco smoke, and cotinine levels in saliva, blood, and urine are often considered the best measure of nicotine consumption (88). Compared with self-report, cotinine levels have been shown to be more accurate indicators of smoking (79) and to be better predictors of pregnancy outcomes (89). Biochemical assessment of smoking behavior is not without limitations, however (83). In addition to the factors of cost and inconvenience, acceptance of appropriately sensitive and specific cutoff points is far from universal. Varying cotinine cutoff levels

Box 1 Pregnancy Smoking Screening Question

Please choose the response that best describes your smoking

(A) I have *never* smoked or I have smoked fewer than 100 cigarettes in my lifetime

(B) I stopped smoking *before* I found out I was pregnant, and I am not smoking now

(C) I stopped smoking *after* I found out I was pregnant, and I am not smoking now

(D) I smoke some now, but I *cut down* on the number of cigarettes I smoke since I found out I was pregnant

(E) I smoke regularly now, about the *same* as before I found out I was pregnant

If the patient responds A, no further follow-up is needed

If the patient responds B or C, reinforce her decision to quit, congratulate her on the success of quitting, and encourage her to remain smoke free

If the patient responds D or E, she should be classified as a smoker. Document and intervene

Source: From Ref. 87.

have been proposed to distinguish smokers from nonsmokers and from those exposed to environmental tobacco smoke (ETS) (90–92). Given varying cut-point recommendations, the use of biochemical assessment may not ever be completely accurate in distinguishing those who smoke, especially intermittently, from those who are only exposed to ETS (93). Thus, using both self-report and biochemical assessment is likely to yield the most accurate information about pregnancy smoking status.

Alcohol

For many years, ACOG has consistently advised clinicians to question all pregnant women at their first prenatal visit about current and past alcohol use (94). A recent survey of more than 600 practicing ACOG members revealed that over 90% asked all women at their first prenatal visit about alcohol use (95). Barriers noted by those who failed to routinely screen prenatal patients for alcohol use included time limitations, patient sensitivity, lack of confidence in skills, and inadequate referral sources.

Even when providers do assess pregnancy alcohol consumption, detection is complicated by many of the same factors that impact the determination of smoking status. Pregnancy alcohol consumption has also become increasingly stigmatized as public awareness of the dangers has increased, leading to the potential for high rates of denial via self-report (96). In addition, and unlike biochemical assessment of smoking status, no reliable biologic marker is available to reveal alcohol use. Although analysis of both meconium and hair samples for fatty acid ethyl esters has been proposed, neither would practically detect alcohol use during pregnancy, and no large population-based studies have validated these methods (97). Similarly, other biochemical markers, such as ethanol metabolites, that reveal only very recent use have not yet been well validated or have not been shown to have adequate diagnostic sensitivity and/or specificity in identifying drinking in pregnant women (98). Thus, most researchers and physicians rely on self-report of maternal alcohol use during pregnancy (53).

Box 2 T-ACE Screening Tool for Pregnancy Risk Drinking^a

Tolerance

“How many drinks does it take to make you feel high?”

A positive answer, scored a 2, is more than two cans of beer, two glasses of wine, or two mixed drinks. This suggests tolerance of alcohol and very likely a history of at least moderate-to-heavy alcohol intake

Annoyed

“Have people annoyed you by criticizing your drinking?”

Cut Down

“Have you felt you ought to cut down on your drinking?”

Eye-Opener

“Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?”

^aThe first question is scored 0 or 2 points. The last three questions are scored 1 point if answered affirmatively. A total score of 2 or more is considered positive for risk drinking. Source: From Ref. 100.

Studies indicate that obstetricians often obtain inaccurate alcohol consumption information from their patients. For example, in a prospective study that included high-risk women, almost twice as many admitted to drinking during a research interview compared with indications from maternal medical records (99). While tools are available to assist prenatal care providers in accurately identifying women who consume alcohol during pregnancy, a recent study revealed that fewer than one quarter who screen for pregnancy alcohol consumption use a standardized screening tool (95). The T-ACE, a modification of a traditional alcohol screening test, the CAGE, but specifically adapted for use before and during pregnancy, consists of four questions that may be asked as part of the medical history by physicians or office personnel (Box 2) (100). It typically identifies 90% or more of potential pregnancy risk drinkers, and follow-up questions can rule out false positives (101). The CAGE, also a four-item scale commonly used in obstetric practices, was developed for and validated with men and has not been shown to be valid with pregnant women (100). The TWEAK, a five-item scale, was developed for and validated with pregnant women (102). However, this tool appears to have lower sensitivity for detection of drinking among minority women and has no additional validity over the T-ACE. The AUDIT-C is a three-item scale to screen for alcohol use during pregnancy, rather than consequences of use as queried in the previously described screens. While this tool includes assessment of quantity and pattern of alcohol use, and initial data suggest good sensitivity across different samples, additional validation of the AUDIT-C is needed. Consequently, ACOG and the National Institute on Alcohol Abuse and Alcoholism have both recommended the T-ACE as the best tool for screening all reproductive-aged women and pregnant women specifically for alcohol use.

