

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Why This Chapter
is Important for
Employers:
An Overview

Alcohol Misuse (Screening and Counseling):

- Fetal exposure to alcohol during pregnancy is one of the leading causes of preventable birth defects, mental retardation, and developmental disorders in the United States.¹
- In 2003, 10% of pregnant women reported alcohol use, including 4% who reported binge drinking.² Approximately 55% of women of childbearing-age drink alcohol and 12% report binge drinking on one or more occasions in the past month.² Because half of all pregnancies in the United States are unintended, many women of childbearing-age who use or abuse alcohol are at risk of an alcohol-exposed pregnancy.
- The direct and indirect costs of alcohol misuse in the United States were estimated to equal nearly \$185 billion in 1998. Medical consequences of fetal alcohol syndrome (FAS) accounted for approximately \$2.9 billion of this amount.³
- Researchers estimate that the excess medical costs for a child with fetal alcohol syndrome (FAS) are \$2,342 per year (in year 1997 dollars).⁴
- Randomized trials demonstrate that brief counseling leads to reduced alcohol consumption among excessive drinkers and to reductions in adverse alcohol-related health outcomes, including excess mortality.⁵⁻⁷
- It is estimated that each \$1 invested in screening and brief counseling interventions saves approximately \$4 in healthcare costs.^{6,8}

Asymptomatic Bacteriuria (Screening):

- Urinary tract infections (UTIs) are the most common bacterial infections among pregnant and non pregnant women; each year 8 million women visit a physician for evaluation of a UTI.⁹
- Physiologic changes that occur during pregnancy make pregnant women more susceptible to UTIs, including asymptomatic bacteriuria (infection in the urine), cystitis (infection in the bladder), and pyelonephritis (infection in the kidneys).⁹
- Asymptomatic bacteriuria occurs in approximately 2% to 14% of pregnant women and 80,000 to 400,000 cases occur each year in the United States.⁹
- Bacteriuria increases the risk for preterm delivery twofold.⁹ It also increases the risk of low birth weight and fetal and perinatal mortality.⁹⁻¹⁰
- Without treatment, asymptomatic bacteriuria can progress to pyelonephritis, a serious kidney infection. Pyelonephritis complicates 1% to 2% of all pregnancies and affects 100,000 women each year.⁹
- Early identification and treatment of asymptomatic bacteriuria improves pregnancy outcomes as it reduces the incidence of pyelonephritis and premature births.

Breastfeeding (Counseling):

- Human milk is universally recognized to be the optimal food for infants and is nutritionally superior to formula: breast milk confers immunity and protects infants from infections and allergens.

- Research shows that children who were breastfed are at significantly lower risk for childhood obesity as well as type 1 and type 2 diabetes compared to their non-breastfed peers.¹¹
- Breastfeeding also has important short- and long-term health benefits for the mother. A woman's risk of breast cancer is decreased 4.3% for every 12-month increment of breastfeeding over her lifetime. Her risk of ovarian and endometrial cancer is decreased through breastfeeding as well.¹²
- Data from 2005 show that 72.9% of all new mothers initiated breastfeeding; but only 39.1% continued to breastfeed for 6 months and only 20.1% continued to breastfeed for the recommended 12-month period.¹³
- A 2001 U.S. Department of Agriculture (USDA) study estimated that at least \$500 million (in year 1998 dollars) could be saved in healthcare costs if breastfeeding rates were increased to match those recommended by the Surgeon General/*Healthy People 2010* goals.¹⁴
- Research indicates that working outside the home reduces the initiation and duration of breastfeeding.¹⁵ Therefore, employers should support women returning to work by offering lactation benefits (such as counseling) and programs.

Folic Acid Supplementation (Counseling and Preventive Medication):

- Neural tube defects (NTD), such as spina bifida and anencephaly, result from a failure of the neural cord to properly fuse.
- Each year, approximately 3,000 pregnancies are affected by neural tube defects (NTDs) and approximately 2,200 infants are born with NTDs.¹⁶
- Folic acid, a B vitamin, helps prevent NTD. Consuming the recommended daily amount of folic acid (0.4mg) can reduce a woman's chance of having a NTD-affected pregnancy by 40% to 80%.¹⁷
- Despite the benefits of supplementation, only 33% of women of childbearing age report taking vitamins that contain folic acid.¹⁸
- NTD rates are highest among the Hispanic population. Efforts to ensure supplementation among this population are important for eliminating health disparities.¹⁹
- The economic impact of NTDs is substantial. The average lifetime cost for a child born with spina bifida is estimated to be \$636,000 (in year 2002 dollars).²⁰ Costs associated with NTDs are shared by parents, employers, and communities.

Group B Streptococcal Disease (Screening and Preventive Medication):

- Group B streptococcus (GBS), a bacterium, has been a leading cause of infection-related infant deaths in the United States since the 1970s.
- GBS disease is a serious infection that causes sepsis (blood poisoning), pneumonia, and meningitis in newborns.
- Each year in the United States between 1,300 and 1,600 infants contract early-onset GBS and 65 to 80 infants die from it.²¹ Those who survive are often left

with lifelong disabilities such as hearing loss, vision impairments, and/or learning disabilities.

- While most women colonized with GBS are asymptomatic (meaning that they can pass the disease to their children, but are not affected by it themselves), some women become infected with GBS and are at risk of womb infections, bladder infections, and stillbirth.²¹
- By identifying women who carry group B streptococcal bacteria, clinicians can administer antibiotic prophylaxis during labor, thus preventing transmission of bacteria to the infant.
- The average neonatal intensive care cost of a GBS-infected infant was estimated to be \$30,100 in 2001.²² The cost of treating an infant with early-onset group B streptococcal sepsis (a severe form of the disease) is estimated to exceed \$123,000 (in year 1993 dollars).²³
- In 1993, researchers estimated that treating high-risk women identified through screening with intrapartum antibiotic prophylaxis could prevent 3,300 cases of GBS annually; saving approximately \$16 million in direct medical costs.²⁴

Hepatitis B Virus (HBV) (Screening, Immunization, and Treatment):

- Over 1 million people in the United States are chronic HBV carriers.²⁵
- In 2003, 73,000 new HBV infections were reported.²⁵
- Screening pregnant women for HBV, and treating the infants of HBV-positive women with post-exposure hepatitis B immune globulin prophylaxis and HBV vaccination can dramatically reduce the incidence of perinatal HBV transmission and thus the number of infants who become chronically infected with hepatitis B.²⁶
- The economic burden of hepatitis B infection can be substantial depending on whether the infection is acute or chronic and what treatment is required.
- From a societal perspective, prevention of perinatal HBV infection was estimated to save \$41.8 million (in year 1993 dollars) in medical and work-loss costs.²⁷

Human Immunodeficiency Virus (HIV) (Screening, Counseling, and Preventive Medication)

- Approximately 120,000 to 160,000 HIV-infected women live in the United States, 80% of whom are of childbearing age. Each year between 1985 and 1995, approximately 6,000 to 7,000 HIV-infected women gave birth.²⁸
- Mother-to-infant HIV transmission, called perinatal transmission, can occur during pregnancy, during labor and delivery, or through breastfeeding. Perinatal HIV transmission is almost entirely preventable.
- Despite screening and treatment advances, perinatal HIV transmission continues to occur; CDC estimates that 280 to 370 infants are born with HIV each year in the United States.²⁸
- In 2000, there were 4,107 hospitalizations among HIV-infected children in the United States, which accounted for approximately \$100 million in hospital charges and more than 30,000 hospital days.²⁹

- The estimated average lifetime healthcare-related cost of a perinatal HIV infection is estimated to range between \$100,000 and \$117,000.³⁰

Influenza (Immunization):

- Pregnant women are considered to be at increased risk for complications from influenza infections.
- Influenza immunization has many benefits. Foremost, when a pregnant woman is immunized during pregnancy, antibodies can be passed to her fetus and can also be passed in breast milk.³¹
- Researchers estimate that an average of 1 to 2 hospitalizations can be prevented for every 1,000 pregnant women vaccinated.³²
- Despite the seriousness of influenza infection and the fact that the inactivated influenza vaccine is safe and effective, only 12% to 13% of pregnant women are inoculated against influenza.^{31,33}
- Immunization of healthy working adults is cost-effective and may result in cost-savings in some years.³⁴ Economic results are likely to be as favorable for pregnant women since they are at high risk for influenza-related complications.

Preeclampsia (Screening):

- Preeclampsia (pregnancy-related high blood pressure) affects 5% to 7% of all pregnancies.³⁵ If preeclampsia is not effectively treated it can lead to eclampsia, a severe condition that is characterized by maternal seizure activity, coma, and death.
- Preeclampsia/eclampsia is the third leading cause of maternal death worldwide³⁶ and is responsible for 18% of all maternal deaths in the United States.³⁷
- Spending on pregnancy-related hypertension totaled nearly \$2.3 billion in the United States in 2003.³⁸
- In 2003, approximately 204,868 pregnant women were admitted to the hospital for hypertension, staying on average 3.5 days. The average per-person charge for such hospital admissions totaled \$11,208.³⁸
- Screening, which involves minimal cost, and early treatment can minimize and prevent otherwise costly medical conditions.

Prenatal Diagnosis of Chromosomal Abnormalities and Neural Tube Defects (NTDs) (Screening and Testing):

- Down syndrome (trisomy 21) is the most common chromosomal abnormality in the United States, affecting 1 in every 800 to 1,000 live-born babies.³⁹
- Spina bifida and anencephaly are common, permanent, and potentially fatal birth defects. Both are neural tube defects (NTD) resulting in failure of the neural cord to properly fuse. Each year in the United States, approximately 3,000 pregnancies are affected by NTDs and approximately 2,200 infants are born with neural tube defects.¹⁶
- The purpose of screening and testing is to identify affected

pregnancies. Early identification of an affected pregnancy allows parents and providers to prepare for the birth of a special needs infant or to terminate the pregnancy.⁴⁰

- Chromosomal abnormalities and NTDs have a substantial economic impact. For example, the average *lifetime* cost for a child born with spina bifida is estimated to be \$636,000 (in year 2002 dollars).⁴¹
- Employers also face productivity losses associated with workdays lost by employees who must care for affected infants and children.⁴²

Rh(D) Incompatibility (Screening and Preventive Medication):

- Rh(D) incompatibility occurs in 9% to 10% of all pregnancies, depending on the race of the pregnant woman and fetus, and may cause severe destruction of an affected fetus's red blood cells.⁴³
- Without treatment, 25% to 30% of affected fetuses will experience hemolytic anemia and hyperbilirubinemia (jaundice) and an additional 20% to 25% will be hydropic and will either die in the womb or shortly after birth.⁴³
- Early identification of Rh(D) incompatibility allows clinicians to begin treatment before damage is done to the fetus. This prevents otherwise expensive medical treatment, lifelong disability, and even death.

Rubella (Screening):

- When contracted during early pregnancy, rubella can cause serious complications including miscarriage, stillbirth, and congenital rubella syndrome (CRS) – a constellation of birth defects that includes hearing impairment, growth retardation, developmental delays, and heart and eye defects.⁴⁴
- CRS and its complications have substantial health consequences and economic costs. A large rubella outbreak in 1964-65 cost an estimated \$840 million.⁴⁵ In 2006, the estimated lifetime cost of treating a child born with CRS exceeded \$200,000.⁴⁵
- Screening allows clinicians to identify childbearing-age women who are at risk for rubella and to immunize them before they become pregnant. Screening pregnant women allows clinicians to identify at-risk women and to encourage them to be immunized immediately after delivery, thereby offering protection during subsequent pregnancies.

Syphilis (Screening):

- In addition to sexual transmission, syphilis can be passed from an infected pregnant woman to her infant during pregnancy and delivery.
- Congenital syphilis is particularly severe and results in fetal or infant death in 40% of cases.⁴⁶
- In 2002, 451 cases of congenital syphilis were reported in the United States.⁴⁷
- The average annual national cost of treating infants with congenital syphilis is approximately \$18.4 million (in year 1995 dollars).⁴⁸
- Screening for syphilis allows clinicians to identify affected patients and begin

treatment earlier in the course of disease, thereby improving outcomes and avoiding the health and economic consequences of latent disease. Further, ensuring that all women receive prenatal care and are screened for syphilis during pregnancy will reduce the incidence of congenital syphilis.⁴⁷

Tetanus (Immunization):

- Neonatal tetanus is a severe and often fatal disease; it accounted for an estimated 200,000 deaths worldwide in 2000⁴⁹ but is extremely rare in the United States.⁵⁰
- Nearly all neonatal tetanus occurs in infants born to women who are not adequately immunized against tetanus. Therefore, it is important for all pregnant women to be vaccinated against tetanus.⁵¹
- There are few economic data on the burden of tetanus disease and no data about the costs of neonatal tetanus in the United States. A recent economic evaluation of the 7-vaccine routine childhood immunization schedule in the United States estimated that, if there had not been a tetanus vaccination program in the U.S., 153 cases of tetanus and 23 deaths from tetanus would have occurred in each birth cohort (all children born in one year) at a total cost of \$29 million (direct and indirect costs in year 2001 dollars).⁵²
- Tetanus immunization offers long-term protection against tetanus for the vaccinated woman, and maternal vaccination confers significant protection to the fetus.⁵³

Tobacco Use Treatment (Screening and Counseling):

- Twenty-five percent (25%) of all childbearing-age women in the United States smoke. Depending on demographic factors, between 11% and 20% of all pregnant women in the United States smoke.⁵⁴
- Women who smoke during their pregnancies are 83% more likely to deliver a low-birth-weight infant, 129% more likely to deliver an infant that will die of SIDS, 30% more likely to deliver an infant with respiratory distress syndrome, and 41% more likely to deliver an infant with a perinatal respiratory condition than are women who do not smoke during pregnancy.
- Each pregnant smoker incurs an additional \$704 in healthcare costs (in year 1996 dollars)⁵⁵ and, annually, smoking-attributable neonatal costs (defined as all costs related to labor/delivery and the care of infants within the first few months of life) are estimated to meet or exceed \$367 million in the United States.⁵⁶⁻⁵⁷
- Tobacco use treatment is considered to be one of the most cost-effective preventive services.⁵⁴ Clinical trials have shown that \$6 are saved in healthcare costs for every \$1 invested in smoking cessation programs for pregnant women.⁵⁸
- A smoking cessation program that could achieve an annual drop of 1 percentage point in smoking prevalence has been estimated to produce an economic benefit of \$21 million in direct medical costs solely by reducing the number of low-birth-weight live births. In 7 years, the cumulative undiscounted saving in direct medical costs would become \$572 million through the prevention of 57,200 low-birth-weight infants (all figures in year 1995 dollars).⁵⁹

References:

Why This Chapter is Important for Employers: An Overview

1. Centers for Disease Control and Prevention. Alcohol use among women of childbearing age – United States, 1991-1999. *MMWR* 2002; 51(13): 273-276.
2. Centers for Disease Control and Prevention. Notice to readers: Surgeon General's advisory on alcohol use in pregnancy. *MMWR* 2005; 54(09): 229.
3. Harwood H. *Updating Estimates of Economic Costs of Alcohol Abuse in the United States: Estimates, Update Methods, and Data*. National Institute of Alcohol Abuse and Alcoholism; 2000. NIH Publication No. 98-4327.
4. Klug MG, Burd L. Fetal alcohol syndrome prevention: annual and cumulative cost savings. *Neurotoxicol Teratol* 2003; 25(6): 763-765.
5. Bertholet N, Daeppen J-B, Fleming M, Burnand B. Reduction of alcohol consumption by brief alcohol intervention in primary care: systematic review and meta-analysis. *Arch Intern Med* 2005;165:986-95.
6. Fleming MF, Mundt MP, French MT, Manwell LB, Stauffacher EA, Barry KL. Brief physician advice for problem alcohol drinkers: long-term efficacy and benefit-cost analysis. A randomized controlled trial in community-based primary care settings. *Alcohol Clin Exp Res* 2002;26:36-43.
7. Cuijpers P, Riper H, Lemmers L. The effects on mortality of brief interventions for problem drinking: a meta-analysis. *Addiction* 2004;99:839-45.
8. Gentilello LM, Ebel BE, Wickizer TM, Salkever DS, Rivara FP. Alcohol interventions for trauma patients treated in emergency departments and hospitals: a cost benefit analysis. *Ann Surg* 2005;241:541-50.
9. Mittal P, Wing DA. Urinary tract infections in pregnancy. *Clin Perinatol* 2005; 32: 749-764.
10. Calogne N; U.S. Preventive Services Task Force. Screening for asymptomatic bacteriuria: Recommendation statement. AHRQ Publication No. 05-0551-A. Rockville, MD: Agency for Healthcare Research and Quality; 2004.
11. Shealy KR, Li R, Benton-Davis S, Grummer-Strawn LM. *The CDC Guide to Breastfeeding Interventions*. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2005.
12. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50,302 women with breast cancer and 96,973 without the disease. *Lancet* 2002; 360: 187-95.
13. Centers for Disease Control and Prevention. National Immunization Survey. [cited 2006 Aug 31]. Available from: http://www.cdc.gov/breastfeeding/data/NIS_data/data_2005.htm.
14. Weimer J. The economical cost of breastfeeding: A review and an analysis. ERS Food Assistance and Nutrition Research Report No. 13, Washington, DC: Economic Research Services, U.S. Department of Agriculture; 2001.
15. United States Breastfeeding Committee. Workplace breastfeeding support. Issue paper. Raleigh, NC: United States Breastfeeding Committee; 2002.
16. Centers for Disease Control and Prevention. Spina bifida and anencephaly before and after folic acid mandate – United States, 1995-1996 and 1999-2000. *MMWR* 2004; 53(17): 362-365.
17. Berry RJ, Li Z, Erickson JD, Li S, Moore CA, Wang H, et al. Prevention of neural-tube defects with folic acid in China. China-US. Collaborative Project for Neural Tube Defect Prevention. *N Engl J Med* 1999; 341:1485–1490.
18. Centers for Disease Control and Prevention. Use of dietary supplements containing folic acid among women of childbearing age – United States, 2005. *MMWR* 54(38); 955-958. Available from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5438a4.htm>.
19. Williams LJ, Rasmussen SA, Flores A, Kirby RS, Edmonds LD. Decline in the prevalence of spina bifida and anencephaly by race/ethnicity: 1995-2002. *Pediatrics* 2005;116(3):580-586.
20. Grosse SD, Waitzman NJ, Romano PS, Mulinare J. Re-evaluating the benefits of folic acid fortification in the United States: Economic analysis, regulation, and public health. *Am J Public Health* 2005;95:1917–1922.
21. Schrag S, Gorwitz R, Fultz-Butts K, Schuchat A. Centers for Disease Control and Prevention. Prevention of perinatal Group B streptococcal disease: Revised guidelines from the CDC. *MMWR* 2002; 51(RR11); 1-22.
22. Benitz WE, Gould JB, Druzin ML. Preventing early-onset Group B Streptococcal Sepsis: strategy development using decision analysis. *Pediatrics* 1999;103(6):76-91.

23. Keenan C. Prevention of neonatal group B streptococcal infection. *Am Fam Physician* 1998; 57(1).
24. Mohle-Boetani JC, Schuchat A, Plikaytis D, Smith JD, Broome CV. Comparison of prevention strategies for neonatal group B streptococcal infection. A population-based analysis. *JAMA* 1993; 270(12):1442-1448.
25. Centers for Disease Control and Prevention, National Center for HIV, STD and TB Prevention, Division of Viral Hepatitis. Disease Burden from Hepatitis A, B, and C in the United States, 1980-2004. [cited 2006 Aug 25]. Available from: http://www.cdc.gov/ncidod/diseases/hepatitis/resource/PDFs/disease_burden2004.pdf.
26. Mast EE, Margolis HS, Fiore AE, Brink EW, Goldstein ST, Wang SA, Moyer LA, Bell BP, Alter MJ. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States. *MMWR* 2005; 54(RR-16): 1-23. [cited 2006 Aug 22] Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5416a1.htm?s_cid=rr5416a1_e.
27. Margolis HS, Coleman PJ, Brown RE, Mast EE, Sheingold SH, Arevalo JA. Prevention of Hepatitis B Virus Transmission by Immunization: an Economic Analysis of Current Recommendations. *JAMA* 1995; 274(15):1201-8.
28. Centers for Disease Control and Prevention. Revised recommendations for HIV screening of pregnant women. *MMWR* 2001; 50(RR19): 59-86.
29. Kourtis AP, Paramsothy P, Posner SE, Meikle SF, Jamieson DJ. National estimates of hospital use by children with HIV infection in the United States: analysis of data from the 2000 KIDS Inpatient database. *Pediatrics* 2006; 118:167-173.
30. Mauskopf JA, Paul JE, Wichman DS, White AD, Tilson HH. Economic impact of treatment of HIV-positive pregnant women and their newborns with zidovudine *JAMA* 1996; 276: 132-138.
31. Centers for Disease Control and Prevention. Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP) *MMWR* 2006; 55(RR-10):1-42.
32. Neuzil KM, Reed GW, Mitchel EF, et al. Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women. *Am J Epidemiol* 1998;148:1094-102.
33. Munoz FM, Greisinger AJ, Wehman OA, et al. Safety of influenza vaccination during pregnancy. *Am J Obstet Gynecol* 2005; 192:1098-1106.
34. Lee PY, Matchar DB, Clements DA, Huber J, Hamilton JD, Peterson ED. Economic analysis of influenza vaccination and antiviral treatment for healthy working adults. *Ann Intern Med* 2002;137:225-231.
35. Wagner L. Diagnosis and management of preeclampsia. *Am Fam Phys* 2004; 70:2317-24.
36. World Health Organization. Postpartum care of the mother and newborn: a practical guide. Geneva, Switzerland: World Health Organization; 1998.
37. Preeclampsia Foundation. [cited 2006 Feb 28]. Available from: <http://www.preeclampsia.org/statistics.asp>.
38. Agency for Healthcare Research and Quality. Health Care Utilization Project Data Source. [cited 2005 Jul 12]. Available from: <http://hcup.ahrq.gov>.
39. The March of Dimes. Down Syndrome Fact Sheet. The March of Dimes 2006; Available from: http://www.marchofdimes.com/professionals/681_1214.asp.
40. Harris RA, Washington AE, Nease Jr RF, Kuppermann M. Cost utility of prenatal diagnosis and the risk-based threshold. *Lancet* 2004; 363:276-82.
41. Grosse SD, Waitzman NJ, Romano PS, Mulinare J. Re-evaluating the benefits of folic acid fortification in the United States: Economic analysis, regulation, and public health. *Am J Public Health* 2005; 95(11): 1917 - 1922.
42. Kelly AE, Haddix AC, Scanlon KS, Helmick CG, Mulinare J. Cost-effectiveness of strategies to prevent neural tube defects. In: Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. *Cost-Effectiveness in Health and Medicine*. New York, Oxford: Oxford University Press; 1996:312-349.
43. Medical Encyclopedia: Rh incompatibility. Available from: <http://www.nlm.nih.gov/medlineplus/ency/article/001600.htm>.
44. Centers for Disease Control and Prevention. Control and prevention of rubella: Evaluation and management of suspected outbreaks, rubella in pregnant women, and surveillance of congenital rubella syndrome. *MMWR* 2001; 50(RR12):1-23.
45. Centers for Disease Control and Prevention. Rubella. In Atkinson W, Hamborsky J, McIntyre L, Wolfe S, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*, 9th ed. Washington DC: Public Health Foundation; 2006:155-70.
46. U.S. Preventive Services Task Force. Screening for syphilis infection. Summary of recommendations / Supporting documents. Rockville, MD: Agency for Healthcare Research and Quality; 2004.