MANAGEMENT

Cigarettes

Addressing cigarette exposure with pregnant smokers should be a top priority for all prenatal care providers, as research has shown that when women quit smoking during pregnancy, the risk of adverse outcomes is nearly reduced to levels experienced by nonsmokers (103). Furthermore, growing

Box 3 The 5 A’s Intervention for Pregnant Smokers

Ask

Tobacco status is queried with a multiple-choice question format and answers are documented in the patient chart

Advise

Urge all tobacco users to quit in a clear, strong, personalized manner. Discuss the benefits of quitting including the potential harms of smoking to the fetus and the long-term health consequences of the mother. Provide pregnancy-specific educational materials

Assess

Determine the patient’s willingness to quit in the next 30 days and encourage the patient to minimize exposure to secondhand smoke. If the patient declines smoking cessation or is ambivalent, work to increase the patient’s motivation to quit

Assist

Provide aid for the patient to quit. Set a quit date. Provide counseling with skills building, pregnancy-specific self-help and smoking cessation materials, and social support. Develop a contract to quit smoking. Encourage a patient diary to record successes, problems, and triggers. Discuss alternate behaviors, potential problem situations, and how to handle slipups

Arrange

Provide follow-up contact, either in person or by telephone soon after the quit date, and further follow-up encounters as needed. Congratulate success during each visit. Review circumstances if relapse occurred and use it as a learning experience for the patient. Consider referral or more intensive treatment. Begin postpartum relapse prevention counseling late in pregnancy

Source: From Ref. 108.

evidence suggests that clinically proven interventions can lead to significant successes in smoking cessation (104). Increasingly, obstetric providers are implementing brief interventions (BIs)—low-cost, time-efficient, and effective self-help treatments involving counseling—with their prenatal smokers. The five A’s BI method of smoking cessation counseling (ask, advise, assess, assist, and arrange), which can be administered in as few as 3 minutes, is considered best practice and has been adapted for use during pregnancy (Box 3) (105). Most physicians have found this model effective and easy to use in the course of a regular prenatal visit.

When properly implemented, the five A’s method results in cessation rates up to four times higher than the rates for those who attempt to quit on their own (106), and 70% higher than traditional physician advice (105). To date, nearly 100 published studies have detailed the effectiveness of various office-based smoking cessation interventions for pregnant women. A 2008 Cochrane Review of clinical trials showed a significant reduction in pregnancy smoking intervention groups compared with controls (107). The most effective interventions were those based on or similar to the five A’s, with these “low-intensity” interventions just as effective as those of higher intensity (i.e., longer and more frequent sessions conducted by counseling professionals encompassing

Box 4 Brief Intervention for Reducing Alcohol Use During Pregnancy—FRAMES Approach

- F: *Feedback* of personal risk. Compare the patient's level and drinking patterns with pregnancy-recommended abstinence. The patient may not be aware that what she considers normal activity is actually risky
- R: *Responsibility* for personal control. Stress to the patient that it is her responsibility to make the change for the health of her baby
- A: *Advice* to change. Give direct advice (not insistence) to the patient to change her drinking behavior
- M: *Menu* of ways to reduce/stop drinking. Identify when the patient is likely to drink and solicit alternate ways that she might handle these situations
- E: *Empathy*. Use a style of interaction that is understanding and involved. Remain positive and encouraging and avoid being judgmental and preachy
- S: *Self-efficacy*. Elicit and reinforce self-motivating statements such as "I am confident that I can stop drinking." Encourage the patient to develop strategies, implement them, and commit to change

Source: From Ref. 111.

multiple types of efforts). In a 2005 bulletin, ACOG established the five A's as a standard component of prenatal care for all smokers (108). And in a 2009, the U.S. Preventive Services Task Force reaffirmed that the net benefit of using a five A's office-based intervention with pregnant smokers is substantial (109).

Alcohol

Once a prenatal patient had been identified as consuming alcohol, the management options available to the provider will depend upon training, expertise, and available resources. For women who drink but are not alcohol dependent, an in-office BI may be all that is needed to reduce the risk of an alcohol-exposed pregnancy. For alcohol-dependent women, a BI, coupled with referral to specialized treatment programs, is recommended (110). BIs, including the structured five A's approach described above for use with smokers, can be delivered by health professionals who are not specialists in the treatment of substance use and dependence. Increasing numbers of physicians have obtained continuing education training in motivational interviewing for use with pregnant women who consume alcohol. Motivational interviewing, a type of BI, helps empower the patient to make lifestyle changes while minimizing resistance (111). Using this approach with pregnant alcohol users specifically, the physician can illustrate the importance of abstinence or decreased alcohol intake and the avoidance of binge-drinking, and offer encouragement and optimism about change (112). The most successful interventions follow the FRAMES approach (Box 4).

Research has suggested that women, even those identified as heavy drinkers, respond to motivational interviewing (113,114). In a multicenter randomized controlled trial to reduce the risk for alcohol-exposed pregnancies, 830 at-risk women received educational information plus motivational interviewing or information alone (115). The intervention

consisted of four counseling sessions and one contraceptive consultation. The intervention group had a 70% decrease in risk for alcohol-exposed pregnancies, more than twice the risk reduction for the information-only group at 3-, 6-, and 9-month follow-up (ORs 2.3, 2.2, and 2.1, respectively). In another randomized controlled trial involving only pregnant women, 255 patients who reported alcohol consumption were recruited from a community-based setting and randomly assigned to receive intervention or assessment only (116). The intervention consisted of multiple BI sessions with a nutritionist that included education and feedback, cognitive behavioral procedures, goal setting, and contracting. Compared with women in the control group, women who received the intervention were five times more likely to report abstinence by the end of the pregnancy. In addition, their newborns had significantly higher birth weights and lengths, and a three times lower fetal mortality rate. In another study, a BI administered by nurses and physicians during a prenatal care visit was evaluated with 300 alcohol-consuming women (117). The BI in this study was a single session, averaging 25 minutes, which included knowledge assessment with feedback, goal setting and contracting, behavioral modification, and tips for handling difficult situations. Although pregnancy alcohol consumption decreased for both those who received the intervention and those who received only an assessment, those who received the BI had the most significant decrease. In addition, the greatest decreases were seen among women with the highest initial consumption and those whose partners also participated in the BI. Still other studies have shown that follow-up is critical, as a series of BIs is generally more effective than a single suggestion to stop drinking (118).

CONCLUSIONS

As many as 20% of pregnancies are complicated by smoking and/or alcohol consumption. Exposure to either substance significantly increases the risk of poor pregnancy outcomes including low birth weight and preterm birth. Prenatal smoke exposure in particular is implicated in substantial health problems early in life, while both smoke and alcohol exposure can lead to long-term growth delays and cognitive and behavioral problems. While biochemical assessment can be used to identify women who smoke during pregnancy, no reliable biomarker for alcohol consumption is yet clinically applicable. Self-report of smoking and alcohol use is typically relied upon in clinical settings, and reliable and well-validated tools are available and recommended for use with all prenatal patients. Once women who smoke or drink during pregnancy are identified, brief proven interventions can aid the busy clinician in working with patients to reduce or eliminate these pregnancy risk behaviors.

REFERENCES

1. Martin JA, Hamilton BE, Sutton PD, et al. Births: final data for 2002. *Natl Vital Stat Rep* 2003; 52: 1–113.
2. March of Dimes. Peristats. [Available from: <http://www.marchofdimes.com/peristats/>]. Accessed 18 February 2008.
3. Bailey BA. Factors predicting pregnancy smoking in Southern Appalachia. *Am J Health Behav* 2006; 30: 413–21.
4. Bailey BA, Jones Cole LK. Rurality and birth outcomes: findings from Southern Appalachia and the potential role of pregnancy smoking. *J Rural Health* 2009; 25: 141–9.