47. Centers for Disease Control and Prevention. Congenital syphilis – United States, 2002. *MMWR* 2004; 50(No. RR-31): 716-719.
48. Nelson HD, Glass N, Huffman L, Villemeyer K, Hamilton A, Frame A, Berg AO. Screening for syphilis: Brief update for the U.S. Preventive Services Task Force. AHRQ Publication No. 04-0545-B. Rockville, MD: Agency for Healthcare Research and Quality; 2004.
49. Vandelaer J, Birmingham M, Gasse F, Kurian M, Shaw C, Garnier S. Tetanus in developing countries: an update on the Maternal and Neonatal Tetanus Elimination Initiative. *Vaccine* 2003; 21:3442-3445.
50. Centers for Disease Control and Prevention. Neonatal tetanus – Montana, 1998. *MMWR* 1998; 47(43):928-930.
51. Centers for Disease Control and Prevention. Tetanus surveillance – United States, 1998-2000. *MMWR* 2003; 52(SS-3):1-8.
52. Zhou F, Santoli J, Messonnier ML, Yusuf HR, Shefer A, Chu SY, et al. Economic evaluation of the 7-vaccine routine childhood immunization schedule in the United States, 2001. *Arch Pediatr Adolesc Med* 2005;159:1136-1144.
53. Wassilak SGF, Orenstein WA, Sutter RW. Chapter 18: Tetanus toxoid. In Plotkin SA, Orenstein WA, eds. *Vaccines*, ed. 3. Philadelphia, PA: W.B. Saunders Company; 1999:441-474.
54. U.S. Public Health Service. Treating tobacco use and dependence: A systems approach. Treating tobacco use and dependence. Rockville, MD: Office of the U.S. Surgeon General; U.S. Public Health Service; U.S. Department of Health and Human Services; 2000.
55. Adams KE, Miller VP, Ernst C, Nishimura BK, Melvin C, Merritt R. Determinants of health: Neonatal health care costs related to smoking during pregnancy. *Health Economics* 2002; 11(3): 193-206.
56. Centers for Disease Control and Prevention. Annual smoking-attributable mortality, years of potential life lost, and economic costs — United States, 1995–1999. *MMWR* 2002; 51(14): 300-303.
57. Centers for Disease Control and Prevention. Cigarette smoking among adults – United States, 2002. Atlanta, GA: Centers for Disease Control and Prevention; 2002.
58. Centers for Disease Control and Prevention. Coverage for tobacco use cessation treatments: Why, what, and how. Atlanta, GA: Centers for Disease Control and Prevention. [cited 2005 Jul 15]. Available from: <http://www.cdc.gov/tobacco>.
59. Lightwood JM, Phibbs, CS, and Glantz SA. Short-term health and economic benefits of smoking cessation: low birth weight. *Pediatrics* 1999; 104:1312-1320.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Alcohol Misuse (Screening and Counseling)

Clinical Preventive Service Recommendations

U.S. Preventive Services Task Force Recommendation

The U.S. Preventive Services Task Force (USPSTF) recommends screening and behavioral counseling interventions to reduce alcohol misuse by adults, including pregnant women, in primary care settings.¹

Evidence Rating: B (Recommended/At Least Fair Evidence)

The evidence on the effectiveness of counseling to reduce alcohol consumption during pregnancy is limited; however, studies in the general adult population show that behavioral counseling interventions are effective among women of childbearing age. The USPSTF concluded that the benefits of behavioral counseling interventions to reduce alcohol misuse by adults outweigh any potential harms.¹

The USPSTF recommendation is supported by the American Academy of Family Physicians (AAFP).²

Recommended Guidance U.S. Surgeon General

The Surgeon General of the United States recommends that clinicians 1) screen pregnant women for alcohol use, 2) inform them of the risks of alcohol consumption, and 3) advise them not to drink alcohol during their pregnancy.³

Evidence Rating:

Not Specified

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- American Academy of Family Physicians (AAFP)
- Centers for Disease Control and Prevention (CDC)
- National Institute of Alcohol Abuse and Alcoholism (NIAAA)
- Peer-reviewed research
- U.S. Preventive Services Task Force (USPSTF)
- U.S. Surgeon General

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

Epidemiology of Condition/Disease

No amount of alcohol can be considered safe during pregnancy: alcohol consumed during any stage of pregnancy increases the risk of alcohol-related birth defects.³ Fetal exposure to alcohol during pregnancy is one of the leading causes of preventable birth defects, mental retardation, and developmental disorders in the United States.⁴

Despite the documented risks associated with fetal alcohol exposure 10% of pregnant women reported consuming alcohol in 2003.⁵ Annually, 55% of

women of childbearing age report alcohol use, and 12% report binge drinking.⁵ This statistic is of particular concern because half of all pregnancies in the United States are unplanned and are at particular risk of unintentional prenatal alcohol exposure. Therefore, experts recommend that women of childbearing age consult their physicians and take steps to reduce the possibility of an alcohol-exposed pregnancy by either 1) using an effective form of contraception or 2) reducing or eliminating alcohol use.⁵

Prenatal alcohol use can lead to one or more fetal alcohol spectrum disorders (FASD). FASD is characterized by permanent disabilities of varying degrees of severity. FASD may result in subtle defects, such as learning disabilities or mild physical abnormalities, or it may result in fetal alcohol syndrome (FAS), the most severe form of FASD, which is characterized by mental retardation, abnormal facial features, growth retardation, and central nervous system complications.³

FASD is identified in 2 of every 1,000 live births, and FAS is identified in between 0.5 to 2 of every 1,000 live births.³ Because many alcohol-related deficits are not identified at the time of birth, the actual prevalence of alcohol-related disorders is much higher. In fact, researchers estimate that, for every case of FAS documented at birth, there are 3 additional cases that are not identified until later in life.³

**Condition/Disease
Risk Factors**

Alcohol misuse (in the form of binge drinking, heavy drinking, alcohol abuse, or alcohol dependence) before pregnancy is highly predictive of continued use.⁴

Value of Prevention

**Economic Burden of
Condition/Disease**

The direct and indirect costs of alcohol misuse in the United States were estimated to equal nearly \$185 billion in 1998. Medical consequences of fetal alcohol syndrome (FAS) accounted for about \$2.9 billion of this amount and approximately \$1.3 billion were attributed to lost earnings due to FAS.⁶

**Workplace Burden
of Condition/Disease**

Data are limited about presenteeism and absenteeism stemming from parental caregiving requirements for FASD/FAS-affected children, but parents are likely to take time off from work to attend to special needs children.

**Economic Benefit of
Preventive
Intervention**

The economic benefits of screening and counseling mainly result from:

- The averted costs of medical care for FAS and related disorders.
- Cost-savings in neonatal care and the management of developmental delays and birth defects.
- Cost-savings associated with special education, the criminal justice system, alcohol and/or drug abuse treatment, and mental health services.

Interventions directed toward alcohol misuse that occur during pregnancy may also improve a pregnant woman's long-term drinking behavior. A permanent or long-term reduction/elimination of alcohol use would generate additional cost-savings due to averted long-term healthcare costs.

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Estimated Cost of Preventive Intervention	Screening patients for alcohol misuse in primary care settings is relatively inexpensive. The cost of follow-up counseling sessions depends on the number of sessions, their mode of delivery (in-office or by telephone), and on the type of provider who delivers the counseling. In 2004, the private-sector cost of the initial health risk assessment and counseling averaged \$23; approximately 95% of all paid claims fell within the range of \$0 to \$81. ⁷
Estimated Cost of Treatment	Treatment costs for pregnant women who misuse alcohol should not differ from general alcohol treatment costs unless there are other pregnancy-related complications.
Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention	Screening and counseling for alcohol misuse have a greater impact and are more cost-effective than most clinical preventive services. ⁸ Screening and counseling for alcohol misuse among all adults (not just pregnant women) reduce both societal and healthcare costs. It is estimated that each \$1 invested in screening and brief counseling interventions saves approximately \$4 in healthcare costs. ⁹⁻¹⁰ Furthermore, researchers estimated that the excess medical costs for a child with fetal alcohol syndrome (FAS) are \$2,342 per year (based on North Dakota Health Claims data for 1996 and 1997). This suggests that a alcohol-reduction program that costs \$50,000 and is able to prevent one case of FAS each year would have paid for itself in 6 years by generating healthcare savings. The benefits are returned even faster if the prevention of alcohol-related conditions other than FAS are included in the analysis. ¹¹
Preventive Intervention Information	
Preventive Intervention: Purpose of Screening and Counseling	Screening for alcohol misuse allows clinicians to identify women who misuse alcohol early in the course of pregnancy (or during the pre- or interconception periods). Pregnant women who misuse alcohol can be counseled to reduce or eliminate their use and referred to treatment services as needed.
Benefits and Risks of Intervention	The benefits of screening and intervention include the prevention of FASD and FAS in addition to the maternal benefits accrued from identifying and intervening with their alcohol misuse. Randomized trials demonstrate that brief counseling leads to reduced alcohol consumption among excessive drinkers and to reductions in adverse alcohol-related health outcomes, including excess mortality. ^{9, 12-13} The USPSTF found little direct evidence regarding harms of screening for alcohol misuse or behavioral counseling interventions to reduce or eliminate alcohol use in general populations. ¹⁴
Initiation, Cessation, and Interval of Screening	All women should be screened for alcohol use with each pregnancy. Because the optimal frequency of screening is unknown, screening is left to the discretion of the clinician. Patients at greater risk for alcohol problems, either because they have a history of past alcohol misuse or may report other risky behaviors, may benefit from re-screening during pregnancy. ¹⁴ Counseling should be conducted as medically indicated. A total of 8 counseling sessions are covered each calendar year.

Intervention Process
Screening

There are several effective screening tools currently available for assessing alcohol use in primary care settings. Non-pregnant women of childbearing age seen in primary care settings should be screened with general tools such as a single questions screen (e.g., AUDIT or AUDIT-C).¹⁵ Pregnant women seen in primary care settings should be screened with a pregnancy-specific tool such as the TWEAK or T-ACE. The TWEAK, a 5-question tool, and the T-ACE, a 4-question tool, were specifically designed to screen pregnant women for “risky drinking”, “harmful drinking”, and alcohol abuse disorders. The T-ACE is very sensitive and has been shown to outperform unaided clinicians in identifying pregnant women who use alcohol.

All pregnant women and women considering pregnancy should be advised of the harmful effects of alcohol on the fetus. Because safe levels of alcohol consumption during pregnancy are unknown, pregnant women should be advised to refrain from drinking alcohol altogether.^{5,14} Non pregnant women should also be advised to use contraception until their drinking can be reduced or eliminated.

Counseling

Clinicians should provide counseling interventions for patients who meet the criteria for alcohol misuse. The USPSTF identifies 3 levels of counseling intervention, differentiated by level of intensity, for these patients. Multi-contact counseling is more effective than single-contact counseling interventions, but providers should tailor counseling intensity to address individual patient needs. Intensity is determined by the duration of the initial contact and whether any follow-up occurs. “Very brief” interventions last up to 5 minutes and have no follow-up. “Brief” counseling interventions last 15 minutes and have no follow-up. “Multi-contact” interventions include one initial session lasting at least 15 minutes and several follow-up contacts.¹ More intensive interventions are typically recommended for those meeting criteria for alcohol dependence.

Effective counseling for alcohol misuse in the primary care setting includes feedback, advice, goal setting, and follow-up. Alcohol misuse counseling should follow the counseling framework known as the “5 As”¹⁵:

- Providers should **assess** the degree of a patient’s drinking, including any problems caused by alcohol and whether the person is alcohol dependent or not.
- Providers should **advise** patients to reduce their alcohol consumption to safer levels or to abstain altogether from drinking.
- Providers should **agree** with patients on their goals for reducing alcohol consumption.
- Providers should **assist** patients in acquiring personal motivation, self-help skills, or outside resources necessary to achieve behavior change.
- Finally, providers should **arrange** for patients to receive appropriate follow-up support services and counseling, depending on the nature of their alcohol misuse.

**Treatment
Information**

Health benefits should include provisions for diagnostic assessment, follow-up, and treatment services.

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Evidence-Based Research:

The U.S. Preventive Services Task Force (USPSTF)

Strength of Evidence: B (Recommended/At Least Fair Evidence)

- The USPSTF found at least fair evidence to support screening and behavioral counseling all adults, including pregnant women, for alcohol misuse.¹

This recommendation is supported by the:

- American Academy of Family Physicians (AAFP)²

Recommended Guidance:

The U.S. Surgeon General

Strength of Evidence: Not Specified

- The U.S. Surgeon General recommends that clinicians should routinely 1) screen pregnant women for alcohol use, 2) inform them of the risks of alcohol consumption, and 3) advise them not to drink alcohol during their pregnancy.³

Authored by:

Campbell KP, Naimi T, Chattopadhyay S. Alcohol misuse during pregnancy evidence-statement: screening and counseling. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Alcohol Misuse (Screening and Counseling)

1. U.S. Preventive Services Task Force. Screening for alcohol misuse. Summary of recommendation. Rockville, MD; Agency for Healthcare Research and Quality; April 2004 [cited 2006 Sep 1]. Available from: <http://www.ahrq.gov/clinic/uspstf/uspstfdrin.htm>.
2. American Academy of Family Physicians. Summary of Policy Recommendations for Periodic Health Examinations. AAFP Policy Action. Revision 6.0; August 2005.
3. Carmona R. U.S. Surgeon General advisory on alcohol use in pregnancy. News release Feb 21, 2005. Department of Health and Human Services, Office of the Surgeon General: Washington, DC; 2005.
4. Centers for Disease Control and Prevention. Alcohol use among women of childbearing age – United States, 1991-1999. *MMWR* 2002; 51(13): 273-276.
5. Centers for Disease Control and Prevention. Notice to readers: Surgeon General's advisory on alcohol use in pregnancy. *MMWR* 2005; 54(09): 229.
6. Harwood H. *Updating Estimates of Economic Costs of Alcohol Abuse in the United States: Estimates, Update Methods, and Data*. National Institute of Alcohol Abuse and Alcoholism; 2000. NIH Publication No. 98-4327.
7. Thomson Medstat. MarketScan. 2004.
8. Maciosek MV, Coffield AB, Edwards NM, Flottemesch TJ, Goodman MJ, Solberg LI. Priorities among effective clinical preventive services. *Am J Prev Med* 2006;31:90-6.
9. Fleming MF, Mundt MP, French MT, Manwell LB, Stauffacher EA, Barry KL. Brief physician advice for problem alcohol drinkers: long-term efficacy and benefit-cost analysis. A randomized controlled trial in community-based primary care settings. *Alcohol Clin Exp Res* 2002;26:36-43.
10. Gentilello LM, Ebel BE, Wickizer TM, Salkever DS, Rivara FP. Alcohol interventions for trauma patients treated in emergency departments and hospitals: A cost benefit analysis. *Ann Surg* 2005;241:541-50.
11. Klug MG, Burd L. Fetal alcohol syndrome prevention: Annual and cumulative cost savings. *Neurotoxicol Teratol* 2003; 25(6): 763-765.
12. Bertholet N, Daepfen J-B, Fleming M, Burnand B. Reduction of alcohol consumption by brief alcohol intervention in primary care: systematic review and meta-analysis. *Arch Intern Med* 2005;165:986-95.
13. Cuijpers P, Riper H, Lemmers L. The effects on mortality of brief interventions for problem drinking: A meta-analysis. *Addiction* 2004;99:839-45.
14. U.S. Preventive Services Task Force. Screening and behavioral counseling interventions in primary care to reduce alcohol misuse. What's new from the USPSTF? Rockville, MD: Agency for Healthcare Research and Quality; April 2004.
15. National Institute of Alcohol Abuse and Alcoholism. Helping patients who drink too much, a clinician's guide. [cited 2006 Aug 21]. Available from: <http://pubs.niaaa.nih.gov/publications/Practitioner/CliniciansGuide2005/guide.pdf#search=%22NIAAA%20clinician's%20guide%22>.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Asymptomatic Bacteriuria (Screening)

Clinical Preventive Service Recommendations

<p>U.S. Preventive Services Task Force Recommendation</p>	<p>The U.S. Preventive Services Task Force (USPSTF) strongly recommends screening for asymptomatic bacteriuria with urine culture for pregnant women at 12 to 16 weeks' gestation.¹</p>
<p>Evidence Rating: A (Strongly Recommended/ Good Evidence)</p>	<p>The USPSTF found good evidence that screening pregnant women for asymptomatic bacteriuria with urine culture significantly reduces symptomatic urinary tract infections, low birth weight, and preterm delivery. The benefits of screening and treatment substantially outweigh any potential harm.¹</p>
<p>Evidence-Based Recommendation American Academy of Family Physicians (AAFP)</p>	<p>The American Academy of Family Physicians (AAFP) strongly recommends that all pregnant women be screened for asymptomatic bacteriuria using urine culture at 12 to 16 weeks' gestation or at the first prenatal visit if after that time.²</p>
<p>Evidence Rating: SR (Strongly Recommends)</p>	<p>Good quality evidence exists which demonstrates the substantial net benefit of screening for asymptomatic bacteriuria over harm; the intervention is perceived to be cost-effective and acceptable to nearly all patients.²</p>
<p>Recommended Guidance American College of Obstetricians and Gynecologists (ACOG)</p>	<p>The American College of Obstetricians and Gynecologists (ACOG) recommends that clinicians screen all pregnant women for asymptomatic bacteriuria by taking a urine culture at the first prenatal visit. They further recommend that a repeat urine culture be obtained during the third trimester.³</p>
<p>Evidence Rating:</p>	<p>Not Specified</p>
<p>Information Sources</p>	<p>The recommendations and supporting information contained in this document came from several sources, including the:</p> <ul style="list-style-type: none">• American Academy of Family Physicians (AAFP)• American College of Obstetricians and Gynecologists (ACOG)• Peer-reviewed research• U.S. Preventive Services Task Force (USPSTF) <p>The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.</p>

Condition/Disease Specific Information

Epidemiology of Condition/Disease

Asymptomatic bacteriuria in pregnancy is defined at the presence of a significant amount of bacterial growth in a urine culture taken from a urine sample⁴ and the absence of symptoms of a urinary infection such as pain or urgency.⁵

Asymptomatic bacteriuria occurs in approximately 2% to 14% of pregnant women and 80,000 to 400,000 cases occur each year in the United States.⁶

Without treatment, 20% to 40% of asymptomatic bacteriuria cases among pregnant women progress to pyelonephritis, a serious kidney infection. Pyelonephritis complicates 1% to 2% of all pregnancies and affects 100,000 women each year.⁶ It is also a leading cause of antepartum hospitalization.¹ With appropriate screening and treatment, only 3% of bacteriuria cases will progress to pyelonephritis.⁶

Condition/Disease Risk Factors

Bacteriuria increases the risk for preterm delivery and low birth weight and may also increase the risk of fetal and perinatal mortality.^{1,6} If fact, the risk of preterm delivery is twice as high among women who had asymptomatic bacteriuria at some point during pregnancy compared to those who did not.⁶

Risk factors for asymptomatic bacteriuria during pregnancy include low socioeconomic urinary tract infections (UTIs) in childhood. Other risk factors include preexisting medical conditions such as diabetes, sickle cell disease, immunosuppression (e.g., HIV/AIDS), urinary tract anatomic anomalies, and spinal cord injuries. UTIs experienced before pregnancy are predictive of the diagnosis of asymptomatic bacteriuria at the first prenatal visit.⁶

Value of Prevention

Economic Burden of Condition/Disease

Specific data about the economic burden of UTIs among pregnant women are not available. The annual cost of all community-acquired urinary tract infections in 1995 was estimated to be approximately \$1.6 billion, including \$659 million in direct costs and \$936 million in indirect costs.⁷ The direct and indirect costs of acute pyelonephritis were estimated to be \$2.14 billion (in year 2000 dollars).⁸

Workplace Burden of Condition/Disease

Lost productivity due to absenteeism associated with pregnancy-related complications of UTIs among working women (in addition to the increased medical care costs of such complications) has important financial ramifications for employers. Specific data on the workplace burden of pregnancy-related UTIs are not available.