5. Missouri Monthly Vital Statistics. Focus...Maternal Smoking Trends in Missouri: 1978-1997. Jefferson City, MO: Missouri Department of Health. Center for Health Information Management and Epidemiology 1998; 32.
6. Zotti ME, Replogle WH, Sappenfield WM. Prenatal smoking and birth outcomes among Mississippi residents. *J MSMA* 2003; 44: 3-9.
7. Jesse DE. Prenatal psychological needs: differences between a TennCare group and a privately insured group in Appalachia. *J Health Care Poor Underserved* 2003; 14: 535-49.
8. Phares TM, Morrow B, Lansky A, et al. Surveillance for disparities in maternal health related behaviors-selected states, pregnancy risk assessment monitoring system (PRAMS), 200-2001. *MMWR* 2004; 53: 1-13.
9. Floyd RL, Sidhu JS. Monitoring prenatal alcohol exposure. *Am J Med Genet C* 2004; 127C: 3-9.
10. CDC. Behavioral Risk Factor Surveillance System. Atlanta, GA: US Department of Health and Human Services, CDC. [Available from: <http://www.cdc.gov/brfss>].
11. Ebrahim SH, Luman ET, Floyd RL, et al. Alcohol consumption by pregnant women in the United States, 1988-1995. *Obstet Gynecol* 1998; 92: 187-92.
12. Stratton K, Howe C, Battaglia F, eds. Fetal Alcohol Syndrome: Diagnosis, Epidemiology, Prevention, and Treatment. Washington, DC: National Academy Press, 1996.
13. Fetal alcohol syndrome - Alaska, Arizona, Colorado, and New York, 1995-1997. *MMWR* 2002; 51: 433-5.
14. Centers for Disease Control and Prevention. Sociodemographic and behavioral characteristics associated with alcohol consumption during pregnancy-United States. *MMWR* 1995; 44: 261-4.
15. Crawford JT, Tolosa JE, Goldenberg RL. Smoking cessation in pregnancy: why, how, and what next. *Clin Obstet Gynecol* 2008; 51: 419-35.
16. Dominguez-Rojas V, de Juanes-Pardo JR, Astasio-Arbiza P, et al. Spontaneous abortion in a hospital population: are tobacco and coffee intake risk factors? *Eur J Epidemiol* 1994; 10: 665.
17. Harger JH, Hsing AW, Tuomala RE, et al. Risk factors for preterm premature rupture of fetal membranes: a multicenter case-control study. *Am J Obstet Gynecol* 1990; 163: 130-7.
18. Ananth CV, Savitz DA, Luther ER. Maternal cigarette smoking as a risk factor for placental abruption, placenta previa, and uterine bleeding in pregnancy. *Am J Epidemiol* 1996; 144: 881.
19. Spinillo A, Capuzzo E, Nicola SE, et al. Factors potentiating the smoking-related risk of fetal growth retardation. *Br J Obstet Gynaecol* 1994; 101: 954.
20. U.S. Department of Health and Human Services. Women and smoking: a report of the surgeon general. Rockville, MD: USDHHS, CDC, National Center for Chronic Disease Prevention and Health Promotion, Office of Smoking and Health, 2001.
21. Chiolerio A, Bovet P, Paccaud F. Association between maternal smoking and low birth weight in Switzerland: the EDEN study. *Swiss Med Wkly* 2005; 135: 525-30.
22. Hammoud AO, Bujold E, Sorokin Y, et al. Smoking in pregnancy revisited: findings from a large population-based study. *Am J Obstet Gynecol* 2005; 192: 1856-62.
23. Kolas T, Nakling J, Salvesen KA. Smoking during pregnancy increases the risk of preterm births among parous women. *Acta Obstet Gynecol Scand* 2000; 79: 644-8.
24. No authors. Medical care expenditures attributable to cigarette smoking during pregnancy-United States. *MMWR* 1997; 46: 1048-50.
25. Rona RJ, China S, DuVe FC. Exposure to cigarette smoking and children's growth. *Int J Epidemiol* 1985; 14: 402-9.
26. Fried PA. Cigarettes and marijuana: are there long term measurable neurobehavioral teratogenic effects? *Neurotoxicol* 1989; 10: 577-84.
27. Fergusson DM, Horwood LJ. Parental smoking and respiratory illness during early childhood: a 6-year longitudinal study. *Pediatr Pulmonol* 1985; 1: 99-106.
28. Seidman DS, Laor A, Stevenson SK. Is maternal and paternal smoking during pregnancy associated with asthma in late adolescence? *Pediatr Res* 1997; 41: 1042A.
29. Toschke AM, Montgomery SM, Pfeiffer U, et al. Early intrauterine exposure to tobacco-inhaled products and obesity. *Am J Epidemiol* 2003; 158: 1068-74.
30. Covington CV, Nordstrom-Klee B, Ager J, et al. Birth to age 7 growth of children prenatally exposed to drugs: a prospective cohort study. *Neurotoxicol Teratol* 2002; 24: 489-96.