Economic Benefit of Preventive Intervention

The preventive treatment of asymptomatic bacteriuria during pregnancy produces economic benefits such as preventing cases of cystitis, pyelonephritis, and premature births. In addition, preventing cases of mild and serious pyelonephritis produce significant improvements in quality of life.⁹

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Estimated Cost of Preventive Intervention	In 2004, the private-sector cost of screening for bacteriuria averaged \$17 per screen; approximately 95% of all paid claims fell within the range of \$1 to \$45 per screen. ¹⁰
Estimated Cost of Treatment	One cost-effectiveness study estimated the cost of antibiotic treatment to be \$11, based on a 7-day course of the generic form of commonly used antibiotics for the treatment of asymptomatic bacteriuria (in year 1994 dollars). ⁷
Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention	Research shows that screening for asymptomatic bacteriuria using urine culture, when compared with use of dipstick analysis, is cost-effective among populations where the prevalence of asymptomatic bacteriuria is at least 9%. ⁶
Preventive Intervention Information	
Preventive Intervention: Purpose of Screening	The purpose of screening for and treating asymptomatic bacteriuria in pregnancy is the prevention of poor maternal and infant outcomes associated with infection including pyelonephritis and prematurity.
Benefits and Risks of Intervention	<p>Good evidence exists that screening pregnant women for asymptomatic bacteriuria with urine culture (rather than urinalysis) — and treating those with the infection — significantly reduces symptomatic urinary tract infections, low birth weight, and preterm delivery. A urine specimen obtained at 12 to 16 weeks' gestation will detect approximately 80% of patients with asymptomatic bacteriuria.^{6,11}</p> <p>The USPSTF did not identify any information on the potential harms of screening for asymptomatic bacteriuria.¹¹</p>
Initiation, Cessation, and Interval	All pregnant women should be screened for asymptomatic bacteriuria at 12 to 16 weeks' gestation. ^{1,3} The optimal frequency of subsequent urine testing during pregnancy is uncertain and is thus left to the discretion of the clinician. The American College of Obstetricians and Gynecologists (ACOG) recommends that clinicians re-screen all pregnant women for asymptomatic bacteriuria by performing a urine culture during the third trimester. ³
Intervention Process	Urine culture is the gold standard for detecting asymptomatic bacteriuria. ¹ Other types of screening tests commonly used in the primary care setting (such as dipstick analysis and direct microscopy) are not as accurate for detecting bacteriuria in asymptomatic persons. ¹
Treatment Information	<p>Asymptomatic bacteriuria can be treated with a range of antibiotics. A Cochrane Collaboration review of 14 randomized trials of asymptomatic bacteriuria in pregnant women showed that antibiotic treatment was significantly associated with decreased incidence of pyelonephritis. The review also determined that antibiotic treatment reduced the rate of preterm delivery and low birth weight.¹²</p> <p>Health benefits should include provisions for diagnostic and treatment services.</p>

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Evidence-Based Research:

U.S. Preventive Services Task Force (USPSTF)

Strength of Evidence: A (Strongly Recommended/Good Evidence)

- The U.S. Preventive Services Task Force (USPSTF) strongly recommends screening for asymptomatic bacteriuria with urine culture for pregnant women at 12 to 16 weeks' gestation.¹ The USPSTF found good evidence that screening pregnant women for asymptomatic bacteriuria with urine culture significantly reduces symptomatic urinary tract infections, low birth weight, and preterm delivery. The benefits of screening and treatment substantially outweigh any potential harm.¹

The American Academy of Family Physicians (AAFP)

Strength of Evidence: SR (Strongly Recommended)

- AAFP strongly recommends that all pregnant women be screened for asymptomatic bacteriuria using urine culture at 12 to 16 weeks' gestation or at the first prenatal visit if after that time. Good quality evidence exists which demonstrates the substantial net benefit of screening for asymptomatic bacteriuria over harm; the intervention is perceived to be cost-effective and acceptable to nearly all patients.²

Recommended Guidance:

American College of Obstetricians and Gynecologists (ACOG)

Strength of Evidence: Not Specified

- The American College of Obstetricians and Gynecologists (ACOG) recommends that clinicians screen all pregnant women for asymptomatic bacteriuria by taking a urine culture at the first prenatal visit. They further recommend that a repeat urine culture be obtained during the third trimester.³

Authored by:

Campbell KP, Chattopadhyay S. Asymptomatic bacteriuria evidence-statement: screening.

In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Asymptomatic Bacteriuria (Screening)

1. Calogne N; U.S. Preventive Services Task Force. Screening for asymptomatic bacteriuria: Recommendation statement. AHRQ Publication No. 05-0551-A. Rockville, MD: Agency for Healthcare Research and Quality; 2004.
2. American Academy of Family Physicians. Summary of policy recommendations for periodic health examinations. AAFP Policy Action. Revision 6.0; August 2005.
3. American College of Obstetricians and Gynecologists. Antimicrobial therapy for obstetric patients. ACOG educational bulletin no. 245 (8-10). Washington, DC: American College of Obstetricians and Gynecologists; March 1998.
4. U.S. National Library of Medicine. Medical Encyclopedia: Asymptomatic bacteriuria. Washington, DC: National Institutes of Health; [cited 2006 Mar 22]. Available from: <http://www.nlm.nih.gov/medlineplus/ency/article/000520.htm>.
5. Sescor NIC, Garingala-Molina FD, Ycasiano CEJ, Saniel MC, Manalastas RM. Prevalence of asymptomatic bacteriuria and associated risk factors in pregnant women. *Philippines Journal of Microbial Disease* 2003; 32(2): 63-69.
6. Mittal P, Wing DA. Urinary tract infections in pregnancy. *Clin Perinatol* 2005; 32: 749-764.
7. Rouse DJ, Andrews WW, Goldenberg RL, Owen J. Screening and treatment of asymptomatic bacteriuria in pregnancy to prevent pyelonephritis: a cost-effectiveness and cost benefit analysis. *Obstet Gynecol* 1995; 86:119-123.
8. Brown P, Ki M, Foxman B. Acute pyelonephritis among adults: cost of illness and considerations for the economic evaluation of therapy. *Pharmacoeconomics* 2005;23:1123-42.
9. Yen Zui-Shen, davis MA, Chen Shyr-Chyr, Chen Wen-Jone. A cost-effectiveness analysis of treatment strategies for acute uncomplicated pyelonephritis in women. *Acad Emerg Med* 2003; 10: 309-314.
10. Thomson Medstat. MarketScan. 2004.
11. U.S. Preventive Services Task Force. Screening for asymptomatic bacteriuria: Recommendation statement. *Guide to Clinical Preventive Services*. 3rd ed. Rockville, MD; Agency for Healthcare Research and Quality; 2001 [cited 2006 Mar 22]. Available from: <http://www.ahrq.gov/clinic/3rduspstf/asymbac/asymbacrs.htm>.
12. U.S. Preventive Services Task Force. Screening for asymptomatic bacteriuria: A brief evidence update for the U.S. Preventive Services Task Force. AHRQ Publication No. 05-551-B. Rockville, MD: Agency for Healthcare Research and Quality; 2004.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Breastfeeding (Counseling)

Clinical Preventive Service Recommendations

U.S. Preventive Services Task Force Recommendation

The U.S. Preventive Services Task Force (USPSTF) recommends that clinicians provide structured breastfeeding education and behavioral counseling to all pregnant and postpartum women to promote the initiation and continuation of breastfeeding.¹

Evidence Rating: B (Recommended/ At Least Fair Evidence)

The USPSTF found fair evidence that programs which combine breastfeeding education with behaviorally-oriented counseling increase the rates of the initiation and continuation of breastfeeding for up to 3 months. The USPSTF notes that effective programs involve at least one in-person session; are usually 30 to 90 minutes in duration; follow structured protocols; and include practical behavioral skills training, problem-solving, and didactic instruction.¹

The USPSTF also found fair evidence to suggest that continued support via in-person visits or telephone contact with a clinician or counselor increases the proportion of women who continue breastfeeding their infants for 6 months.¹

CDC Recommendation

The CDC *Guide to Breastfeeding Interventions* recognizes the critical role returning to work plays in women's infant feeding decisions, and identifies a strong need to establish lactation support in the workplace.²

Evidence Rating:

Not Specified

Other Evidence Based Recommendations American Academy of Family Physicians (AAFP)

The American Academy of Family Physicians (AAFP) recommends structured breastfeeding education and behavioral counseling programs to promote breastfeeding.³

Evidence Rating: R (Recommends)

Although evidence exists which demonstrates the net benefit of counseling to promote breastfeeding, either the benefit is only moderate in magnitude or the evidence supporting a substantial benefit is only fair. The intervention is perceived to be cost-effective and acceptable to most patients.³

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- American Academy of Family Physicians (AAFP)
- Centers for Disease Control and Prevention (CDC)
- *Healthy People 2010*, U.S. Department of Health and Human Services
- Peer-reviewed research
- U.S. Preventive Services Task Force (USPSTF)

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document

should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

Epidemiology of Condition/Disease

Breastfeeding provides protective immune globulins from the mother to the infant, completing the development of the infant's immune system after birth and thereby reducing the risk that the infant will acquire some serious infections. This immunologic protection is impossible to replicate with infant formula. Infants who are breastfed are thus better prepared to fight off infections and allergens than their non-breastfed counterparts. Additionally, human breast milk is universally recognized to be the optimal food for infants and is nutritionally superior to formula. Evidence suggests that breastfed infants are less likely to develop obesity, and type 1 and type 2 diabetes than bottle-fed infants.² Further, children who were breastfed have lower rates of otitis media (ear infections), respiratory infections, gastroenteritis, and eczema (a skin disorder).²

Despite the benefits of breastfeeding for both women and infants, breastfeeding rates in the United States remain suboptimal, especially among certain subpopulations. Data from 2005 show that 72.9% of all new mothers initiated breastfeeding and 39.1% continued to breastfeed for 6 months.⁴ However, only 63.5% of low income mothers and 55.4% of African-American mothers initiated breastfeeding. Further, only 29.7% of low income mothers and 24.8% of African-American mothers continued to breastfeed their infants for the recommend 6-month period.⁴

The *Healthy People 2010* goals for breastfeeding aim to increase breastfeeding rates so that 75% of all new mothers initiate breastfeeding, 50% continue breastfeeding for at least 6 months postpartum, and 25% continue to breastfeed at least 1 year postpartum.⁵

Breastfeeding rates should be of paramount importance to employers as working outside the home negatively affects initiation and duration of breastfeeding.⁶ Furthermore, one-third of working mothers return to work within 3 months of the birth of their child, and two-thirds return within 6 months, the exact time period when breastfeeding is most critical.⁶

Condition/Disease Risk Factors

The mothers at highest risk for not breastfeeding are first-time mothers, those who have less formal education, those who are non-white, and those who are ill postpartum.⁷

Value of Prevention

Economic Burden of Condition/Disease

Healthcare costs of treating respiratory tract infections, ear infections, and gastrointestinal illnesses represent the majority of healthcare expenses for children less than one year of age.⁸ Because all of these illnesses are significantly more common among formula-fed infants than breastfed infants, support of breastfeeding initiation and continuation saves healthcare dollars.⁸ Indirect costs include time and income lost from work to take care of a sick child.

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

<p>Workplace Burden of Condition/Disease</p>	<p>Children who are not breastfed contribute to huge additional healthcare expenditures for the employers of their parents. Their parents are also responsible for significant productivity losses in the workplace associated with absenteeism and presenteeism. A study that compared infant feeding among employed mothers found that 75% of all 1-day maternal absences were among formula-feeding mothers.⁹ The study also found that infants who were formula fed were much more likely to fall ill. In fact, only 14% of infants with no illnesses were formula-fed (comparatively 86% of infants with no illnesses were breastfed).⁹</p>
<p>Economic Benefit of Preventive Intervention</p>	<p>Breastfeeding offers important economic benefits to families, employers, and society at large. Breastfeeding allows the family to save the money that otherwise would be spent on infant formula, other human milk substitutes, and feeding equipment.</p> <p>Further, a 2001 U.S. Department of Agriculture (USDA) study estimated that at least \$3.6 billion (in year 1998 dollars) would be saved if breastfeeding rates were increased from the current rates to those recommended by the U.S. Surgeon General (75% in-hospital and 50% at 6 months). This estimate includes \$3.1 billion in savings from prevented premature deaths, \$500 million in savings from reduced healthcare costs (e.g., hospital visits, etc), and savings from averted indirect costs such as forgone earnings of parents.⁸</p>
<p>Estimated Cost of Preventive Intervention</p>	<p>In 2004, the private-sector cost of counseling to promote breastfeeding initiation and continuation averaged \$23 per session; approximately 95% of all paid claims fell within the range of \$0 to \$81 per session.¹⁰</p>
<p>Estimated Cost of Treatment</p>	<p>Not Applicable</p>
<p>Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention</p>	<p>A study based on 1993-1994 data from the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) in Colorado found that compared with formula-feeding, breastfeeding each infant enrolled in WIC saved \$478 in WIC costs and Medicaid expenditures during the first 6 months of the infant's life, or \$161 after consideration of the formula manufacturers' rebate.¹¹ The cost saving was realized by the averted WIC costs for formula and foods for infants and mothers as well as reduced administrative expenses and lower Medicaid health care costs including costs for pharmacy reimbursement for the breastfed infants.¹¹</p>
<p>Preventive Intervention Information</p>	
<p>Preventive Intervention: Purpose of Counseling</p>	<p>The purpose of counseling is to educate women on the benefits of breastfeeding and to provide support and skills-training for women who choose to breastfeed, thereby increasing the number of women who initiate and maintain breastfeeding for the minimum recommended period of 12 months.</p>
<p>Benefits and Risks of Intervention</p>	<p>Breastfeeding has important short- and long-term health outcomes for children. Research shows that children who were breastfed are at significantly lower risk for childhood obesity as well as type 1 and type 2 diabetes than their non-breastfed</p>

peers. Breastfed infants and children also have lower rates of otitis media (ear infections), respiratory infections, gastroenteritis, and eczema (a skin disorder).¹²

Breastfeeding also has important short- and long-term health benefits for the mother. A woman's risk of breast cancer is decreased 4.3% for every 12-month increment of breastfeeding over her lifetime.¹² Her risk of ovarian and endometrial cancer is decreased by breastfeeding as well. Breastfeeding improves uterine tone, helps to stop post-birth bleeding, assists postpartum weight loss, and temporarily suppresses ovulation to aid in child-spacing.²

Educational programs have been shown to increase the proportion of women who initiate breastfeeding immediately after birth by 23% and the number of women who continue to breastfeed for 1 to 3 months by 39%. The efficacy of education programs is enhanced by ongoing support for breastfeeding initiation and continuation.¹³

There are no known risks of counseling to promote breastfeeding. In the United States, only women with the following conditions should be advised to avoid breastfeeding: women who are HIV positive; are taking antiretroviral medications; have untreated, active tuberculosis; are infected with human T-cell lymphotropic virus type I or type II; are using illicit drugs; are taking prescribed cancer chemotherapy agents that interfere with DNA replication; and whose infants who are diagnosed with galactosemia. Women undergoing radiation therapies need to temporarily interrupt breastfeeding but do not need to discontinue breastfeeding permanently.¹⁴

Initiation, Cessation, and Interval of Counseling

Counseling to promote breastfeeding should be offered to all women of childbearing age. It should begin during prenatal care and continue throughout the intrapartum hospital stay and into the postpartum period. Counseling should be given, according to need, throughout the course of lactation.

Intervention Process Counseling

Counseling should include breastfeeding initiation advice as well as skills and referrals to support breastfeeding continuation. The most effective breastfeeding education and counseling interventions last approximately 30 to 90 minutes and feature directive health education combined with behaviorally-oriented skills training and problem-solving.¹

Effective breastfeeding education and behavioral counseling programs¹:

- Begin during the prenatal period.
- Use face-to-face individual or group sessions.
- Are led by specially trained nurses, midwives, or lactation specialists.
- Sessions last 30 to 90 minutes.
- Include education on the benefits of breastfeeding for mother and infant, basic physiology, technical training on positioning and latch-on techniques, skills on how to overcome common barriers, skills to garner social support, how to use basic lactation support equipment such as breast pumps, etc.

Treatment Information

Not Applicable

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Evidence-Based Research:

U.S. Preventive Services Task Force (USPSTF)

Strength of Evidence: B (Recommended/At Least Fair Evidence)

- The USPSTF found at least fair evidence to support the provision of structured breastfeeding education and behavioral counseling to all pregnant and postpartum women to promote the initiation and continuation of breastfeeding.¹
- The USPSTF also found at least fair evidence to suggest that continued support via in-person visits or telephone contact with a clinician or counselor increases the proportion of women who continue breastfeeding their infants for 6 months.¹

The American Academy of Family Physicians (AAFP)

Strength of Evidence: R (Recommended)

- AAFP recommends structured breastfeeding education and behavioral counseling programs to promote breastfeeding. Although evidence exists which demonstrates the net benefit of counseling to promote breastfeeding, either the benefit is only moderate in magnitude or the evidence supporting a substantial benefit is only fair. The intervention is perceived to be cost-effective and acceptable to most patients.³

Authored by:

Campbell KP, Chattopadhyay S. Breastfeeding evidence-statement: counseling. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Breastfeeding (Counseling)

1. Berg AO. Behavioral interventions to promote breastfeeding: Recommendations and rationale. U.S. Preventive Services Task Force. *Ann Fam Med* 2003; 1(2): 79-80.
2. Shealy KR, Li R, Benton-Davis S, Grummer-Strawn LM. *The CDC Guide to Breastfeeding Interventions*. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2005.
3. American Academy of Family Physicians. Summary of Policy Recommendations for Periodic Health Examinations. AAFP Policy Action. Revision 6.0; August 2005.
4. Centers for Disease Control and Prevention. National Immunization Survey. [cited 2006 Aug 31]. Available from: http://www.cdc.gov/breastfeeding/data/NIS_data/data_2005.htm.
5. U.S. Department of Health and Human Services. *Healthy People 2010*. 2nd ed. 2 vols. Washington, DC: U.S. Government Printing Office, November 2000 [cited 2006 Aug 21]. Available from: <http://www.healthypeople.gov/Publications>.
6. United States Breastfeeding Committee. Workplace breastfeeding support. Issue paper. Raleigh, NC: United States Breastfeeding Committee; 2002.
7. Donnelly A, Snowden HM, Renfew MJ, Woolridge MW. Commercial hospital discharge packs for breastfeeding women (Cochrane review). In: *The Cochrane Library*, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd.
8. Weimer J. The economical cost of breastfeeding: A review and an analysis. ERS Food Assistance and Nutrition Research Report No. 13, Washington, DC: Economic Research Services, U.S. Department of Agriculture; 2001.
9. Cohen R, Mrtek MB, Mrtek RG. Comparison of maternal absenteeism and infant illness rates among breast-feeding and formula-feeding women in two corporations. *Am J Health Promot* 1995;10(2):148-53.
10. Donnelly A, Snowden HM, Renfew MJ, Woolridge MW. Commercial hospital discharge packs for breastfeeding women (Cochrane review). In: *The Cochrane Library*, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd.
11. Montgomery DL, Splett PL. Economic benefit of breast-feeding infants enrolled in WIC. *J Am Diet Assoc* 1997;97:379-385.
12. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50,302 women with breast cancer and 96,973 without the disease. *Lancet* 2002; 360: 187-95.
13. Guise JM, Palda V, Westhoff C, Chan BKS, Helfand M, Lieu TA. The effectiveness of primary care-based interventions to promote breastfeeding. U.S. Preventive Services Task Force. *Ann Fam Med* 2003; 1(2): 70-78.
14. Centers for Disease Control and Prevention. Breastfeeding: Infectious diseases and specific conditions affecting human milk: When should a mother avoid breastfeeding. [cited 2005 Dec 21]. Available from: <http://www.cdc.gov/breastfeeding/disease/contraindicators.htm>.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Folic Acid Supplementation (Counseling and Preventive Medication)

Clinical Preventive Service Recommendations

U.S. Preventive Services Task Force Recommendation

In 1996, the U.S. Preventive Services Task Force (USPSTF) recommended that all women of childbearing age who are capable of becoming pregnant (even those currently using contraception) consume 0.4 micrograms of folic acid per day to reduce the risk of a pregnancy affected by either spina bifida, anencephaly, or another neural tube defect.

This recommendation is archived and considered out of date.

CDC Recommendation

The CDC concurs with the U.S. Public Health Service (see description below).