31. Batstra L, Hadders-Algra M, Neeleman J. Effect of antenatal exposure to maternal smoking on behavioral problems and academic achievement in childhood: prospective evidence from a Dutch birth cohort. *Early Hum Dev* 2003; 75: 21-33.
32. Fried PA. Adolescents prenatally exposed to marijuana: examination of facets of complex behaviors and comparisons with the influence of in utero cigarettes. *J Clin Pharmacol* 2002; 42: 97S-102S.
33. Sexton M, Fox NL, Hebel JR. Prenatal exposure to tobacco: II. Effects on cognitive functioning at age 3. *Int J Epidemiol* 1990; 19: 72-7.
34. Fergusson DM, Horwood LJ, Lynskey MT. Maternal smoking before and after pregnancy: effects on behavioral outcomes in middle childhood. *Pediatr* 1993; 92: 815-22.
35. Fergusson DM, Woodward LJ, Horwood LJ. Maternal smoking during pregnancy and psychiatric adjustment in late adolescence. *Arch Gen Psychiatr* 1998; 55: 721-7.
36. Wakschlag LS, Pickett KE, Cook E, Benowitz NL, Leventhal BL. Maternal smoking during pregnancy and severe antisocial behavior in offspring: a review. *Am J Public Health* 2002; 92: 966-74.
37. Nigg JT, Breslau N. Prenatal smoking exposure, low birth weight, and disruptive behavior disorders. *J Am Acad Child Adolesc Psychiatr* 2007; 46: 362-9.
38. Milberger S, Biederman J, Faraone SV, Jones J. Further evidence of an association between maternal smoking during pregnancy and attention deficit hyperactivity disorder: findings from a high-risk sample of siblings. *J Clin Child Psychol* 1998; 27: 352-8.
39. Williams GM, O'Callaghan M, Najman JM, et al. Maternal cigarette smoking and child psychiatric morbidity: a longitudinal study. *Pediatrics* 1998; 102: e11.
40. Rasanen P, Hakko H, Isohanni M, et al. Maternal smoking during pregnancy and risk of criminal behavior among adult male offspring in the northern Finland 1966 birth cohort. *Am J Psychiatr* 1999; 156: 857-62.
41. Brennan PA, Grekin ER, Mortensen EL, Mednick SA. Relationship of maternal smoking during pregnancy with criminal arrest and hospitalization for substance abuse in male and female adult offspring. *Am J Psychiatr* 2002; 159: 48-54.
42. Weissman MM, Warner V, Wickramaratne PJ, Kandel DB. Maternal smoking during pregnancy and psychopathology in offspring followed to adulthood. *J Am Acad Child Adolesc Psychiatr* 1999; 38: 892-9.
43. Buka SL, Shenassa ED, Niaura R. Elevated risk of tobacco dependence among offspring of mothers who smoked during pregnancy: a 30-year prospective study. *Am J Psychiatr* 2003; 160: 1978-84.
44. Cornelius MD, Leech SL, Goldschmidt L, Day NL. Is prenatal tobacco exposure a risk factor for early adolescent smoking? A follow-up study. *Neurotoxicol Teratol* 2005; 27: 667-76.
45. Andres RL, Day MC. Perinatal complications associated with maternal tobacco use. *Semin Neonatal* 2000; 5: 231-41.
46. Lehtovirta P, Forss M. The acute effects of smoking on intervillous blood flow of the placenta. *Br J Obstet Gynaecol* 1978; 85: 729-31.
47. Ingvarsson RF, Bjarnason AO, Dagbjartsson A, et al. The effects of smoking in pregnancy on factors influencing fetal growth. *Acta Paediatr* 2007; 96: 383-6.
48. Mansi G, Raimondi F, Pichini S, et al. Neonatal urinary cotinine correlates with behavioral alterations in newborns prenatally exposed to tobacco smoke. *Pediatr Res* 2007; 61: 257-61.
49. Fergusson DM. Prenatal smoking and antisocial behavior. *Arch Gen Psychiatry* 1999; 56: 223-4.
50. Falk L, Nordberg A, Seiger A, Kjaeldgaard A, Hellstrom-Lindahl E. Smoking during early pregnancy affects the expression pattern of both nicotinic and muscarinic acetylcholine receptors in human first trimester brainstem and cerebellum. *Neuroscience* 2005; 132: 389-97.
51. Roza SJ, Verburg BO, Jaddoe VVW, et al. Effects of maternal smoking in pregnancy on prenatal brain development. The Generation R Study. *Eur J Neurosci* 2007; 25: 611-17.
52. Jones KL, Smith DW. Recognition of the fetal alcohol syndrome in early infancy. *Lancet* 1973; 2: 999-1001.
53. Sokol RJ, Delaney-Black V, Nordstrom B. Fetal alcohol spectrum disorder. *JAMA* 2003; 290: 2996-9.

54. Sokol RJ, Miller SI, Reed G. Alcohol abuse during pregnancy: an epidemiological study. *Alcohol Clin Exp Res* 1980; 4: 135–45.
55. Bada HS, Das A, Bauer CR, et al. Low birth weight and preterm births: etiologic fraction attributable to prenatal drug exposure. *J Perinatol* 2005; 25: 631–7.
56. Jaddoe VVW, Bakker R, Hoffman A, et al. Moderate alcohol consumption during pregnancy and the risk of low birth weight and preterm birth. The Generation R Study. *Ann Epidemiol* 2007; 17: 834–40.
57. Windham GC, Fenster L, Hopkins B, et al. The association of moderate maternal and paternal alcohol consumption with birthweight and gestational age. *Epidemiol* 1995; 6: 591–7.
58. Sokol RJ, Janisse JJ, Louis JM, et al. Extreme prematurity: an alcohol-related birth effect. *Alcohol Clin Exp Res* 2007; 31: 1031–7.
59. Hack M, Kline NK, Taylor HG. Long-term development outcomes of low birth infants. *Future Child* 1995; 5: 35–6.
60. Day NL, Leech SL, Richardson GA, et al. Prenatal alcohol exposure predicts continued deficits in offspring size at 14 years of age. *Alcohol Clin Exp Res* 2002; 26: 1584–91.
61. Barr HM, Streissguth AP, Darby BL, et al. Prenatal exposure to alcohol, caffeine, tobacco and aspirin: effects on fine and gross motor performance in 4-year-old children. *Dev Psychol* 1990; 26: 339–48.
62. Mattson SN, Riley FP, Gramling L, et al. Neuropsychological comparison of alcohol-exposed children with or without physical features of fetal alcohol syndrome. *Neuropsychol* 1998; 12: 146–53.
63. Streissguth AP, Barr HM, Sampson PD. Moderate prenatal alcohol exposure: effect on child IQ and learning problems at age 7 ½ years. *Alcohol Clin Exp Res* 1990; 14: 662–9.
64. Burden MJ, Jacobson SW, Jacobson JL. Relation of prenatal alcohol exposure to cognitive processing speed and efficiency. *Alcohol Clin Exp Res* 2005; 29: 1473–83.
65. Russell M, Czarnecki DM, Cowan R, et al. Measures of maternal alcohol use as predictors of development in early childhood. *Alcohol Clin Exp Res* 1991; 15: 991–1000.
66. Stressguth AP, Barr HM, Carmichael Olson H, et al. Drinking during pregnancy decreases word attack and arithmetic scores on standardized tests: adolescent data from a population-based prospective study. *Alcohol Clin Exp Res* 1994; 18: 248–54.
67. Nanson JL, Hiscock M. Attention deficits in children exposed to alcohol prenatally. *Alcohol Clin Exp Res* 1990; 14: 656–61.
68. Bailey BN, Delaney-Black V, Covington CY, et al. Prenatal exposure to binge drinking and cognitive and behavioral outcomes at age 7 years. *Am J Obstet Gynecol* 2004; 191: 1037–43.
69. Carmichael Olson H, Sampson PD, Barr HM, et al. Prenatal exposure to alcohol and school problems in late childhood: a longitudinal prospective study. *Dev Psychopathol* 1992; 4: 341–59.
70. Barr HM, Bokstein FL, O'Malley KD, et al. Binge drinking during pregnancy as a predictor of psychiatric disorders on the Structured Clinical Interview for DSM-IV in young adult offspring. *Am J Psychiatry* 2006; 163: 1061–5.
71. Guerri C, Bazanet A, Riley EP. Foetal alcohol spectrum disorders and alterations in brain and behavior. *Alcohol* 2009; 44: 108–14.
72. Lee S, Choi I, Kang S, Rivier C. Role of various neurotransmitters in mediating the long-term endocrine consequences of prenatal alcohol exposure. *Ann NY Acad Sci* 2008; 1144: 176–88.
73. Jones PJ, Leichter J, Lee M. Placental blood flow in rats fed alcohol before and during gestation. *Life Sci* 1981; 29: 1153–9.
74. Anton RF, Becker HC, Randall CL. Ethanol increases PGE and thromboxane production in mouse pregnant uterine tissue. *Life Sci* 1990; 46: 1145–53.
75. Pennigton S. Ethanol-induced growth inhibition: the role of cyclic AMP-dependant protein kinase. *Alcohol Clin Exp Res* 1988; 12: 125–9.
76. American College of Obstetricians and Gynecologists. ACOG educational bulletin: Smoking cessation during pregnancy, Number 260, September 2000. *Int J Gynaecol Obstet* 2001; 75: 345–8.
77. Jordan TR, Dake JA, Price JH. Best practices for smoking cessation in pregnancy: do obstetrician/gynecologists use them in practice. *J Womens Health* 2006; 15: 400–11.