**Evidence-Based Recommendation
American Academy of Family Physicians (AAFP)**

The American Academy of Family Physicians (AAFP) recommends that clinicians prescribe 0.4-0.8 mg/day of folic acid supplementation from at least 1 month prior to conception through the first trimester of the pregnancy to women who have not had a previous pregnancy affected by a neural tube defect.¹

**Evidence Rating: SR
(Strongly Recommends)**

Good quality evidence exists which demonstrates the substantial net benefit of folic acid supplementation over harm; the intervention is perceived to be cost-effective and acceptable to nearly all patients.¹

American Academy of Family Physicians (AAFP)

The American Academy of Family Physicians (AAFP) recommends that clinicians prescribe 0.4 mg folic acid supplementation to women not planning a pregnancy but of childbearing potential who have not had a previous pregnancy affected by a neural tube defect.¹

**Evidence Rating: R
(Recommended)**

Although evidence exists which demonstrates the net benefit of folic acid supplementation, either the benefit is only moderate in magnitude or the evidence supporting a substantial benefit is only fair. The intervention is perceived to be cost-effective and acceptable to most patients.¹

American Academy of Family Physicians (AAFP)

The American Academy of Family Physicians (AAFP) recommends that clinicians prescribe 4 mg/day of folic acid supplementation from 1 to 3 months prior to conception through the first trimester of pregnancy to women who are planning a pregnancy and have had a previous pregnancy affected by a neural tube defect.¹

**Evidence Rating: SR
(Strongly Recommended)**

Good quality evidence exists which demonstrates the substantial net benefit of folic acid supplementation over harm; the intervention is perceived to be cost-effective and acceptable to nearly all patients.¹

**Other Recommended
Guidance
U.S. Public Health
Service**

The U.S. Public Health Service recommends that²⁻³:

- All women of childbearing age in the United States who are capable of becoming pregnant should consume 0.4 mg of folic acid per day for the purpose of reducing their risk of having a pregnancy affected with spina bifida or other neural tube defects.
- Women who have had a prior NTD-affected pregnancy are at high risk of having a subsequent affected pregnancy and should consult their physicians when planning to become pregnant again.

Evidence Rating:

Not Specified

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- American Academy of Family Physicians (AAFP)
- American College of Obstetricians and Gynecologists (ACOG)
- Centers for Disease Control and Prevention (CDC)
- National March of Dimes Birth Defects Foundation
- Peer-reviewed research
- U.S. Public Health Service (USPHS)

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

**Epidemiology of
Condition/Disease**

Spina bifida and anencephaly are severe, potentially fatal birth defects. Both are neural tube defects (NTD) resulting in failure of the neural tube to fuse correctly. Approximately 3,000 pregnancies are affected by NTDs, and approximately 2,200 infants are born with neural tube defects each year.⁴ Many NTD-affected pregnancies do not result in a live birth because they are electively or spontaneously aborted (commonly referred to as a miscarriage) or result in fetal death or stillbirth.⁴

Anencephaly is always fatal and affected infants die shortly after birth. The majority of infants born with spina bifida grow into adulthood, but have severe medical complications such as paralysis and varying degrees of bowel and bladder incontinence.²

Folic acid, a B vitamin, prevents NTDs. Evidence (from populations not consuming foods fortified with folic acid) shows that consuming the recommended daily amount of synthetic folic acid (0.4 mg) through folic acid supplements can reduce a woman's chance of having a NTD-affected pregnancy by 40% to 80%.⁵

	<p>Synthetic folic acid can be consumed via folic acid supplements, folic acid-containing multivitamins, cereals that have been fortified with folic acid, and fortified grains. The natural form of this vitamin, folate, can be found in foods such as green leafy vegetables, orange juice, and beans. Synthetic folic acid vitamin supplementation is recommended because it is easier for the body to absorb than folate found in food and because up to 50% of naturally occurring folate is lost during cooking.⁶</p>
<p>Condition/Disease Risk Factors</p>	<p>Despite the known benefit of folic acid, only 33% of women of childbearing age report taking vitamins that contain folic acid and certain subpopulations have even lower rates of vitamin supplementation.⁷</p> <p>NTD rates are highest among the Hispanic population. Efforts to ensure supplementation among this population are important for eliminating health disparities.⁸</p>
<p>Value of Prevention</p>	
<p>Economic Burden of Condition/Disease</p>	<p>The economic burden of NTDs is substantial. The total lifetime cost for a child born with spina bifida is estimated to be \$636,000 (in year 2002 dollars).⁹ Applying the prevalence rate for spina bifida from the National Birth Defect Prevention Network data¹⁰ to the 4 million live births each year, that amounts to \$814 million in lifetime costs for each one-year cohort of births (all children born in one year).⁹ Costs associated with NTDs are shared by parents, employers, and communities.</p>
<p>Workplace Burden of Condition/Disease</p>	<p>Apart from the excess medical costs for affected children, employers face productivity loss costs associated with employees' absences to care for children with spina bifida. The present value of the cost of such caregiver time was estimated to be \$252,000 per child (in year 1993 dollars).¹¹</p>
<p>Economic Benefit of Preventive Intervention</p>	<p>The economic benefit of folic acid supplementation is based on the cost savings that result from averted direct and indirect costs of each NTD that is prevented with supplementation.</p>
<p>Estimated Cost of Preventive Intervention</p>	<p>In 2004, the private-sector cost of counseling to promote folic acid supplementation averaged \$23 per session; approximately 95% of all paid claims fell within the range of \$0 to \$81 per session.¹²</p> <p>The cost of supplementation is highly variable, depending on the type of vitamin supplement that is taken and for how long. The cost of over-the-counter vitamins is relatively cheap and is an out-of-pocket cost for beneficiaries. Prescription strength folic acid (recommended for women who have had a previous pregnancy affected by a NTD) costs approximately \$100 per year.¹³</p>
<p>Estimated Cost of Treatment</p>	<p>Not Provided</p>

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention

At present there is no evidence on the incremental cost-effectiveness of folic acid supplementation. A study undertaken before the implementation of the folic acid fortification program, examined a public and provider education program as a possible strategy to increase folic acid consumption through consumption of vitamin supplements and estimated that, compared to no program, the cost-effectiveness of supplementation was approximately \$5,000 per quality-adjusted life year (QALY).¹¹

Preventive Intervention Information

Preventive Intervention: Purpose of Counseling and Preventive Medication

Encouraging a woman to increase her folic acid intake prior to pregnancy via support, counseling, and/or prescription vitamins can lead to improved nutrition, thereby improving her chance of a healthy pregnancy and reducing her risk of an NTD-affected pregnancy.

Benefits and Risks of Intervention

A double-blind, placebo-controlled, randomized trial showed that folic acid supplementation before and during pregnancy decreased the risk of a first occurrence of a neural tube defect.¹⁴⁻¹⁵ The efficacy of such folic acid supplementation has since been confirmed by many other studies.

The South Carolina NTD prevention program has reported great success in preventing the recurrence of isolated NTDs by providing counseling and vitamins to women who have had a previous NTD-affected pregnancy.¹⁶

Initiation, Cessation, and Interval of Counseling and Preventive Medication

Folic acid supplementation is believed to have minimal risks. Folic acid is considered nontoxic even at very high doses and is rapidly excreted in the urine.

Folic acid supplementation information should be provided during routine healthcare visits and throughout the first trimester of pregnancy. Folic acid supplements should be prescribed/recommended, as medically indicated.

Intervention Process, Counseling, and Preventive Medication

Clinicians should 1) advise all women of child-bearing age who are capable of becoming pregnant about the importance of folic acid supplementation and 2) provide them with guidance on folic acid supplementation and, if needed, a prescription for folic acid supplements.

Treatment Information

Not Applicable

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Evidence-Based Research:

The American Academy of Family Physicians (AAFP)
 Strength of Evidence: SR (Strongly Recommended), R (Recommended)
 SR (Strongly Recommended)

- AAFP recommends that clinicians prescribe 0.4-0.8 mg/day of folic acid supplementation from at least 1 month prior to conception through the first trimester of the pregnancy to women planning to become pregnant who have not had a previous pregnancy affected by a neural tube defect. Good quality evidence exists which demonstrates the substantial net benefit of folic acid supplementation over harm; the intervention is perceived to be cost-effective and acceptable to nearly all patients.¹

R (Recommended)

- AAFP recommends that clinicians prescribe 0.4 mg folic acid supplementation to women not planning a pregnancy but of childbearing potential who have not previously had a baby with a neural tube defect. Although evidence exists which demonstrates the net benefit of folic acid supplementation, either the benefit is only moderate in magnitude or the evidence supporting a substantial benefit is only fair. The intervention is perceived to be cost-effective and acceptable to most patients.¹
- AAFP recommends that clinicians prescribe 4 mg/day of folic acid supplementation from 1-3 months prior to conception through the first trimester of pregnancy to women who are planning a pregnancy and had a previous pregnancy affected by a neural tube defect.¹ Good quality evidence exists which demonstrates the substantial net benefit of folic acid supplementation over harm; the intervention is perceived to be cost-effective and acceptable to nearly all patients.¹

Recommended Guidance:

U.S. Public Health Service (USPHS)

Strength of Evidence: Not Specified

- The U.S. Public Health Services recommends that all women of childbearing age in the United States who are capable of becoming pregnant should consume 0.4 mg of folic acid per day for the purpose of reducing their risk of having a pregnancy affected with spina bifida or other neural tube defects. Women who have had a prior NTD-affected pregnancy are at high risk of having a subsequent affected pregnancy, and should consult their physicians when planning to become pregnant again.²⁻³

Authored by:

Campbell KP, Grosse S, Chattopadhyay S. Folic acid supplementation evidence-statement: counseling and preventive medication. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Folic Acid Supplementation (NTD) (Preventive Medication)

1. American Academy of Family Physicians. Summary of Policy Recommendations for Periodic Health Examinations. AAFP Policy Action. Revision 6.0; August 2005.
2. Centers for Disease Control and Prevention. Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. MMWR 1992; 41(RR14): 001.
3. Centers for Disease Control and Prevention. Folic Acid. Centers for Disease Control and Prevention; 2006. Available from: http://www.cdc.gov/ncbddd/folicacid/health_recomm.htm.
4. Centers for Disease Control and Prevention. Spina bifida and anencephaly before and after folic acid mandate – United States, 1995-1996 and 1999-2000. MMWR 2004; 53(17): 362-365.
5. Berry RJ, Li Z, Erickson JD, Li S, Moore CA, Wang H et al. Prevention of neural-tube defects with folic acid in China. China-US Collaborative Project for Neural Tube Defect Prevention. N Engl J Med 1999; 341:1485–1490.
6. March of Dimes. Spina bifida. Quick Facts and Reference Sheets. Updated 2005 [cited 2005 Jul 6]. Available from: <http://www.marchofdimes.com>.
7. Centers for Disease Control and Prevention. Use of dietary supplements containing folic acid among women of childbearing age – United States, 2005. MMWR 54(38); 955-958. Available from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5438a4.htm>.
8. Williams LJ, Rasmussen SA, Flores A, Kirby RS, Edmonds LD. Decline in the prevalence of spina bifida and anencephaly by race/ethnicity: 1995-2002. Pediatrics 2005;116(3):580-586.
9. Grosse SD, Waitzman NJ, Romano PS, Mulinare J. Re-evaluating the benefits of folic acid fortification in the United States: Economic analysis, regulation, and public health. Am J Public Health 2005;95:1917–1922.
10. Canfield MA, Collins JS, Botto LD, Williams LJ, Mai CT, Kirby RS, et al. Changes in the birth prevalence of selected birth defects after grain fortification with folic acid in the United States: findings from a multi-state population-based study. Birth Defects Res A Clin Mol Teratol 2005;73:679-689.
11. Kelly AE, Haddix AC, Scanlon KS, Helmick CG, Mulinare J. Cost-effectiveness of strategies to prevent neural tube defects. In: Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. *Cost-Effectiveness in Health and Medicine*. New York, Oxford: Oxford University Press; 1996:312–349.
12. Thomson Medstat. Marketscan 2004.
13. Pricegrabber.com cost estimate for a one-year supply of prescription strength (1 mg) folic acid. [cited 2006 Aug 31]. Available from: http://www.pricegrabber.com/search_attrib.php?form_keyword=folic+acid&topcat_id=&page_id=1776&lo_p=0&hi_p=0.
14. Medical Research Council Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. Lancet 1991;338:131–137.
15. Czeizel AE, Dudas I. Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. N Engl J Med 1992;327:1832–1835.
16. Stevenson RE, Allen WP, Pai GS, Best R, Seaver LH, Dean J, Thompson S. Decline in prevalence of neural tube defects in a high-risk region of the United States. Pediatrics 2000;106:677-683.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

**Group B Streptococcal Disease (GBS)
(Screening and Preventive Medication)**

Clinical Preventive Service Recommendations

U.S. Preventive Services Task Force Recommendation

Not Applicable

CDC Recommendation

The Centers for Disease Control and Prevention (CDC) recommends that clinicians screen all pregnant women for vaginal and rectal group B streptococcal (GBS) colonization at 35 to 37 weeks' gestation.¹

- Women should be tested for GBS at each pregnancy as colonization at a prior pregnancy is not an indication for antibiotic prophylaxis in subsequent pregnancies.
- Women who are identified through screening as GBS carriers should be given intrapartum antibiotic prophylaxis.
- Women whose screening status is unknown at the time of labor should receive intrapartum antibiotic prophylaxis if they present with any of the following risk factors: delivery at less than 37 weeks' gestation, membrane rupture \geq 18 hours, or intrapartum fever \geq 38C.
- Women with GBS isolated from the urine at any time in the current pregnancy should also be given intrapartum antibiotic prophylaxis.
- Women who have previously given birth to an infant with invasive GBS disease should receive intrapartum antibiotic prophylaxis.
- Women who are expected to deliver preterm (less than 37 weeks' gestation) should be assessed for their need for intrapartum antibiotic prophylaxis to prevent perinatal GBS disease.
- GBS colonized women who have a planned cesarean before rupture of the membranes are at a low risk for delivering an infant with early-onset GBS disease and should thus not routinely receive intrapartum antibiotic prophylaxis.

Evidence Rating:

Not Specified

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- Centers for Disease Control and Prevention (CDC)
- Royal College of Obstetricians and Gynecologists
- Peer-reviewed research

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

Epidemiology of Condition/Disease

Group B streptococcus (GBS), a bacterium, has been a leading cause of infection-related infant death in the United States since the 1970s.¹ GBS disease is a serious infection that causes sepsis (blood poisoning), pneumonia, and meningitis in newborns. GBS can be lethal: 1 in every 20 babies born with GBS dies. Each year in the United States between 1,300 and 1,600 infants contract early-onset GBS and 65 to 80 infants die from it.¹ Those who survive are often left with lifelong disabilities such as hearing loss, vision impairments, and/or learning disabilities.¹

In the 1980s, scientists discovered that administering antibiotics during labor to women who carry GBS could prevent early-onset GBS disease from developing in newborns. One in every 4 to 5 pregnant women carries GBS in her vagina or rectum.¹ While most women colonized with GBS are asymptomatic (meaning that they can pass the disease to their child, but are not affected by it themselves), some women become infected with GBS and are at risk of womb infections, bladder infections, and stillbirth.¹

Condition/Disease Risk Factors

Pregnant women are at a higher risk of delivering an infant with GBS disease if they have GBS in their urine, are colonized with GBS at the time of labor, have a fever during labor, rupture their membranes 18 hours or more before delivery, or if they have previously had a baby with GBS disease.¹

Value of Prevention

Economic Burden of Condition/Disease

While the rate of neonatal GBS infections has declined since the 1990s due to widespread screening and treatment, GBS continues to have an economic toll in the United States.² The average neonatal intensive care cost of a GBS-infected infant was estimated to be \$30,100 in 2001.³ The excess average discounted lifetime healthcare cost for an infant disabled by an early-onset GBS (over that for a healthy infant) was estimated to equal \$261,000 (in year 2001 dollars).⁴

Workplace Burden of Condition/Disease

Productivity losses associated with absenteeism and presenteeism for parents of GBS-affected children have not been quantified.

Economic Benefit of Preventive Intervention

Preventing a case of infant disability due to GBS can reduce the discounted lifetime healthcare costs for an infant by \$261,000, on average (year 2001 dollars).⁴ In 1993, researchers estimated that treating high-risk women identified through screening with intrapartum antibiotic prophylaxis could prevent 3,300 cases of GBS annually; saving approximately \$16 million in direct medical costs.²

Estimated Cost of Preventive Intervention

In 2004, the private-sector cost of screening for GBS averaged \$13 per screen; approximately 95% of all paid claims fell within the range of \$4 to \$33 per screen.⁶ When women with a positive test result are treated with antibiotic therapy during labor (an initial dose of 2g of ampicillin intravenously, followed by 1g every 4 hours) the preventive medication costs are estimated to equal \$63 per course of therapy.⁴

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

<p>Estimated Cost of Treatment</p>	<p>The cost of treating an infant with early-onset group B streptococcal sepsis (a severe form of the disease) was estimated to exceed \$123,000 (in year 1993 dollars).⁴</p>
<p>Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention</p>	<p>Screening to prevent early-onset GBS is estimated to cost less than \$12,000 (in year 1997 dollars) per prevented case. Preventive intervention may also generate net cost-savings if the high cost of managing a case of early-onset GBS is considered.³</p> <p>In comparison to other preventive interventions and to commonly accepted cost-effectiveness benchmarks, screening for GBS is cost-effective.</p>
<p>Preventive Intervention Information</p>	
<p>Preventive Intervention: Purpose of Screening</p>	<p>Identifying women who carry group B streptococcal bacteria allows clinicians to administer antibiotic prophylaxis during labor, thus preventing transmission of the bacteria to the infant. Vaccines to prevent GBS disease are under development but are not currently available. Thus, universal prenatal GBS culture-based screening is the best available prevention strategy.¹</p>
<p>Benefits and Risks of Intervention</p>	<p>The risks of screening for GBS colonization are minimal. However, there are risks associated with intrapartum antibiotic prophylaxis. Severe anaphylaxis is associated with the use of penicillin in some women. Anaphylaxis occurs in 1 out of every 10,000 treatments and can be fatal. Also, the widespread use of antibiotics, particularly broad-spectrum antibiotics such as ampicillin, contributes to the development of resistant organisms.¹</p> <p>Despite the risks associated with prevention, screening for group B streptococcal colonization and intrapartum antibiotic prophylaxis can reduce the rate of neonatal infection death and prevent infants from significant disability. These significant benefits outweigh the risks and costs associated with screening.</p>
<p>Initiation, Cessation, and Interval of Screening and Preventive Medication</p>	<p>All pregnant women should be screened for vaginal and rectal group B streptococcal (GBS) colonization between 35 and 37 weeks' gestation. Preventive medication should be given to colonized women, as medically indicated.</p>
<p>Intervention Process Screening</p>	<p>All women should be screened for vaginal and rectal group B streptococcal colonization using recommended laboratory methods for GBS isolation and identification. Women should be screened for GBS with each pregnancy as colonization at a prior pregnancy is not an indication for antibiotic prophylaxis in subsequent pregnancies.</p>
<p>Preventive Medication</p>	<p>Intrapartum antibiotic prophylaxis should be given, as medically indicated, to:</p> <ul style="list-style-type: none"> • Women who are identified as GBS carriers. • Women whose screening status is unknown at the time of labor <i>if</i> they present with any of the following risk factors: delivery at less than 37 weeks' gestation, membrane rupture \geq18 hours, or intrapartum fever \geq 38C.

- Women with GBS isolated from the urine at any time in the current pregnancy.
- Women who have previously given birth to an infant with invasive GBS disease.

Women who are expected to deliver preterm (less than 37 weeks gestation) should be assessed for their need for intrapartum antibiotic prophylaxis to prevent perinatal GBS disease.

GBS colonized women who have a planned cesarean before rupture of the membranes are at a low risk for delivering an infant with early-onset GBS disease and should thus not routinely receive intrapartum antibiotic prophylaxis.¹

Treatment Information

Health benefits should include provisions for treatment services for affected women and infants.

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Recommended Guidance:

The Centers for Disease Control and Prevention (CDC)

Strength of Evidence: Not Specified

- The CDC recommends screening all pregnant women for vaginal and rectal group B streptococcal (GBS) colonization between 35 and 37 weeks' gestation.¹

Authored by:

Campbell KP, Chattopadhyay S. Group B streptococcal disease evidence-statement: screening and preventive medication. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Group B Streptococcal Disease (Screening and Preventive Medication)

1. Schrag S, Gorwitz R, Fultz-Butts K, Schuchat A. Centers for Disease Control and Prevention. Prevention of perinatal Group B streptococcal disease: Revised guidelines from the CDC. *MMWR* 2002; 51(RR11); 1-22.
2. Keenan C. Prevention of neonatal group B streptococcal infection. *Am Fam Physician* 1998; 57(1).
3. Mohle-Boetani JC, Schuchat A, Plikaytis D, Smith JD, Broome CV. Comparison of prevention strategies for neonatal group B streptococcal infection. A population-based analysis. *JAMA* 1993; 270(12):1442-1448.
4. Haberland CA, Benitz WE, Sanders GD, Pietzsch JB, Yamada S, Nguyen L, et al. Perinatal screening for Group B Streptococci: Cost-Benefit analysis of rapid polymerase chain reaction. *Pediatrics* 2002;110(3):471-480.
5. Benitz WE, Gould JB, Druzin ML. Preventing early-onset Group B streptococcal sepsis: Strategy development using decision analysis. *Pediatrics* 1999;103(6):76-91.
6. Thomson Medstat. MarketScan. 2004.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Hepatitis B Virus (HBV) (Screening, Immunization, and Treatment)

Clinical Preventive Service Recommendations

**Preventive Services
Task Force
Recommendation**

Screening

The U.S. Preventive Services Task Force (USPSTF) strongly recommends screening for hepatitis B virus (HBV) infection in pregnant women at their first prenatal visit.¹

**Evidence Rating: A
(Strongly
Recommended/
Good Evidence)**

The USPSTF found good evidence that universal prenatal screening for HBV infection using HBsAg substantially reduces prenatal transmission of HBV and the subsequent development of chronic HBV infection. The current practice of vaccinating all infants against HBV infection and post-exposure prophylaxis with hepatitis B immune globulin administered at birth to infants of HBV-infected women substantially reduces the risk for acquiring HBV infection.¹

Immunization

The U.S. Preventive Services Task Force (USPSTF) defers to the Advisory Committee on Immunization Practices (ACIP) and the Centers for Disease Control and Prevention (CDC) on recommendations surrounding immunization.