78. Bailey BA, Jones Cole LK. Are obstetricians following best-practice guidelines for addressing pregnancy smoking? Results from Northeast Tennessee. *South Med J* 2009; 102: 894–899.
79. Russell T, Crawford M, Woodby L. Measurements for active cigarette smoke exposure in prevalence and cessation studies: why simply asking pregnant women isn't enough. *Nicotine Tob Res* 2004; 6: 141–51.
80. George L, Granath F, Johansson AL, Cnattingius S. Self-reported nicotine exposure and plasma levels of cotinine in early and late pregnancy. *Acta Obstet Gynecol Scand* 2006; 85: 1331–7.
81. McDonald SD, Perkins SL, Walker MC. Correlation between self-reported smoking status and serum cotinine during pregnancy. *Addict Behav* 2005; 30: 853–7.
82. Kendrick JS, Zahniser SC, Miller N, et al. Integrating smoking cessation into routine public prenatal care: the Smoking Cessation in Pregnancy project. *Am J Public Health* 1995; 85: 217–22.
83. Patrick DL, Cheadle A, Thompson DC, et al. The validity of self reported smoking: a review and meta-analysis. *Am J Public Health* 1994; 84: 1086–93.
84. England LJ, Grauman A, Qian C, et al. Misclassification of maternal smoking status and its effects on an epidemiologic study of pregnancy outcomes. *Nicotine Tob Res* 2007; 9: 1005–13.
85. Dolan-Mullen P, Carbonari JP, Tabak ER, Glenday MC. Improving disclosure of smoking by pregnant women. *Am J Obstet Gynecol* 1991; 165: 409–13.
86. Kharrazi M, Epstein D, Hopkins B, et al. Evaluation of four maternal smoking questions. *Public Health Rep* 1999; 114: 60–70.
87. Mullen PD, Carbonari JP, Tabak ER, Glenday MC. Improving disclosure of smoking by pregnant women. *Am J Obstet Gynecol* 1991; 165: 409–13.
88. Perez-Stable EJ, Benowitz NL, Marin G. Is serum cotinine a better measure of cigarette smoking than self-report? *Prev Med* 1995; 24: 171–9.
89. Haddow JE, Knight GJ, Palomaki GE, et al. Cigarette consumption and serum cotinine in relation to birth weight. *Br J Obstet Gynaecol* 1987; 94: 678–81.
90. Parna K, Rahu M, Youngman LD, et al. Self-reported and serum cotinine-validated smoking in pregnant women in Estonia. *Matern Child Health J* 2005; 9: 385–92.
91. Etter JF, Vu Duc T, Perneger TV. Saliva cotinine levels in smokers and nonsmokers. *Am J Epidemiol* 2000; 151: 251–8.
92. U.S. Department of Health and Human Services. Third national report on human exposure to environmental chemicals (NCEH Pub No 05-0570). Centers for Disease Control and Prevention, National Center for Environmental Health, 2005.
93. Boyd NR, Windsor RA, Perkins LL, Lowe JB. Quality of measurement of smoking status by self-report and saliva cotinine among pregnant women. *Matern Child Health J* 1998; 2: 77–83.
94. ACOG Committee Opinion. No. 422: at-risk drinking and illicit drug use: ethical issues in obstetric and gynecologic practice. *Obstet Gynecol* 2008; 112: 1449–60.
95. Diekman ST, Floyd RL, Decoufle P, et al. A survey of obstetrician-gynecologists on their patients' alcohol use during pregnancy. *Obstet Gynecol* 2000; 95: 756–63.
96. Ernhart CB, Morrow-Tluak M, Sokol RJ, Martier S. Underreporting of alcohol use in pregnancy. *Alcohol Clin Exp Res* 1988; 12: 506–11.
97. Klein J, Chan D, Koren G. Neonatal hair analysis as a biomarker for in utero alcohol exposure. *N Engl J Med* 2002; 347: 2086.
98. Cook JD. Biochemical markers of alcohol use in pregnant women. *Clin Biochem* 2003; 36: 9–19.
99. Stoler JM, Holmes LB. Under-recognition of prenatal alcohol effects in infants of known alcohol abusing women. *J Pediatr* 1999; 135: 430–6.
100. Sokol RJ, Martier SS, Ager JW. The T-ACE questions: practical prenatal detection of risk –drinking. *Am J Obstet Gynecol* 1989; 160: 863–8.
101. Chang G, Wilkins-Haug L, Berman S. Alcohol use and pregnancy: improving identification. *Obstet Gynecol* 1998; 91: 892–8.
102. Russell M. New assessment tools for risk drinking during pregnancy: T-ACE, TWEAK, and others. *Alcohol Health Res World* 1994; 8: 55–61.
103. England LJ, Kendrick JS, Wilson HG, et al. Effects of smoking reduction during pregnancy on the birth weight of term infants. *Am J Epidemiol* 2001; 154: 694–701.
104. Melvin C, Gaffney C. Treating nicotine use and dependence of pregnant and parenting smokers: an update. *Nicotine Tobacco Res* 2004; 6: S107–124.

105. Melvin CL, Dolan-Mullen P, Windsor RA, et al. Recommended cessation counseling for pregnant women who smoke: a review of the evidence. *Tobacco Control* 2000; 9: III80–4.
106. Fiore MC, Bailey WC, Cohen SJ, et al. Treating tobacco use and dependence: clinical practice guideline. Rockville, MD: US Dept of Health and Human Services, 2000.
107. Lumley J, Oliver SS, Chamberlain C, et al. Interventions for promoting smoking cessation during pregnancy. *Cochrane Database Syst Rev* 2004; 8: CD001055.
108. American College of Obstetricians and Gynecologists. ACOG educational bulletin: smoking cessation during pregnancy, Number 316, October 2005. *Obstet Gynecol* 2005; 106: 883–8.
109. U.S. Preventive Services Task Force. Counseling and interventions to prevent tobacco use and tobacco-caused disease in adults and pregnant women: U.S. Preventive Services Task Force reaffirmation recommendation statement. *Ann Intern Med* 2009; 150: 551–5.
110. Bailey BA, Sokol RJ. Pregnancy and alcohol use: evidence and recommendations for prenatal care. *Clin Obstet Gynecol* 2008; 51: 436–44.
111. Miller WR, Rollnick S. *Motivational interviewing: preparing people to change addictive behavior*. New York, NY: Guilford Press, 1991.
112. Handmaker NS, Wilbourne P. Motivational interventions in prenatal clinics. *Alcohol Res Health* 2001; 25: 219–29.
113. Chang G, Goetz MA, Wilkins-Haug L, et al. A brief intervention for prenatal alcohol use: an in-depth look. *J Subst Abuse Treat* 2000; 18: 365–9.
114. Handmaker NS, Miller WR, Manicke M. Findings of a pilot study of motivational interviewing with pregnant drinkers. *J Stud Alcohol* 1999; 60: 285–7.
115. Floyd RL, Sobell M, Velasquez MM, et al. Project Choices – a brief intervention with Motivational Interviewing (MI) to reduce pregnancy alcohol exposure. *Am J Prev Med* 2007; 32: 1–10.
116. O'Connor MJ, Whaley SE. Brief intervention for alcohol use by pregnant women. *Am J Pub Health* 2007; 97: 252–8.
117. Chang G, McNamara TK, Orav J, et al. Brief intervention for prenatal alcohol use: a randomized trial. *Obstet Gynecol* 2005; 105: 991–8.
118. Larsson G. Prevention of fetal alcohol effects: an antenatal program for early detection of pregnancies at risk. *Acta Obstet Gynecol Scand* 1983; 62: 171–8.