**CDC
Recommendation**

Screening

**Advisory Committee
on Immunization
Practices (ACIP)**

The Advisory Committee on Immunization Practices (ACIP) recommends that all pregnant women be tested routinely for hepatitis B surface antigen (HBsAg) during an early prenatal visit (i.e., first trimester) in each pregnancy, even if they have been previously vaccinated or tested. Women who were not screened prenatally, those who engage in behaviors that put them at high risk for infection (e.g., injection-drug use, having had more than one sex partner in the previous 6 months or an HBsAg-positive sex partner, evaluation or treatment for a sexually transmitted infection [STI], or recent or current injection-drug use) and those with clinical hepatitis should be tested at the time of admission to the hospital for delivery.^{2,3}

Immunization

The ACIP further recommends the hepatitis B vaccine for pregnant women at risk for hepatitis B virus infection. Pregnant women who are identified as being at risk for HBV infection during pregnancy (see list of risk factors in preceding paragraph) should be vaccinated. Pregnant women at risk for HBV infection during pregnancy should be counseled concerning other methods to prevent HBV infection.^{2,3}

Management of Exposed or Potentially Exposed Infants/Treatment

The ACIP recommends that all infants born to HBsAg-positive women should receive single-antigen hepatitis B vaccine and hepatitis B immune globulin prophylaxis (HBIG) (0.5 mL) within the first 12 hours following the birth, administered at different injection sites.^{2,3}

Women admitted for delivery without documentation of HBsAg test results should have blood drawn and tested as soon as possible after admission. While test results are pending, all infants born to women without documentation of HBsAg test results should receive the first dose of single-antigen hepatitis B vaccine (without HBIG) within 12 hours following the birth.²⁻³

A summary of guidelines for the immunization of pregnant women can be found online (www.cdc.gov/nip/publications/preg_guide.htm).

Evidence Rating:

Expert Consensus

**Other Evidence-Based Recommendations
American Academy of Family Physicians (AAFP)**

The American Academy of Family Physicians (AAFP) strongly recommends screening for hepatitis B virus (HBV) infection in pregnant women at their first prenatal visit.⁵

**Evidence Rating: SR
(Strongly Recommended)**

Good quality evidence exists which demonstrates the substantial net benefit of screening for HBV over harm; the intervention is perceived to be cost-effective and acceptable to nearly all patients.⁵

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- Advisory Committee on Immunization Practices (ACIP)
- American Academy of Family Physicians (AAFP)
- Centers for Disease Control and Prevention (CDC)
- Peer-reviewed research
- U.S. Preventive Services Task Force (USPSTF)

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

Epidemiology of Condition/Disease

Over 1 million people in the United States are chronic carriers of HBV.⁴ In 2003, an estimated 73,000 new HBV infections were reported in the United States.⁴ Hepatitis infection can lead to liver disease, including liver cancer, which without treatment can result in death. Between 4,000 and 5,000 chronic carriers of HBV die each year in the United States.⁴ Hepatitis B can be treated with medications if diagnosed early, but some individuals do not respond to treatment and require liver transplants to survive.

The severity of hepatitis B infection depends on the age at which an individual becomes infected and the presence of other comorbid conditions such as alcohol abuse, HIV/AIDS, or other types of liver disease.⁶ Most adolescents and adults with acute HBV infections recover fully, but 30% of children aged 1 to 5 years

	<p>and 2% to 6% of adults become chronically infected with hepatitis B.⁷ Immunization against HBV is the single most effective way of preventing hepatitis B infection and its consequences.²</p>
<p>Condition/Disease Risk Factors</p>	<p>The risk factors for hepatitis B include intravenous drug use, concurrent infection with a sexually transmitted infection (STI), multiple sexual partners, household contact with an infected person, and being a healthcare worker with exposure to bodily fluids. However, 30% to 40% of infected individuals have no identified risk factors.⁶</p> <p>Infants can contract hepatitis B from an infected woman during labor and delivery and as many as 90% of infants infected through perinatal transmission become chronic carriers of HBV.²</p>
<p>Value of Prevention</p>	
<p>Economic Burden of Condition/Disease</p>	<p>The economic burden of hepatitis B infection depends on whether the infection is acute or chronic and what treatment is required. The direct medical cost of outpatient treatment for symptomatic acute hepatitis B has been estimated at \$272 per occurrence, while the cost of hospitalization for symptomatic hepatitis B infection is \$8,080 per occurrence (both in year 2000 dollars).⁸ If a patient develops liver disease as a result of chronic HBV infection, the direct medical cost of treatment is estimated to be \$59,308 (before discounting)⁸ and patients who require a liver transplant can have first-year billed charges of up to \$244,600 (in year 1999 dollars).⁹</p>
<p>Workplace Burden of Condition/Disease</p>	<p>HBV is also responsible for disability costs, costs associated with work-loss and absenteeism, and other indirect costs.</p>
<p>Economic Benefit of Preventive Intervention</p>	<p>Screening pregnant women for HBV, and treating the infants of HBV-positive women with post-exposure hepatitis B immune globulin prophylaxis and HBV vaccination can dramatically reduce the incidence of perinatal HBV transmission and thus the number of infants who become chronically infected with hepatitis B.² The additional recommended step of vaccinating all infants with HBV at birth also serves as a safety net to prevent perinatal hepatitis B transmission.² The averted direct and indirect costs of illness from each case of HBV prevented constitute the predominant economic benefit of the preventive intervention. From a societal perspective, prevention of perinatal HBV infection was estimated to save \$41.8 million (in year 1993 dollars) in medical and work-loss costs.¹⁰</p>
<p>Estimated Cost of Preventive Intervention</p>	<p>In 2004, the private-sector cost of¹¹:</p> <ul style="list-style-type: none"> • Screening for HBV via the hepatitis B surface antigen test averaged \$22; approximately 95% of all paid claims fell within the range of \$0 to \$64 per test. • An adult HBV vaccine averaged \$35; approximately 95% of all paid claims fell within the range of \$0 to \$77. • Vaccine administration averaged \$10; approximately 95% of all paid claims fell within the range of \$0 to \$20 (3 doses are usually needed for full protection).

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

<p>Estimated Cost of Treatment</p>	<p>In 2004, the private-sector cost of post-exposure hepatitis B immune globulin prophylaxis (for infants born to HBV-positive women) averaged \$178 and approximately 95% of all paid claims fell within the range of \$0 to \$514.¹¹</p> <p>The cost of therapeutic treatment of chronic hepatitis B varies according to the medication required; a single course of interferon therapy costs \$5,570 including provider visits and laboratory costs (in year 1995 dollars).¹²</p>
<p>Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention</p>	<p>The estimated cost of preventing a perinatal HBV infection is \$164 per year of life saved, (in year 1993 dollars).¹⁰ In comparison to other preventive interventions and to commonly accepted cost-effectiveness benchmarks, hepatitis B screening is highly cost-effective.</p>
<p>Preventive Intervention Information</p>	
<p>Preventive Intervention: Purpose of Screening and Immunization</p>	<p>Screening pregnant women for HBV, immunizing women at high-risk of HBV, and treating the infants of HBV-positive women with post-exposure hepatitis B immune globulin prophylaxis and HBV vaccination, can dramatically reduce perinatal HBV transmission and, thus, the number of infants who become chronically infected with hepatitis B.²</p>
<p>Benefits and Risks of Intervention</p>	<p>The benefits of screening, immunization, and treatment are substantial; an untreated maternal hepatitis B viral infection may result in severe disease for the woman and chronic infection for the newborn.²</p> <p>There is no apparent risk of adverse effects for developing fetuses when a hepatitis B vaccine is administered to a pregnant woman.³</p>
<p>Initiation, Cessation, and Interval Screening</p>	<p>Screening for hepatitis B should be conducted at the first prenatal visit in each pregnancy. Women at increased risk of acquiring HBV may be screened again during the third trimester and/or during labor and delivery and should be offered the hepatitis B vaccine. Household contacts of women with a positive HBsAg test should also be screened for HBV infection. Women admitted for delivery without documentation of HBsAg test results should have blood drawn and tested as soon as possible after admission.²</p>
<p>Immunization</p>	<p>HBV immunization should be given to high-risk pregnant women as deemed appropriate by the clinician.²</p> <p>All infants should receive their first hepatitis B immunizations at the time of birth. Infants born to HBV-infected women should be immunized and given immune globulin within 12 hours of birth. Infants born to women with unknown HBsAg status should receive one dose of single-antigen hepatitis B vaccine (without HBIG) within 12 hours of birth, while awaiting the woman's test results.²</p>
<p>Treatment</p>	<p>Post-exposure hepatitis B immune globulin prophylaxis should be given, as medically indicated.²</p>

Intervention Process Screening	The principal screening test for detecting an HBV infection (acute or chronic) is the identification of HBsAg in the blood. Testing methods include the HBsAg Immunoassay and the “rapid test,” an assay that detects HBsAg and the hepatitis B e-antigen HBeAg simultaneously.
Immunization	HBV immunizations are administered via injection.
Treatment	Post-exposure hepatitis B immune globulin prophylaxis.
Treatment Information	Please refer to the “Intervention Process” section for information on preventive treatment.

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Evidence-Based Research:

The U.S. Preventive Services Task Force (USPSTF)

Strength of Evidence: A (Strongly Recommended/Good Evidence)

- The USPSTF found good evidence that universal prenatal screening for HBV infection using HBsAg substantially reduces prenatal transmission of HBV and the subsequent development of chronic HBV infection. The current practice of vaccinating all infants against HBV infection and post-exposure prophylaxis with hepatitis B immune globulin administered at birth to infants of HBV-infected women substantially reduces the risk for acquiring HBV infection.¹

The American Academy of Family Physicians (AAFP)

Strength of Evidence: SR (Strongly Recommended)

- AAFP strongly recommends screening for hepatitis B virus (HBV) infection in pregnant women at their first prenatal visit.⁵ Good quality evidence exists which demonstrates the substantial net benefit of screening for HBV over harm; the intervention is perceived to be cost-effective and acceptable to nearly all patients.⁵

Recommended Guidance:

The Advisory Committee on Immunization Practices (ACIP)

Strength of Evidence: Expert Consensus

Screening

The ACIP recommends that all pregnant women be tested routinely for HBsAg during an early prenatal visit (e.g., first trimester) in each pregnancy, even if they have been previously vaccinated or tested. Women who were not screened prenatally, those who engage in behaviors that put them at high risk for infection (e.g., injection-drug use, having had more than one sex partner in the previous 6 months or an HBsAg-positive sex partner, evaluation or treatment for a sexually transmitted infection [STI], or recent or current injection-drug use) and those

with clinical hepatitis should be tested at the time of admission to the hospital for delivery.^{2,3}

Immunization

The ACIP recommends the hepatitis B vaccine for pregnant women at risk for hepatitis B virus infection.

This recommendation is supported by:
The U.S. Preventive Services Task Force (USPSTF)

Management of Exposed Infants/Treatment

The ACIP recommends that all infants born to HBsAg-positive women should receive single-antigen hepatitis B vaccine and HBIG (0.5 mL) within 12 hours of birth, administered at different injection sites.²

The ACIP recommends that all infants born to women without documentation of HBsAg test results should receive the first dose of single-antigen hepatitis B vaccine (without HBIG) within 12 hours of birth, while the woman's test results are pending.²

Authored by:

Campbell KP, Lindley MC, Lentine D, Bhatt A. Hepatitis B virus evidence-statement: screening, immunization, and treatment. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Hepatitis B Virus (Screening and Immunization)

1. U.S. Preventive Services Task Force. Screening for hepatitis B virus infection. Rockville, MD; Agency for Healthcare Research and Quality; February 2004 [cited 2006 Sep 11]. Available from: <http://www.ahrq.gov/clinic/uspstf/uspshpb.htm>.
2. Mast EE, Margolis HS, Fiore AE, Brink EW, Goldstein ST, Wang SA, Moyer LA, Bell BP, Alter MJ. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States. MMWR 2005 [cited 2006 Aug 22]; 54(RR-16): 1-23. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5416a1.htm?s_cid=rr5416a1_e.
3. Centers for Disease Control and Prevention. Guidelines for vaccinating pregnant women: From recommendations of the Advisory Committee on Immunization Practices (ACIP). October 1998; [updated July 2005; cited 2006 Aug 28]. Available from: http://www.cdc.gov/nip/publications/preg_guide.htm.
4. Centers for Disease Control and Prevention. Disease burden from hepatitis A, B, and C in the United States, 1980-2004. National Center for HIV, STD and TB Prevention, Division of Viral Hepatitis. [cited 2005 Aug 25]. Available from: http://www.cdc.gov/ncidod/diseases/hepatitis/resource/PDFs/disease_burden2004.pdf
5. American Academy of Family Physicians. Summary of policy recommendations for periodic health examinations. AAFP Policy Action. Revision 6.0; August 2005.
6. U.S. Preventive Services Task Force. Screening for hepatitis B infection: Recommendation statement. Rockville, MD: Agency for Healthcare Research and Quality; February 2004 [cited 2006 Sep 15]. Available from: <http://www.ahrq.gov/clinic/3rduspstf/hepbscr/hepbrs.htm>.
7. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2006. MMWR 2006; 55 (RR-11): 1-94.
8. Chesson HW, Blandford JM, Gift TL, Tao G, Irwin KL. The estimated direct medical cost of sexually transmitted diseases among American youth, 2000. *Perspect Sex Reprod Health* 2004; 36(1):11-19.
9. Hauboldt RH. *Cost Implications of Human Organ and Tissue Transplantations*, An Update. Seattle, WA: Milliman & Robertson, INC; 1999.
10. Margolis HS, Coleman PJ, Brown RE, Mast EE, Sheingold SH, Arevalo JA. Prevention of hepatitis B virus transmission by immunization: An economic analysis of current recommendations. *JAMA* 1995; 274(15):1201-8.
11. Thomson Medstat. MarketScan. 2004.
12. Wong J, Koff R, Tine F, Pauker S. Cost-effectiveness of interferon-alpha2b treatment for hepatitis B e antigen-positive chronic hepatitis B. *Ann Intern Med* 1995; 122:664-675.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Human Immunodeficiency Virus (HIV) (Screening, Counseling, and Preventive Medication)

Clinical Preventive Service Recommendations (Screening)

U.S. Preventive Services Task Force Recommendation

The U.S. Preventive Services Task Force recommends that clinicians screen all pregnant women for HIV.¹

Evidence Rating: A (Strongly Recommend/Good Evidence)

The USPSTF found good evidence that both standard and FDA-approved rapid screening tests accurately detect HIV infection in pregnant women and fair evidence that introduction of universal prenatal counseling and voluntary testing increases the proportion of HIV-infected women who are diagnosed and are treated before delivery. There is good evidence that recommended regimens of highly active antiretroviral therapy (HAART) are acceptable to pregnant women and lead to significantly reduced rates of mother-to-child transmission. Early detection of maternal HIV infection also allows for discussion of elective cesarean section and avoidance of breastfeeding, both of which are associated with lower HIV transmission rates. There is no evidence of an increase in fetal anomalies or other fetal harm associated with currently recommended antiretroviral regimens (with the exception of efavirenz). Serious or fatal maternal events are rare using currently recommended combination therapies. The USPSTF concluded that the benefits of screening all pregnant women substantially outweigh potential harms.¹

CDC Recommendation

The Centers for Disease Control and Prevention (CDC) recommends that clinicians screen all pregnant women for HIV.²

- HIV screening should be a routine part of prenatal care for all women. Providers should inform all of their obstetric patients of the substantial benefit that knowledge of HIV status has for the health of a woman and her infant.
- HIV screening should occur as early as possible during pregnancy so that informed therapeutic decisions can be made and treatment can begin early. For women at high-risk of HIV infection (e.g., women who have a history of sexually transmitted infections [STIs], women who exchange sex for money or drugs, women who have multiple sex partners during pregnancy, and women who use illicit drugs during pregnancy) should be re-tested during the third trimester (at or before 36 weeks' gestation).
- Women who are admitted for labor and delivery who have not been screened for HIV or whose HIV status is unknown should be tested immediately so that timely prophylactic treatment can be initiated if appropriate. In such cases, rapid testing or the expedited return of standard testing results is recommended. After delivery, the standard confirmatory testing should be completed.
- HIV screening should be voluntary and free of coercion. Women should not be tested without their knowledge, and a woman's decision to decline testing must not have detrimental consequences for the quality of prenatal care or labor and delivery care she receives.

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

CDC recommends that all pregnant women receive counseling and educational information on HIV and HIV screening *before* they are screened/tested.²

- Information regarding HIV and the risks of HIV infection should be given to all pregnant women as a part of routine prenatal care health education.
- Pregnant women who have behaviors that place them at high risk for acquiring HIV infection (e.g., multiple sex partners, history of STIs, substance abuse, etc) should be referred to an HIV risk-reduction service (e.g., HIV centers with personnel trained in HIV counseling, drug treatment centers, etc).

Other Recommended Guidance

The U.S. Public Health Service concurs with the CDC recommendations regarding screening and counseling.

Important Screening Information

Regulations, laws, and policies regarding HIV screening of pregnant women and infants differ throughout the United States and its territories. Healthcare providers should adhere to local laws and regulations concerning maternal HIV screening.³

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- Centers for Disease Control and Prevention (CDC)
- Peer-reviewed research
- U.S. Public Health Service (USPHS)
- U.S. Preventive Services Task Force (USPSTF)

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

Epidemiology of Condition/Disease

Approximately 120,000 to 160,000 HIV infected women live in the United States, 80% of whom are of childbearing age.³ Each year between 1985 and 1995, approximately 6,000 to 7,000 HIV infected women gave birth. Infected women can pass on HIV to their infants (called perinatal HIV transmission) during pregnancy, during labor and delivery, or after delivery through breastfeeding.³

During the early 1990s, before preventive medication was available to prevent HIV transmission from an infected pregnant woman to her infant, an estimated 1,000 to 2,000 infants were born with HIV infection each year and the risk for mother-to-child transmission ranged from 16% to 25%.³ Widespread universal screening and perinatal use of combination antenatal antiretroviral drugs and/or zidovudine combined with cesarean section sharply reduced transmission risk and thus the number of perinatally acquired HIV infections.³ By 2001, the perinatal transmission rate was reduced to less than 2%.³

However, despite important screening and treatment advances, perinatal HIV transmission continues to occur; the CDC estimates that each year in the United

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

<p>Condition/Disease Risk Factors</p>	<p>States 280 to 370 infants are born with HIV.³ Most exposed infants are born to women who were not tested for HIV prenatally or whose test results were unknown at the time of delivery.³</p> <p>Risk factors for perinatal HIV transmission include immunologically or clinically advanced HIV disease in the woman, a high plasma viral load, preterm delivery, injection drug use during pregnancy, and breastfeeding. The risk of perinatal transmission also increases with protracted labor after the rupture of membranes, maternal infection with a secondary STI, and the use of certain obstetrical procedures.³</p>
<p>Value of Prevention</p>	
<p>Economic Burden of Condition/Disease</p>	<p>Analysis of the KIDS Inpatient Database of the Healthcare Cost and Utilization Project (HCUP) estimated that there were 4,107 hospitalizations among HIV-infected children in the United States in 2000, which accounted for approximately \$100 million in hospital charges and more than 30,000 hospital days.⁴</p> <p>The estimated <i>lifetime</i> health care related cost of a pediatric HIV infection is estimated to range between \$100,000 and \$117,000 (in year 1994 dollars). The total costs depends on how rapidly an infant’s HIV progresses to AIDS and the length of his or her life.⁵</p>
<p>Workplace Burden of Condition/Disease</p>	<p>Not Provided</p>
<p>Economic Benefit of Preventive Intervention</p>	<p>The economic benefit of the preventive intervention includes the value of life years saved plus savings that accrue by avoiding the lifetime cost of managing an HIV infection.</p>
<p>Estimated Cost of Preventive Intervention</p>	<p>The cost of screening, testing, and treating HIV varies significantly, depending on where the test is administered, whether counseling is also provided, and what treatment protocol is followed. In 2004, the private-sector cost of HIV screening averaged \$29 (range \$4 to \$90); the cost of counseling averaged \$39 (range \$0-to-\$129).⁶</p>
<p>Estimated Cost of Treatment</p>	<p>The average wholesale price (AWP) for a 1-month supply of oral zidovudine (ZDV) tablets is \$219.02 (generic) or \$410.54 (brand – Retrovir®).⁷ The AWP for 6 weeks worth of zidovudine syrup — the recommended treatment for exposed infants — is \$48.13 (generic) or \$54.73 (brand – Retrovir®). Retrovir® treatment for HIV-positive women during labor/delivery is \$246.71 (cost varies depending on dose, which is based on the woman’s weight).⁷</p>
<p>Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention</p>	<p>Researchers studied the costs associated with screening and treating HIV/AIDS in pregnant women and found that universal screening can be cost-saving in this population. For example, compared to no screening, a universal screening program targeting pregnant women would save an estimated \$3.69 million dollars and prevent 64.6 cases of pediatric HIV infection for every 100,000 pregnant women screened.⁸</p>

Preventive Intervention Information

<p>Preventive Intervention: Purpose of Screening, Counseling, and Preventive Medication</p>	<p>The purpose of screening is to identify infected women early in the course of pregnancy. Early identification and the administration of preventive medication can reduce perinatal transmission rates to less than 2%.³ Counseling services are required to educate women on the benefits and risks of screening, risk reduction strategies, and, for those who screen positive, treatment options.</p>
<p>Benefits and Risks of Intervention</p>	<p>The risks associated with screening for HIV include the potential negative consequences of HIV infection such as discrimination and stigmatization, loss of relationships, domestic violence, and adverse psychological reactions such as depression or anxiety. The benefit of identification and early treatment — both necessary to prevent perinatal HIV transmission — outweigh the risks and costs associated with screening. Further, many of the aforementioned risks can be reduced through appropriate education and counseling.³</p>
<p>Initiation, Cessation, and Interval of Screening</p>	<p>HIV screening should occur as early as possible during pregnancy so that informed therapeutic decisions can be made and treatment can begin early. For women at high risk of HIV infection (e.g., women who have a history of STIs, women who exchange sex for money or drugs, women who have multiple sex partners during pregnancy, and women who use illicit drugs during pregnancy) should be re-tested during the third trimester (at or before 36 weeks' gestation).</p> <p>Women who are admitted for labor and delivery who have not been screened for HIV or whose HIV status is unknown should be tested immediately so that timely prophylactic treatment can be initiated if appropriate. In such cases, rapid testing or the expedited return of standard testing results is recommended. After delivery, the standard confirmatory testing should be completed.²</p>
<p>Counseling</p>	<p>Counseling should be provided before and after screening, as medically indicated.</p>
<p>Preventive Medication</p>	<p>Preventive medication should be provided, as medically indicated, to prevent perinatal transmission.</p>
<p>Intervention Process: Screening</p>	<p>Screening for HIV should be conducted with an Food and Drug Administration (FDA)-licensed enzyme immunoassay (EIA). If positive, the EIA should be followed by a confirmatory test with an FDA-licensed supplemental test such as the Western blot test. If a woman is being screened for the first-time during labor and delivery, a rapid assay test should be used in place of the EIA. A rapid test can provide a definitive negative result and a preliminary positive result, thus identifying women who could benefit from antiretroviral treatment and a cesarean delivery, and identifying infants who could benefit from antiretroviral prophylactic treatment. Rapid tests should be confirmed by a supplemental test, but, due to time constraints, suspected HIV positive women may be offered treatment before the results of the supplemental test are received. Only one FDA-approved rapid HIV test is currently available in the United States, the Abbott</p>

Counseling

Murex Single Use Diagnostic System HIV-1 test. Other tests are pending approval.²

All pregnant women should receive counseling and educational information on HIV and HIV screening before they are screened.² Pregnant women who have behaviors that place them at high risk for acquiring HIV infection (e.g., multiple sex partners, history of STIs, substance abuse, etc) should be referred to an HIV risk-reduction service (e.g., HIV centers with personnel trained in HIV counseling, drug treatment centers, etc).¹ HIV-infected pregnant women should receive HIV prevention counseling. This counseling should include discussion of the risk for perinatal HIV transmission, ways to reduce this risk, and the prognosis for infants who become infected. HIV-infected pregnant women should be counseled regarding antiretroviral therapy during pregnancy to improve their health and prevent perinatal transmission.³

Preventive Medication

The primary strategy to prevent perinatal transmission (in addition to avoidance of breastfeeding) is antiretroviral chemoprophylaxis using zidovudine (ZDV), now often part of a combined antiretroviral therapy regimen that reduces viral load as low as possible near the time of delivery. ZDV should be administered orally to the mother during the second and third trimesters of pregnancy; intravenous administration of ZDV should be given to the woman during labor and delivery. Infants born to HIV-positive women should be given ZDV during the first 6 weeks of life.³

Treatment Information

Health benefits should include provisions for ongoing treatment for HIV-positive women and their infants.

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Evidence-Based Research:

U.S. Preventive Services Task Force (USPSTF)

Strength of Evidence: A (Strongly Recommended/Good Evidence)

- The USPSTF found good evidence to recommend that clinicians screen all pregnant women for HIV.¹

Recommended Guidance:

The Centers for Disease Control and Prevention (CDC)

Strength of Evidence: Not Specified

- The CDC recommends that clinicians screen all pregnant women for HIV.²
- The CDC recommends that all pregnant women receive counseling and educational information on HIV and HIV screening before they are screened/tested.²
- The CDC recommends that zidovudine be administered orally to HIV-positive pregnant women during the second and third trimesters of pregnancy and

intravenously during labor and delivery. The CDC also recommends that oral ZDV be administered to exposed infant during the first 6 weeks of life.²

These recommendations are supported by the:

- U.S. Public Health Service

Authored by:

Lentine D, Campbell KP. Human immunodeficiency virus evidence-statement: screening, counseling, and preventive medication. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Human Immunodeficiency Virus (HIV) (Screening)

1. U.S. Preventive Services Task Force. Screening for Human Immunodeficiency Virus Infection. Rockville, MD: Agency for Healthcare Research and Quality; July 2005. Available from: <http://www.ahrq.gov/clinic/uspstf/uspshivi.htm>.
2. Centers for Disease Control and Prevention. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health care settings. MMWR. 2006;55(RR14):1-17.
3. Centers for Disease Control and Prevention. Revised recommendations for HIV screening of pregnant women. MMWR 2001; 50(RR19): 59-86.
4. Kourtis AP, Paramsothy P, Posner SF, Meikle SF, Jamieson DJ. National estimates of hospital use by children with HIV infection in the United States: analysis of data from the 2000 KIDS Inpatient database. Pediatrics 2006; 118:167-173.
5. Mauskopf JA, Paul JE, Wichman DS, White AD, Tilson HH. Economic impact of treatment of HIV-positive pregnant women and their newborns with zidovudine JAMA 1996; 276: 132-138.
6. Thomson Medstat. Marketscan. 2004.
7. Fleming T. 2006 Redbook: *Pharmacy's Fundamental Reference*. Thomson PDR; Rev Ed edition. May 2006.
8. Immergluck LC, Cull WL, Schwatz A, Elstein AS. Cost-effectiveness of universal compared with voluntary screening for human immunodeficiency virus among pregnant women in Chicago. Pediatrics 2000; 105(4): E54.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Influenza (Immunization)

Clinical Preventive Service Recommendations

U.S. Preventive Services Task Force Recommendation

Not Applicable – The U.S. Preventive Services Task Force defers to the Advisory Committee on Immunization Practices and the CDC on recommendations surrounding immunization.

CDC Recommendation

The Advisory Committee on Immunization Practices (ACIP) recommends that all women who are pregnant during the influenza season (October to mid-May) be vaccinated with trivalent inactivated influenza vaccine.¹ Because this population is considered at risk for influenza-related complications, it should be given priority access to the vaccine in case of shortage.²

Note: Live attenuated influenza vaccine (LAIV) is contraindicated during pregnancy. Because the intranasal vaccine spray contains live virus, it should not be administered to pregnant women.¹

A summary of guidelines for the immunization of pregnant women can be found online (www.cdc.gov/nip/publications/peg_guide.htm).

Evidence Rating:

Expert Consensus

Other Recommended Guidance

The American Academy of Family Physicians (AAFP) and the American College of Obstetricians and Gynecologists (ACOG) concur with the ACIP recommendations.

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- Advisory Committee on Immunization Practices (ACIP)
- American Academy of Family Physicians (AAFP)
- American College of Obstetricians and Gynecologists (ACOG)
- Centers for Disease Control and Prevention (CDC)
- Peer-reviewed research

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

Epidemiology of Condition/Disease

Influenza is a viral respiratory tract infection that occurs during the winter months in temperate climates. Uncomplicated cases of the illness usually resolve within several days to weeks and include fever, cough, sore throat, headache, muscle aches, and tiredness.

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Influenza infection can exacerbate other underlying medical conditions and can lead to hospitalization or even death.¹ Throughout the 1990s in the United States, influenza infection was associated with an average of 36,000 deaths and over 200,000 hospitalizations per year.³⁻⁴

Pregnant women are considered to be at increased risk for complications from influenza infection. Healthy pregnant women in their third trimester are hospitalized for influenza at rates as high as 250 per 100,000 reported cases.¹ Rates are higher among pregnant women with other underlying medical conditions. Researchers estimate that an average of 1 to 2 hospitalizations can be prevented for every 1,000 pregnant women vaccinated.⁵

Despite the seriousness of influenza infection and the fact that the inactivated influenza vaccine is safe and effective, only 12% to 13% of pregnant woman are inoculated against influenza.^{1,6}

Condition/Disease Risk Factors

All pregnant women who are not immunized against influenza are at risk of infection.

Value of Prevention

Economic Burden of Condition/Disease

The overall national economic burden of influenza-attributable illness for adults aged 18 to 64 years is \$4.6 billion in direct medical costs and an additional \$5.6 billion in lost productivity resulting from 17 million missed workdays.⁷ Furthermore, adult hospitalizations from influenza-attributable illness result in 3.1 billion dollars per year in direct hospitalization costs (in year 2003 dollars).⁷

Workplace Burden of Condition/Disease

Influenza-related complications during pregnancy increase medical care costs and productivity losses triggered by lost work days. An infected employee may also spread infection to other employees or family members.

Economic Benefit of Preventive Intervention

Although no study specifically examined the case for pregnant women, studies of the economic benefit of immunization in working adults commonly include reduced hospitalizations, physician visits, and lost workdays; and an increase in quality-adjusted days due to symptom relief from influenza-like illness.⁸⁻⁹

Estimated Cost of Preventive Intervention

In 2004, the private-sector cost of an adult influenza vaccine averaged \$13 and approximately 95% of all paid claims fell within the range of \$3 to \$24 per vaccine.¹⁰ Vaccine administration averaged \$10 per dose and approximately 95% of all paid claims fell within range of \$0 to \$20 per dose.¹⁰

Estimated Cost of Treatment

Zanamivir and oseltamivir, the antiviral medications recommended for treatment of influenza, have not been studied in pregnant women. Because of the unknown effects of these drugs, they should only be used during pregnancy if the potential benefit justifies the potential risk to the embryo or fetus.¹

Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention

A review of several economic studies shows that vaccination of healthy working adults is cost-effective and may result in cost-savings in some years.¹¹ Though no specific study was conducted with reference to pregnant women, economic results are likely to be at least as favorable for this group since pregnant women are at high risk for influenza-related complications.

Preventive Intervention Information

Preventive Intervention: Purpose of Immunization

Immunization against influenza reduces the chance that a pregnant woman will contract influenza thereby reducing her chance of experiencing influenza-related illness, hospitalization, and associated costs.

Benefits and Risks of Intervention

There are many benefits to influenza vaccination. First, when a pregnant woman is immunized during pregnancy, antibodies can be passed to her fetus and can also be passed in breast milk.⁶ Because children under 6 months are at high risk of complications from influenza, but cannot be vaccinated themselves, the vaccination of persons who may transmit influenza to infants is recommended.¹ That includes parents, siblings, and other caregivers. Second, healthy, working adults who receive influenza shots (in a year when the vaccine is well matched to the circulating influenza viruses) experience significantly fewer days of influenza-like illness (ILI), make fewer doctor visits for such illnesses, and take fewer days off from work due to ILIs, compared to unvaccinated workers.⁸⁻⁹

Influenza vaccination with inactivated virus is considered to be safe for both pregnant women and their fetuses. Two studies with a total of over 2,250 pregnant women found no adverse events after vaccination, regardless of when during pregnancy the vaccine is given.^{6,12}

Initiation, Cessation, and Interval of Immunization

No studies have been conducted on the safety of LAIV in pregnant women. All women who will be pregnant during the influenza season (October to mid-May) should be given the inactivated influenza vaccine at some point during pregnancy. This single-dose vaccine may be administered during any trimester.¹ The ideal time to vaccinate is October and November, although vaccination in December or even later can still be beneficial since influenza activity peaks in February or later in most years.¹

It is important to note that a woman should receive an influenza vaccination with each pregnancy to protect herself and her fetus. Immunity gained from the influenza vaccine does not carry from year to year. Influenza vaccination is also recommended for all household contacts of children less than 5 years of age and particularly for households with children less than 6 months of age since infants are at very high risk of influenza complications but are too young to receive the influenza vaccine.¹

Intervention Process

Inactivated influenza vaccine is administered via intra-muscular injection. Injections can be administered in various settings including doctor office visits or at the worksite.

Treatment Information

Influenza-specific antiviral medications are available, but no safety studies have been conducted in pregnant women. Because of the unknown effects of these

drugs on fetuses, they should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.¹

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Recommended Guidance:

Advisory Committee on Immunization Practices (ACIP)

Strength of Evidence: Expert Consensus

- The ACIP recommends vaccinating all women who are/will be pregnant during the influenza season (October to mid-May) with trivalent inactivated influenza vaccine.¹

This recommendation is supported by the:

- American Academy of Family Physicians (AAFP)
- American College of Obstetricians and Gynecologists (ACOG)
- U.S. Preventive Services Task Force (USPSTF)

Authored by:

Lindley MC, Bhatt A. Influenza evidence-statement: immunization. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Influenza (Immunization)

1. Centers for Disease Control and Prevention. Prevention and control of influenza: Mortality associated with recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR 2006; 55(RR-10):1-42.
2. Centers for Disease Control and Prevention. Updated interim influenza vaccination recommendations: 2004-2005 influenza season. MMWR 2004; 53(50):1183-4.
3. Thompson WW, Shay DK, Weintraub E, Brammer L, Bridges CB, Cox NJ, et al. Influenza-associated hospitalizations in the United States. JAMA 2004; 292(11):1333-40.
4. Thompson WW, Shay DK, Weintraub E, Brammer L, Cox N, Anderson LJ, et al. Mortality associated with respiratory syncytial virus in the United States. JAMA 2003; 289(2):179-86.
5. Neuzil KM, Reed GW, Mitchel EF, Simonsen L, Griffin MR. Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women. Am J Epidemiol 1998;148:1094-102.
6. Munoz FM, Greisinger AJ, Wehmanen OA, Mouzoon ME, Hoyle JC, Smith FA, et al. Safety of influenza vaccination during pregnancy. Am J Obstet Gynecol 2005; 192:1098-1106.
7. Molinari N, Ortega-Sanchez I, Messonnier M, Thompson W, Wortley P, Weintraub E, et al. National expenditures on influenza: Estimating medical and indirect costs. Draft manuscript.

8. Rothberg MB, Rose DN. Vaccination versus treatment of influenza in working adults: a cost-effectiveness analysis. *Am J Med* 2005;118:68-77.
9. Bridges CB, Thompson WW, Meltzer MI, Reeve GR, Talamonti WJ, Cox NJ, et al. Effectiveness and cost benefit of influenza vaccination of healthy working adults: A randomized controlled trial. *JAMA* 2000; 284 (13) 1655-63.
10. Thomson Medstat. Marketscan. 2004.
11. Lee PY, Matchar DB, Clements DA, Huber J, Hamilton JD, Peterson ED, et al. Economic analysis of influenza vaccination and antiviral treatment for healthy working adults. *Ann Intern Med* 2002;137:225-231.
12. Heinonen OP, Shapiro S, Monson RR, Hartz SC, Rosenberg L, Slone D, et al. Immunization during pregnancy against poliomyelitis and influenza in relation to childhood malignancy. *Int J Epidemiol* 1973;2:229-35.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Preeclampsia (Screening)

Clinical Preventive Service Recommendations

U.S. Preventive Services Task Force Recommendation

In 1996, the U.S. Preventive Services Task Force (USPSTF) recommended that clinicians screen all pregnant women for preeclampsia by taking a blood pressure measurement at the first prenatal visit and periodically throughout the pregnancy.¹

Given the availability of new evidence, the USPSTF decided to update its 1996 recommendation. This work is in a queue to be scheduled for review.

**Other Recommended Guidance
American College of Obstetricians and Gynecologists (ACOG)**

The American College of Obstetricians and Gynecologists (ACOG) recommends that clinicians monitor blood pressure at the first prenatal visit, every 4 weeks until 28 weeks' gestation, every 2 to 3 weeks until 36 weeks' gestation, and weekly thereafter.²

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- American Academy of Pediatrics (AAP)
- American College of Obstetricians and Gynecologists (ACOG)
- Agency for Healthcare Quality and Research (AHRQ)
- National Vital Statistics
- Peer-reviewed research
- Preeclampsia Foundation
- World Health Organization (WHO)

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

Epidemiology of Condition/Disease

Preeclampsia occurs when a woman with normal blood pressure experiences acute hypertension (140 mm Hg or higher systolic or 90 mm Hg or higher diastolic) or an increase blood pressure (an increase of ≥ 30 mm Hg in systolic blood pressure or ≥ 15 mm Hg in diastolic blood pressure) after 20 weeks' of gestation.³ While more common towards the end of pregnancy, preeclampsia can appear as early as 20 weeks' gestation. Symptoms of the condition include the presence of protein in the urine, swollen extremities, sudden weight gain, headaches, and changes in vision. However, many women report no symptoms.⁴

Preeclampsia affects 5% to 7% of all pregnancies.⁵ Women with preeclampsia are at an increased risk for placental abruption, acute renal failure, cerebral hemorrhage, disseminated intravascular coagulation, pulmonary edema,

circulatory collapse, and progression to full-blown eclampsia, an extremely serious condition characterized by maternal seizure activity, coma, and death. Preeclampsia can also cause severe problems for the fetus such as delayed growth, low birth weight, and the risk of premature birth.⁶

Preeclampsia/eclampsia is the third leading cause of maternal death worldwide¹ and is responsible for 18% of all maternal deaths in the United States.⁷ In the United States during 2002, preeclampsia/eclampsia caused:

- Maternal death in 56 out of every 100,000 live birth.⁸
- Neonatal death in 71 out of every 100,000 live births.⁹

Condition/Disease Risk Factors

Research indicates that women that are pregnant for the first time, women with multiple gestations, molar pregnancy or fetal hydrops, chronic hypertension or diabetes, and those with a personal or family history of eclampsia or preeclampsia are at increased risk for preeclampsia and eclampsia. Overweight and obese women are also at increased risk of preeclampsia.¹⁰

Value of Prevention

Economic Burden of Condition/Disease

According to the Hospital Cost Utilization Project (HCUP) Nationwide Inpatient Survey (NIS), spending on hypertension during pregnancy totaled nearly \$2.3 billion in the United States in 2003.¹¹ During that year, approximately 204,868 pregnant women were admitted to the hospital for hypertension, staying an average of 3.5 days. The average per-person charge for such hospital admissions totaled \$11,208.¹¹ Few data are available about the incremental costs for infants because of preeclampsia or the value of years of life lost due to preeclampsia and its complications, including maternal or neonatal deaths.

Workplace Burden of Condition/Disease

The medical care costs of maternal and neonatal complications due to preeclampsia impose an additional financial burden on employer-sponsored health insurance plans.

Pregnancy-related complications affecting their own health or the health of their children may also require working mothers to take significant time off from work, resulting in additional productivity losses at the workplace.

Economic Benefit of Preventive Intervention

Screening, which involves minimal cost, and early treatment can minimize and prevent otherwise costly medical conditions. For example, although there is a lack of recent research, there is acceptance of the finding that women with preeclampsia or eclampsia stay in the hospital substantially longer than do normotensive women (i.e., women having blood pressure typical of the group to which they belong), regardless of their method of delivery. The longer hospital stays and higher rates of cesarean section delivery among women with preeclampsia and eclampsia lead to more costly obstetric medical claims. For example, 217,700 excess hospital days for delivery admissions were attributable to preeclampsia and eclampsia in 1986.¹⁰

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Estimated Cost of Preventive Intervention	Blood pressure screening is a standard procedure at each office visit and involves minimal cost. Screening for preeclampsia is conducted as a part of routine prenatal care and does not require a separate visit.
Estimated Cost of Treatment	Not Provided
Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention	Complete cost-effectiveness analyses are not available.

Preventive Intervention Information

Preventive Intervention: Purpose of Screening	Screening allows clinicians to identify affected women early in the course of their pregnancies and begin treatment, thereby reducing the risk of complications for affected women <i>and</i> their infants.
Benefits and Risks of Intervention	Regular blood pressure screening during pregnancy is used to detect preeclampsia. Early detection of hypertension permits continuous monitoring and early intervention (e.g., bed rest, medications, early delivery). Although studies have not shown that early identification of hypertension and preeclampsia is associated with better outcomes, clinical experience suggests that to be the case. As such, the medical community considers regular blood pressure screening to be in the best interest of both mother and fetus. At the same time, blood pressure screening is simple, inexpensive, and acceptable to patients.
Initiation, Cessation, and Interval of Screening	ACOG recommends that clinicians monitor blood pressure at the first prenatal visit, every 4 weeks until 28 weeks' gestation, every 2 to 3 weeks until 36 weeks' gestation, and weekly thereafter.
Intervention Process	Screening for preeclampsia can be conducted via conventional measures (arm cuff and a mercury calibrated aneroid or digital sphygmomanometer) or ambulatory blood pressure monitoring. Before a diagnosis of preeclampsia can be made, the patient must have two elevated blood pressure readings (defined as $\geq 140/90$ mmHg) taken at least 6 hours apart. Preeclampsia may also be diagnosed if a woman has undergone an increase of 30 mmHg or more in systolic pressure or 15 mmHg or more in diastolic pressure since becoming pregnant. Clinicians should be aware that overweight and obese patients may need to be monitored more closely, especially if they have preexisting hypertension, due to their increased risk of preeclampsia. ²
Treatment Information	Treatment methods for preeclampsia include bed rest, medication, and delivery. Health benefits should include provisions for follow-up and treatment services.

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Recommended Guidance:

The American College of Obstetricians and Gynecologists (ACOG)
Strength of Evidence: Not Specified

- The American College of Obstetricians and Gynecologists recommends screening pregnant women for preeclampsia by monitoring blood pressure at the first prenatal visit, every 4 weeks until 28 weeks' gestation, every 2 to 3 weeks until 36 weeks' gestation, and weekly thereafter.²

Authored by:

Campbell KP, Chattopadhyay S. Preeclampsia evidence-statement: screening. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Preeclampsia (Screening)

1. U.S. Preventive Service Task Force. Prenatal Disorders: Screening for preeclampsia. *Guide to Clinical Preventive Services*. 2nd ed. Washington, DC: U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion; 1996.
2. American Academy of Pediatrics and American College of Obstetricians and Gynecologists. *Guidelines for Perinatal Care*. 3rd ed. Washington, DC: American College of Obstetricians and Gynecologists.
3. Werner L. Diagnosis and management of pre-eclampsia. *Am Fam Physician* 2004 Dec 15;70(12):2317-24.
4. Conde-Agudelo A, Villar J, Lindheimer M. World Health Organization Systemic Review of Screening Tests for Preeclampsia. *Obstet Gynecol* 104(6):1367-91.
5. Wagner L. Diagnosis and management of preeclampsia. *Am Fam Phys* 2004; 70:2317-24.
6. American Academy of Family Physicians. Preeclampsia. Kansas City, MO: American Academy of Family Physicians; 2006.
7. Preeclampsia Foundation. [cited 2006 Feb 28]. Available from: <http://www.preeclampsia.org/statistics.asp>.
8. National Vital Statistics 2004; 53(5): 97.
9. American College of Obstetricians & Gynecologists. Committee opinion: Obesity in pregnancy. *Obstet Gynecol* 2005; 106(3): 671-675.
10. Saftlas AF, Olson DR, Franks AL, Atrash HK, Pokras R. Epidemiology of preeclampsia and eclampsia in the United States, 1979-1986. *Am J Obstet Gynecol* 1990; 163:460-465.
11. Agency for Healthcare Research and Quality. Health Care Utilization Project Data Source. [cited 2005 Jul 12]. Available from: <http://hcup.ahrq.gov>.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Prenatal Diagnosis of Chromosomal Abnormalities and Neural Tube Defects (Screening and Testing)

Clinical Preventive Service Recommendations

U.S. Preventive Services Task Force Recommendations

In 1996, the U.S. Preventive Services Task Force (USPSTF) recommended that clinicians offer serum multiple marker screening to all pregnant women at low risk for Down syndrome and amniocentesis or chorionic villus sampling (CVS) testing to all pregnant women at high risk for Down syndrome.

This recommendation is considered out of date and has been archived.

In 1996, the U.S. Preventive Services Task Force recommended that clinicians offer neural tube defect screening to all pregnant women who have access to adequate prenatal care, counseling, and follow-up services.

Screening for neural tube defects during pregnancy is currently considered part of standard prenatal care. The USPSTF knows of no reason at the present time to update its 1996 recommendation.

Recommended Guidance

Offering pregnant women screening and testing (prenatal diagnosis) to detect chromosomal abnormalities is standard clinical practice. All pregnant women are candidates for screening services. Most clinical guidelines recommend that women age 35 and older (and those who have equivalent risk) be offered testing in place of, or in addition to, screening.¹

Offering all pregnant women (irrespective of age) screening services to detect neural tube defects (NTDs) and offering testing services (prenatal diagnosis) to women at elevated risk is standard clinical practice.²

There are several screening and prenatal diagnosis methods available. There is no single current authoritative source on which of the various methods provides the best outcome. Therefore, it is recommended that employers provide healthcare coverage for all screening and testing methods, including — but not limited to — the following:

- All types of maternal serum screening tests
- Amniocentesis
- Chorionic villus sampling (CVS)
- Ultrasound

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- American Academy of Obstetricians and Gynecologists (ACOG)
- Centers for Disease Control and Prevention (CDC)
- March of Dimes
- Peer-reviewed research

- U.S. Preventive Services Task Force (USPSTF)
- U.S. Public Health Service

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

Epidemiology of Condition/Disease

Chromosomal Abnormalities

Down syndrome (trisomy 21) is the most common chromosomal abnormality in the United States, affecting 1 in every 800 to 1,000 live-born babies.³ Children with Down syndrome have physical abnormalities including heart defects, short stature, characteristic facial abnormalities, and varying degrees of mental retardation. Although Down syndrome and its complications cannot be cured, early intervention programs that begin in infancy may help those living with Down syndrome achieve certain developmental milestones in a more timely fashion.

Life expectancy among individuals with Down syndrome has increased substantially over the past three decades. In 1983, the average life expectancy for an individual with Down syndrome was 25 years; by 1997, life expectancy had risen to 49 years.⁴ However, life expectancy gains have not been equal among individuals with Down syndrome, and large survival disparities have been noted between white and black infants.⁴

Other chromosomal abnormalities include trisomy 13, trisomy 18, and sex-chromosome abnormalities. Trisomy 13 and 18 are very severe and usually cause fetal or infant death.⁵ Sex-chromosome abnormalities are the most mild form of chromosomal abnormality and occur in approximately 1 in every 2,000 to 2,500 female infants and 1 in every 600 to 800 male infants.⁵ These abnormalities lead to sexual development problems (including infertility) and, sometimes, behavioral or learning problems.⁵

Neural Tube Defects (NTDs)

Spina bifida and anencephaly are common and permanent neural tube defects (NTDs) which result from the failure of the neural cord to properly fuse. Each year in the United States, approximately 3,000 pregnancies are affected by NTDs and approximately 2,200 infants are born with neural tube defects.⁶ Many NTD-affected pregnancies do not result in a live birth since they are electively or spontaneously aborted (commonly referred to as a miscarriage) or result in fetal death or stillbirth.

Anencephaly is fatal; all affected infants die shortly after birth. Approximately 92% of infants born with spina bifida survive with varying degrees of disability. Debilitating medical complications associated with spina bifida include paralysis and bowel and bladder incontinence.⁷

**Condition/Disease
Risk Factors**

Chromosomal Abnormalities

The risk of Down syndrome increases dramatically with advancing maternal age. For example, the risk of delivering a baby with Down syndrome is about 1 in 1,250 for a 25-year-old woman, 1 in 1,000 for a 30-year-old woman, 1 in 400 for a 35-year-old woman, and 1 in 100 for a 40-year-old woman.⁸ Risk factors other than age are poorly understood, and 97% of Down syndrome pregnancies occur in families with no previous history of the syndrome.¹

As with Down syndrome, the risk of trisomy 13 and trisomy 18 increases with advancing maternal age; women age 35 or older are most at risk for these conditions.⁵

Neural Tube Defects (NTDs)

Inadequate folic acid consumption is the major risk factor for NTDs. Consuming the recommended daily amount of folic acid (0.4-0.8mg) can reduce a woman's chance of having a NTD-affected pregnancy by 40% to 80%.⁹ However, only 33% of childbearing-age women report taking vitamins that contain folic acid.⁹

Spina bifida, the most common type of NTD, occurs most frequently among Hispanics and European whites and least frequently among African-Americans and Asians. Low socioeconomic status has been reported to be a risk factor for NTDs.¹⁰

Value of Prevention

**Economic Burden of
Condition/Disease**

The economic impact of chromosomal abnormalities and NTDs is substantial.

The *lifetime* cost of live-born infants with Down syndrome includes the incremental medical, developmental, and special education costs as well as lost productivity and earnings due to death and disability. The total *lifetime* cost for all cases of Down syndrome (based on 1988 cross-sectional data) was estimated to exceed \$1.8 billion in year 1992 dollars.¹¹

The total lifetime cost for a child born with spina bifida is estimated at \$636,000 (in year 2002 dollars).¹² Applying that cost to the prevalence rate for spina bifida from National Birth Defect Prevention Network data¹³ (4 million live births each year) yields an estimated \$814 million in *lifetime* costs for each cohort.¹² Costs associated with NTDs are shared by parents, employers, and communities.

**Workplace Burden of
Condition/Disease**

Lost productivity attributable to premature morbidity and mortality due to Down syndrome was estimated to total \$1.18 billion in 1992 dollars, comprising nearly 64% of total *lifetime* cost for all cases of Down syndrome.¹¹

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Apart from the incremental excess cost of medical care for affected children, employers face productivity losses of employees who must care for affected children. The present value of lost workdays for a typical caregiver was estimated to be \$252,000 in year 1993 dollars.¹⁴

<p>Economic Benefit of Preventive Intervention</p>	<p>The economic benefit of prenatal screening is defined as the averted cost from preventing the birth of a child with a chromosomal abnormality or NTD. These averted costs include savings from the direct costs of medical, developmental, and special education services as well as the indirect costs associated with lost productivity due to morbidity and mortality.¹²</p>
<p>Estimated Cost of Preventive Intervention</p>	<p>In 2004, the private-sector cost of⁵:</p> <ul style="list-style-type: none"> • Screening for NTDs via ultrasound averaged \$155; approximately 95% of all paid claims fell within the range of \$41 to \$352 per ultrasound. • Screening for chromosomal abnormalities averaged \$56; approximately 95% of all paid claims fell within the range of \$0 to \$158 per test. The full range of tests totaled, on average, \$8,255. • Genetic testing (including complete gene sequence analysis) averaged \$408 per test; approximately 95% of all paid claims fell within the range of \$0 to \$1,852. The full range of tests totaled, on average, \$5,013. • Genetic counseling averaged \$39; approximately 95% of all paid claims fell within the range of \$1 to \$129. • An amniocentesis averaged \$296. • Chorionic villus sampling averaged \$355.
<p>Estimated Cost of Treatment</p>	<p>When birth defects are detected, the cost of treatment may include costs associated with genetic counseling and termination.</p>
<p>Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention</p>	<p>California is one of two states with a public prenatal screening program, which is supported by fees paid by prenatal care providers and insurers. In 1998, the fee paid by payers was \$105, which covered the cost of the State's expanded screening program for chromosomal abnormalities and NTDs. The fee covered both the initial screening and reimbursements for genetic counseling, ultrasound, amniocentesis, and genetic testing.¹⁶ The California prenatal screening program estimated a benefit-to-cost ratio of 2.7, meaning that, on average, each \$1 spent on the program would be offset by \$2.70 in economic benefits calculated using a discount rate of 5% per year.¹⁶</p>

Preventive Intervention Information

Preventive Intervention: Purpose of Screening and Testing

The major benefit of screening for and diagnosing chromosomal abnormalities and NTDs is the opportunity to inform women and their partners of the likelihood that they are carrying an affected fetus. The usefulness of this information depends on the values and preferences of the parents. With appropriate information and counseling, parents can decide whether to terminate or continue a pregnancy. Parents who decide to continue the pregnancy have an opportunity to prepare emotionally and financially for the birth of their child.

Benefits and Risks of Intervention

The knowledge gained by screening can help women and their families make an informed decision as to whether or not to undergo prenatal diagnosis (testing). In turn, prenatal diagnosis can help women and their families make an informed decision about whether to continue or terminate the pregnancy. Prenatal diagnosis of a chromosomal abnormality or NTD may preclude trauma associated with the unexpected delivery of an affected infant.¹ Furthermore, information gained from prenatal diagnosis may help providers better prepare for the delivery of an affected infant.^{1,17} For example, some studies show reduced severity of paralysis in infants with spina bifida delivered by cesarean section compared with those having vaginal delivery.¹⁷

The risks of screening and prenatal diagnosis depend on the method used. The major risk associated with screening is the chance of a false-positive result, which can lead to unnecessary anxiety.¹⁶ Thus, confirmatory testing (prenatal diagnosis) is considered to be essential. Risks of prenatal diagnosis include the risks associated with amniocentesis or CVS (in very rare cases the fetus can be injured, suffer an infection, or miscarry), the psychological effects for the woman and her partner of a positive result, and the risks associated with abortion.

Many women who test positive for an NTD-affected pregnancy choose to terminate their pregnancy. Screening thus leads to the prevention of the births of affected infants. In fact, some studies have shown that the availability of screening, testing, and the opportunity for termination reduces the number of infants born with NTDs by up to 70%.¹⁶ However, termination rates vary depending on the ethnic and religious backgrounds of the families and many other factors. In one study of an ethnically diverse population in California, termination rates for spina bifida averaged 67%.¹⁶ It is important to remember that many women who choose to carry the pregnancy to term will have either a stillborn fetus or an infant who will die in the first few hours or days after birth.

Initiation, Cessation, and Interval of Screening and Testing

The screening and testing process is defined by several factors: the type of test utilized, whether there is need for follow-up testing, and the risk-status of the pregnant woman. Timing is left to the discretion of the physician and should be determined by the pregnant woman's needs and the stage of pregnancy when she began prenatal care.

Intervention Process

Several screening methods are used to determine risk for chromosomal abnormalities and NTDs. Most methods examine biological markers in maternal blood samples.

Down syndrome can be diagnosed prenatally by identifying an extra chromosome 21 through a cell sample. Fetal cell samples can be obtained through an amniocentesis, chorionic villus sampling (CVS), or cordocentesis.¹

Treatment Information

Health benefits should include provisions for follow-up services such as:

- Genetic counseling
- Termination *or* continuing prenatal care and labor and delivery.

Cures for chromosomal abnormalities and NTDs are not available, but various interventions can be used to improve the functioning or quality of life of those who are affected.

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Recommended Guidance:

Offering pregnant women screening and testing (prenatal diagnosis) to detect chromosomal abnormalities is standard clinical practice. All pregnant women are candidates for screening services. Most clinical guidelines recommend that women age 35 and older, (and those who have equivalent risk) be offered testing in place of, or in addition to, screening.²⁻³

Offering all pregnant women (irrespective of age) screening to detect neural tube defects (NTDs) and offering testing (prenatal diagnosis) to women at elevated risk is standard clinical practice.²⁻³

There are several screening and prenatal diagnosis methods available. There is no single current authoritative source on which of the various methods provides the best outcome. Therefore, it is recommended that employers provide healthcare coverage for all screening and testing methods, including — but not limited to — the following:

- All types of maternal serum screening tests
- Amniocentesis
- Chorionic villus sampling (CVS)
- Ultrasound

Authored by:

Campbell KP, Grosse S, Chattopadhyay S. Prenatal diagnosis of chromosomal abnormalities and neural tube defects evidence-statement: screening and testing. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Prenatal Diagnosis of Chromosomal Abnormalities and Neural Tube Defects (Screening)

1. American College of Obstetricians and Gynecologists. Prenatal diagnosis of fetal chromosomal abnormalities. Washington, DC: American College of Obstetricians and Gynecologists, 2001; 27.
2. American College of Obstetricians and Gynecologists. Neural tube defects. Clinical management guidelines for obstetrician-gynecologist. ACOG Practice Bulletin 2004; 44: 1-11.
3. The March of Dimes. Down syndrome fact sheet. The March of Dimes 2006; Available from: http://www.marchofdimes.com/professionals/681_1214.asp.
4. Rasmussen SA, Wong LY, Correa A, Gambrell D, Friedman JM. Survival in infants with Down syndrome, Metropolitan Atlanta, 1979-1998. *J Pediatr* 2006;148:806-812.
5. March of Dimes. Chromosomal Abnormalities. Quick reference fact sheet for professionals. [cited 2005 Jul 6]. Available from: http://www.marchofdimes.com/professionals/681_1209.asp.
6. Centers for Disease Control and Prevention. Spina bifida and anencephaly before and after folic acid mandate – United States, 1995-1996 and 1999-2000. *MMWR* 2004; 53(17): 362-365.
7. Centers for Disease Control and Prevention. Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. *MMWR* 1992; 41(RR14): 001.
8. March of Dimes. Chromosomal abnormalities. [cited 2005 July 6]. Available from: http://www.marchofdimes.com/professionals/681_1209.asp.
9. Centers for Disease Control and Prevention. Use of dietary supplements containing folic acid among women of childbearing age – United States, 2005. *MMWR* 54(38); 955-958. Available from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5438a4.htm>.
10. Wasserman CR, Shaw GM, Selvin S, Gould JB, Syme SL. Socioeconomic status, neighborhood social conditions, and neural tube defects. *Am J Public Health* 1998; 88(11): 1674-1680.
11. Centers for Disease Control and Prevention. Economic costs of birth defects and cerebral palsy – United States, 1992. *MMWR* 1995; 44(37): 694-649.
12. Grosse SD, Waitzman NJ, Romano PS, Mulinare J. Re-evaluating the benefits of folic acid fortification in the United States: Economic analysis, regulation, and public health. *Am J of Public Health* 2005; 95(11): 1917 - 1922.
13. Canfield MA, Collins JS, Botto LD, Williams LJ, Mai CT, Kirby RS, Pearson K, et al. Changes in the birth prevalence of selected birth defects after grain fortification with folic acid in the United States: findings from a multi-state population-based study. *Birth Defects Res A Clin Mol Teratol* 2005;73:679-689.
14. Kelly AE, Haddix AC, Scanlon KS, Helmick CG, Mulinare J. Cost-effectiveness of strategies to prevent neural tube defects. In: Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. *Cost-Effectiveness in Health and Medicine*. New York, Oxford: Oxford University Press; 1996:312–349.
15. Thomson Medstat. MarketScan. 2004.
16. Cunningham GC, Tompkinson DG. Cost and effectiveness of the California triple marker prenatal screening program. *Genet Med* 1999; 1(5): 199-206.
17. The March of Dimes. Maternal blood screening for Down syndrome and neural tube defects. March of Dimes 2006.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Rh (D) (Screening and Preventive Medication)

Clinical Preventive Service Recommendations

U.S. Preventive Services Task Force Recommendation

The U.S. Preventive Services Task Force (USPSTF) strongly recommends Rh (D) blood typing and antibody testing for all pregnant women during their first visit for pregnancy-related care.¹

The USPSTF also recommends repeated Rh (D) antibody testing for all unsensitized Rh (D)-negative women between 24 and 28 weeks' gestation, unless the biological father is known to be Rh (D)-negative.¹

Evidence Rating: A (Strongly Recommend/Good Evidence)

The USPSTF found good evidence that Rh (D) blood typing, anti-Rh (D) antibody testing, and intervention with Rh (D) immunoglobulin, as appropriate, prevents maternal sensitization and improves outcomes for newborns. The benefits substantially outweigh any potential harms.¹

B (Recommend/At Least Fair Evidence)

The USPSTF found fair evidence that repeated antibody testing for unsensitized Rh (D)-negative women (unless the father is also known to be Rh [D]-negative) and intervention with Rh (D) immunoglobulin, as appropriate, provides additional benefit over a single test at the first prenatal visit in preventing maternal sensitization and improving outcomes for newborns. The benefits of repeated testing substantially outweigh any potential harms.¹

The American Academy of Family Physicians (AAFP) concurs with the USPSTF.

Other Recommended Guidance American College of Obstetricians and Gynecologists (ACOG)

The American College of Obstetricians and Gynecologists (ACOG) concurs with the U.S. Preventive Service Task Force (USPSTF) recommendations, with the exception that ACOG strongly recommends that clinicians administer immunoglobulin to Rh (D)-negative pregnant women after undergoing invasive procedures such as chronic villus sampling or fetal blood sampling.²

ACOG further recommends that immunoglobulin be administered following a possible spontaneous or elective abortion, second or third trimester bleeding, external cephalic version, or abdominal trauma.²

Evidence Rating:

Expert Consensus

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- American Academy of Family Physicians (AAFP)
- American Academy of Pediatricians (AAP)
- The American College of Obstetricians and Gynecologists (ACOG)
- National Institutes of Health (NIH)
- U.S. Preventive Services Task Force (USPSTF)

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

Epidemiology of Condition/Disease

Rh (D) incompatibility refers to a condition that develops when a pregnant women with Rh-negative blood type carries a fetus with an Rh-positive blood type. In reaction to what is perceived to be a foreign substance, the woman's body makes antibodies that attack fetal red blood cells (isoimmunization). Since it takes time to build up antibodies, first pregnancies are typically not affected by Rh incompatibility. However, in subsequent pregnancies, Rh incompatibility may cause destruction of fetal red blood cells (hemolysis), which leads to anemia and an accumulation of bilirubin in the fetus's bloodstream (hyperbilirubinemia) that produces jaundice. Extreme jaundice leads to kernicterus, a form of brain damage associated with cerebral palsy and mental retardation. The hemolytic destruction of red blood cells can also lead to hydrops fetalis, a severe anemia resulting in fetal heart failure, total body swelling, respiratory distress or total circulatory collapse, and often death.³

Rh incompatibility occurs in approximately 10% of all pregnancies, depending on the race of the pregnant woman and her fetus. Without treatment, 25% to 30% of these fetuses will show various degrees of hemolytic anemia and hyperbilirubinemia. An additional 20% to 25% will be hydropic and will either die *in utero* (resulting in a stillbirth) or shortly after birth. Hemolytic disease of the fetus accounts for 4 to 5 deaths per 100,000 births in the United States.³

Condition/Disease Risk Factors

Only Rh-negative women are at risk of having a baby with Rh disease. If an Rh-negative woman and Rh-positive man conceive an Rh-positive fetus, there is a chance that some of the fetus's Rh-positive red blood cells may enter the woman's blood stream, which stimulates the woman's immune system to produce antibodies against the fetus's Rh-positive cells. The risk of Rh disease becomes greater with each subsequent pregnancy.⁴

Value of Prevention

Economic Burden of Condition/Disease

No data exist that estimate the total direct or indirect costs of Rh (D) incompatibility in the United States.

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

	<p>The value of life years lost due to fetal loss, stillbirth, neonatal and post-neonatal deaths, and productivity loss associated with disability constitute the major components of the economic burden of Rh (D) incompatibility. Costs would be even higher if the additional medical care costs and productivity losses of working pregnant women are considered.</p>
Workplace Burden of Condition/Disease	<p>In addition to the incremental medical care utilization costs due to complications from Rh (D) incompatibility, there can be significant productivity losses at the workplace when working parents need to take time off from work to care for short- or long-term health problems of their children.</p>
Economic Benefit of Preventive Intervention	<p>Early identification of Rh (D) incompatibility allows clinicians to begin treatment before damage is done to the fetus. This prevents otherwise expensive medical treatment, lifelong disability, and even death.</p>
Estimated Cost of Preventive Intervention	<p>In 2004, the private-sector cost of screening for Rh (D) incompatibility averaged \$15 per screen; approximately 95% of all paid claims fell within the range of \$0 to \$38. The cost of immune globulin averaged \$111 and approximately 95% of all paid claims fell within the range of \$0 to \$178.⁵</p>
Estimated Cost of Treatment	<p>Not Provided</p>
Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention	<p>A review undertaken on behalf of the National Institute of Clinical Excellence in the United Kingdom, the governmental unit responsible for producing evidence-based recommendations for the UK, found that routine antenatal anti-D preventive medication (immunoglobulin) provides a cost-effective intervention for preventing the incidence of hemolytic disease of the newborn in pregnancies of Rh (D)-negative women.⁶</p>

Preventive Intervention Information

Preventive Intervention: Purpose of Screening and Preventive Medication	<p>Early identification of Rh (D) incompatibility allows clinicians to begin treatment before damage is done to the fetus. This prevents otherwise expensive medical treatment, lifelong disability, and even death.</p>
Benefits and Risks of Intervention	<p>Early detection of Rh (D)-negative blood type in a pregnant woman is of substantial benefit (when the woman is not yet isoimmunized and the father of the fetus is not known to be Rh (D)-negative) because it makes prevention of isoimmunization possible. Clinicians can administer anti-D immune globulin to Rh (D)-negative pregnant women, thereby preventing the maternal isoimmunization that would adversely affect subsequent pregnancies. This course of treatment prevents isoimmunization in 96% of women at risk.⁴ Screening and treatment with immunoglobulins have few adverse affects.⁴</p>
Initiation, Cessation, and Interval	<p>The USPSTF strongly recommends that all pregnant women undergo Rh (D) blood typing and antibody testing at their first prenatal visit. Furthermore, the</p>

USPSTF recommends that women known to be Rh (D)-negative and unsensitized undergo a repeat Rh (D) antibody test between 24 and 28 weeks' gestation to determine their degree of sensitivity. This second step is unnecessary if the fetus's father is known to be Rh (D)-negative.

A full dose (300mg) of immunoglobulin should be administered to¹⁻²:

- All unsensitized Rh (D)-negative women after their repeated antibody screen between 24 and 28 weeks' gestation.
- D-negative women within 72 hours of delivering a Rh (D)-positive infant.
- D-negative women following amniocentesis or either induced or spontaneous abortion (a 50 mg dose should be administered when abortion occurs prior to 13 weeks).

Clinicians have discretion regarding the provision of immunoglobulin to Rh (D)-negative pregnant women after undergoing invasive procedures such as chorionic villus sampling or fetal blood sampling and/or following a possible spontaneous or elective abortion, second or third trimester bleeding, external cephalic version, or abdominal trauma.²

Intervention Process

Rh (D) blood typing and antibody testing is conducted via an analysis of the blood. Immunoglobulin is administered to those at risk of Rh disease through an injection.

Treatment Information

Health benefit coverage should include provisions for follow-up and treatment services.

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Evidence-Based Research:

The U.S. Preventive Services Task Force (USPSTF)
Strength of Evidence: A (Strongly Recommended/Good Evidence),
B (Recommended/At Least Fair Evidence)

A (Strongly Recommended/Good Evidence)

- The USPSTF found good evidence to support Rh (D) blood typing and antibody testing for all pregnant women during their first visit for pregnancy-related care.¹

B (Recommended/At Least Fair Evidence)

- The USPSTF found fair evidence to support Rh (D) antibody testing for all unsensitized Rh (D)-negative women between 24 and 28 weeks' gestation, unless the biological father is known to be Rh (D)-negative.¹

This recommendation is supported by the:

- American Academy of Family Physicians (AAFP)

Recommended Guidance:

The American College of Obstetricians and Gynecologists (ACOG)

Strength of Evidence: Expert Consensus

- The ACOG concurs with the USPSTF recommendations, with the exception that ACOG strongly recommends that clinicians 1) administer immunoglobulin to Rh (D)-negative pregnant women after undergoing invasive procedures such as chorionic villus sampling or fetal blood sampling, and 2) administer immunoglobulin following a possible spontaneous or elective abortion, second or third trimester bleeding, external cephalic version, or abdominal trauma.²

Authored by:

Campbell KP, Chattopadhyay S. Rh (D) incompatibility evidence-statement: screening and preventive medication. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors.

A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage.

Washington, DC: National Business Group on Health; 2006.

References

Rh (D) Incompatibility (Screening and Preventive Medication)

1. U.S. Preventive Service Task Force. Screening for Rh (D) incompatibility: Recommendations statement. November 2004. AHRQ Pub. No. 05-0566-A.
2. American College of Obstetricians and Gynecologists. Prevention of Rh (D) alloimmunization. Washington, DC: American College of Obstetricians and Gynecologists; 1999 May 8. (ACOG practice bulletin; no 4).
3. Medical Encyclopedia: Rh incompatibility. Available from: <http://www.nlm.nih.gov/medlineplus/ency/article/001600.htm>.
4. March of Dimes. Quick reference and fact sheets. Rh Disease. [cited 2006 Jul 18]. Available from: http://www.marchofdimes.com/professionals/681_1220.asp.
5. Thomson Medstat. Marketscan. 2004.
6. Chilcott J, Lloyd Jones M, Wight J, Forman K, Wray J, Beverley C, et al. A review of the clinical effectiveness and cost-effectiveness of routine anti-D antibiotic prophylaxis for pregnant women who are rhesus-negative. Health Technol Assess 2003;7(4).

EVIDENCE-STATEMENT:**HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)****Rubella (Screening)****Clinical Preventive Service Recommendations****U.S. Preventive Services Task Force Recommendation**

Not Applicable – The U.S. Preventive Services Task Force defers to the Advisory Committee on Immunization Practices and the CDC on recommendations surrounding immunization.

CDC Recommendation

Rubella vaccine is contraindicated during pregnancy. Because the vaccine contains live virus, it should not be administered to pregnant women.¹

The Advisory Committee on Immunization Practices (ACIP) recommends that clinicians screen all women of childbearing age, including pregnant women, for rubella susceptibility during their first clinical encounter. A history of vaccination (proved by written documentation of receipt of ≥ 1 dose of a rubella-containing vaccine after the age of 1 year) or a serologic test for antibodies (offering laboratory evidence of immunity) can be used to document immunity against rubella. Susceptible, nonpregnant women should be vaccinated, and susceptible pregnant women should be vaccinated immediately after delivery or at the end of their pregnancies (such as following miscarriage). Nonpregnant women may be offered vaccination without serologic screening.¹

A summary of guidelines for the immunization of pregnant women can be found online (www.cdc.gov/nip/publications/preg_guide.htm).

Evidence Rating:

Expert Consensus

Other Recommended Guidance

The American Academy of Family Physicians (AAFP) concurs with the ACIP recommendations.

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- Advisory Committee on Immunization Practices (ACIP)
- American Academy of Family Physicians (AAFP)
- Centers of Disease Control and Prevention (CDC)
- Peer-reviewed research

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information**Epidemiology of Condition/Disease**

For most people, rubella is a mild illness. However, when contracted during early pregnancy, particularly during the first trimester, rubella can cause serious complications including miscarriage, stillbirth, and congenital rubella syndrome (CRS) – a constellation of birth defects that include hearing impairment, growth

retardation, developmental delays, and heart and eye defects.² Because rubella infection can affect all the organs of a developing fetus, the earlier a woman is infected with rubella during her pregnancy, the more severe the complications are for the developing fetus. Approximately 90% of infants born to women who contracted rubella during the first 11 weeks of pregnancy develop CRS and about 20% of infants born to women who contracted rubella during the first 20 weeks of pregnancy develop CRS.²

In 1964-1965, an epidemic of rubella hit the United States: over 12 million individuals were infected resulting in 11,000 fetal losses (as a result of miscarriage or abortion) and 20,000 cases of CRS.³

In 1969, rubella vaccines were licensed in the United States to protect individuals from rubella. Widespread vaccine use led to a 99% reduction in the number of rubella cases over 3 decades; this reduced the rubella caseload from a high of 57,686 cases in 1969 to only 271 cases in 1999.²

Since universal childhood immunization was initiated in 1969, there has not been another rubella epidemic, although isolated outbreaks do occur. The United States experienced a resurgence of rubella in the early 1990s with 1,124 cases reported in 1990 and 1,412 in 1991. During this time period 66 infants were born with CRS.⁴

In 2004, an expert panel convened by CDC concluded that rubella and CRS have been eliminated from the United States; however, continued vaccination of susceptible women and children is necessary to maintain this success.³

Because pregnant women are most susceptible to the complications of rubella, experts recommend the targeted screening and vaccination of childbearing-aged women. Such a practice would reach those individuals who were not vaccinated in childhood. The rubella vaccine is contraindicated for use during pregnancy due to the theoretical possibility that the live virus rubella vaccine could cause fetal infection and CRS; however, there have been no documented cases of CRS related to use of the rubella vaccine.¹

**Condition/Disease
Risk Factors**

Since the mid-1990s, rubella and CRS has disproportionately affected foreign-born ethnic minorities. In 1999, 73% of all rubella cases in the United States occurred among Hispanics, most of whom were from Mexico and Central America (CDC, unpublished data). Between 1998 and 2000, over 90% of all CRS cases occurred among infants of Hispanic women 96% of whom were foreign-born.³

Value of Prevention

**Economic Burden of
Condition/Disease**

CRS and its complications have substantial health consequences and economic costs. A large rubella outbreak in 1964-1965 cost an estimated \$840 million.⁵ In 2006, the estimated *lifetime* cost of treating a child born with CRS exceeded \$200,000.⁵

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

<p>Workplace Burden of Condition/Disease</p>	<p>Rubella and CRS result in excess direct medical costs. Indirect costs constitute the major workplace burden of rubella, however. Indirect costs include permanent disability caused by CRS as well as productivity losses associated with the missed work time of employed caregivers attending to their sick children.</p>
<p>Economic Benefit of Preventive Intervention</p>	<p>The economic benefits of immunization result from reducing hospitalizations and outpatient visits and by avoiding productivity losses caused by rubella or CRS-related disabilities.</p>
<p>Estimated Cost of Preventive Intervention</p>	<p>In 2004, the private-sector cost of screening for rubella antibodies averaged \$21; approximately 95% of paid claims fell within the range of \$0 to \$50.⁶ The cost of the rubella vaccine averaged \$20 and approximately 95% of all paid claims fell within the range of \$0 to \$40 per dose (1 to 2 doses are required for protection against rubella).⁶</p>
<p>Estimated Cost of Treatment</p>	<p>In 2006, the <i>lifetime</i> cost of treating a child born with CRS exceeded \$200,000.⁵</p>
<p>Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention</p>	<p>Although there is a lack of economic evidence about the cost-effectiveness of screening pregnant women, one study that investigated the current 2-dose MMR vaccination program for children through a decision-tree-based analysis demonstrated that the program resulted in substantial cost-savings and high benefit-to-cost ratios. The estimated total cost savings to society of \$7.6 billion (in year 2001 dollars) included a savings of \$549 million from rubella and CRS prevention.⁷</p>

Preventive Intervention Information

<p>Preventive Intervention: Purpose of Screening</p>	<p>Screening allows clinicians to identify childbearing-age women who are at risk for rubella and to immunize them before they become pregnant. Screening pregnant women allows clinicians to identify at-risk women and to encourage them to be immunized immediately after delivery, thereby offering protection during subsequent pregnancies.</p>
<p>Benefits and Risks of Intervention</p>	<p>Screening for rubella susceptibility involves minimal risk, although false-positive test results may lead to unnecessary treatment. The rubella vaccine is very effective; more than 90% of individuals vaccinated show long-term protection from the illness.¹ Adverse reactions to the rubella vaccine may include pain at the injection site or temporary rash, which are usually mild in both children and adults, although adults — particularly women — commonly complain of temporary joint pain after vaccination.</p>
<p>Initiation, Cessation, and Interval of Screening</p>	<p>All women of childbearing age, including pregnant women, should be screened for rubella susceptibility during their first clinical encounter. All women of childbearing age who are not pregnant should be vaccinated at their first clinical encounter if not immune to rubella. A susceptible pregnant woman should be vaccinated immediately after delivery or at the end of her pregnancy (e.g., miscarriage).</p>

**Intervention Process
Screening**

Screening is conducted by ascertaining an individual's risk for rubella. Immunity to rubella can be documented by 1) a history of immunization (proved by written documentation of receipt of ≥ 1 dose of a rubella-containing immunization after the age of 1 year), or 2) a serologic test for antibodies (offering laboratory evidence of immunity). Individuals who cannot document immunity are considered at risk for rubella.

Immunization

Rubella immunization is administered via an injection.

**Treatment
Information**

Health benefits should include provisions for treatment services.

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Recommended Guidance:

Advisory Committee on Immunization Practices (ACIP)

Strength of Evidence: Expert Consensus

The ACIP recommends that clinicians screen all women of childbearing age, including pregnant women, for rubella susceptibility during their first clinical encounter. Susceptible non-pregnant women should be vaccinated and susceptible pregnant women should be vaccinated immediately after delivery or at the end of their pregnancy (e.g., miscarriage).¹

This recommendation is supported by the:

- U.S. Preventive Services Task Force (USPSTF)

Authored by:

Campbell KP, Lindley MC, Bhatt A, Chattopadhyay S. Rubella evidence-statement: screening. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Rubella (Screening)

1. Centers for Disease Control and Prevention. Measles, mumps, and rubella – vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: Recommendations of the Advisory Committee on Immunization Practices. *MMWR* 1998; 47(RR-8):1-57.
2. Centers for Disease Control and Prevention. Control and prevention of rubella: Evaluation and management of suspected outbreaks, rubella in pregnant women, and surveillance of congenital rubella syndrome. *MMWR* 2001; 50(RR12):1-23.
3. Centers for Disease Control and Prevention. Achievements in public health: elimination of rubella and congenital rubella syndrome – United States, 1969-2004. *MMWR* 2005; 54(11):279-282.
4. Reef SE, Frey TK, Theall K, Abernathy E, Burnett CL, Icenogle J, et al. The changing epidemiology of rubella in the 1990s: On the verge of elimination and new challenges for control and prevention. *JAMA* 2002; 287(4):464-72.
5. Centers for Disease Control and Prevention. Rubella. In Atkinson W, Hamborsky J, McIntyre L, Wolfe S, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*, 9th ed. Washington DC: Public Health Foundation; 2006:155–70.
6. Thomson Medstat. MarketScan. 2004.
7. Zhou F, Reef S, Massoudi M, Papania MJ, Yusuf HR, Bardenheier B, et al. An economic analysis of the current universal 2-dose measles-mumps-rubella vaccination program in the United States. *J Infect Dis* 2004;189:S131-S145.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Syphilis (Screening)

Clinical Preventive Service Recommendations

U.S. Preventive Services Task Force Recommendation

The U.S. Preventive Services Task Force (USPSTF) strongly recommends that clinicians screen all pregnant women for syphilis infection.¹

Evidence Rating: A (Strongly Recommended/ Good Evidence)

The USPSTF found good evidence that screening pregnant women decreases the proportion of infants with clinical manifestations of syphilis infection and those with positive serologies. The USPSTF concludes that the benefits of screening substantially outweigh the potential harms.¹

CDC Recommendation

The Centers for Disease Control and Prevention (CDC) recommends a serologic test for syphilis for all pregnant women at the first prenatal visit. Women who are at high risk for syphilis morbidity, are previously untested, or have a positive serology in the first trimester should be screened again early in the third trimester (28 weeks gestation) and at delivery. Infants should not be discharged from the hospital unless the syphilis serologic status of the mother has been determined at least one time during pregnancy and preferably again at delivery.²

Evidence Rating:

Not Specified

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- Centers for Disease Control and Prevention (CDC)
- Peer-reviewed research
- U.S. Preventive Services Task Force (USPSTF)

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

Epidemiology of Condition/Disease	<p>Syphilis is a serious sexually transmitted infection (STI) that, if left untreated, may result in cardiovascular and neurological complications leading to disability and ultimately death.¹</p> <p>In addition to sexual transmission, syphilis can be passed from an infected mother to her infant during pregnancy and delivery. Congenital syphilis is particularly severe and results in fetal or infant death in 40% of cases.¹ In 2002, 451 cases of congenital syphilis were reported in the United States.³ Of these cases, 333 (73.8%) occurred because the mother had no documented treatment or received inadequate treatment of syphilis before or during pregnancy.³ Infected infants who survive may suffer serious central nervous system abnormalities, deafness, bone and joint deformities, skin abnormalities, blood disorders, and other problems.³</p>
Condition/Disease Risk Factors	<p>Populations at increased risk for syphilis infection (as determined by incidence rates) include commercial sex workers, persons who exchange sex for drugs, and those in adult correctional facilities.</p> <p>The prevalence of syphilis infection varies widely among communities and patient populations.¹ Some populations have a particularly high risk of infection, specifically African-Americans and people living in the Southeastern United States.⁴</p>
Value of Prevention	
Economic Burden of Condition/Disease	<p>The average annual national cost of treating infants with congenital syphilis is approximately \$18.4 million (in year 1995 dollars).⁵</p>
Workplace Burden of Condition/Disease	<p>The health, disability, and life insurance costs of syphilis-infected employees impose a significant economic burden on employers. Affected women may also lose work time in order to seek treatment for themselves or for their affected infants.</p>
Economic Benefit of Preventive Intervention	<p>Screening and early detection are key to averting costs associated with disease progression, long-term complications, and neonatal transmission. For example, treatment for early stage syphilis (\$41.26) is much less expensive than treatment for later stage disease (\$2,062) (both figures in year 2001 dollars).⁶</p>
Estimated Cost of Preventive Intervention	<p>In 2004, the private-sector cost of screening for syphilis averaged \$12; approximately 95% of all paid claims fell within the range of \$0 to \$32.⁷</p>
Estimated Cost of Treatment	<p>The cost of treating syphilis will vary depending on the medication used and other factors. For azithromycin therapy, the 2001 public-sector price of the 1-g sachet formulation was \$11.50 and the wholesale price for a 1-g dose ranged from \$17.32 for the sachet formulation to \$27.89 for tablets. The public sector cost of standard IM benzathine penicillin therapy ranged from \$18.64 to \$22.22 (in year 2001 dollars).⁶</p>

<p>Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention</p>	<p>Serological screening of pregnant women is cost-effective even when there is a very low prevalence of maternal infection because screening is inexpensive but treating congenital syphilis is costly.⁸</p>
<p>Preventive Intervention Information</p>	
<p>Preventive Intervention: Purpose of Screening</p>	<p>Screening for syphilis allows clinicians to identify affected patients and begin treatment early in the course of disease. Early intervention improves outcomes and avoids the health and economic consequences of latent disease in the mother and the occurrence of congenital syphilis.² Treatment also reduces the risk of transmission between the affected woman and her sexual partner(s).</p>
<p>Benefits and Risks of Intervention</p>	<p>No studies have documented harms associated with screening for syphilis. Theoretical harms include partner discord, stigma, unnecessary anxiety, treatment in the case of a false-positive result, and opportunity costs (in terms of time and resources) to both the clinician and patient. Harms of treatment include allergic reactions to penicillin and other side effects of treatment medications such as the Jarisch-Herxheimer reaction (fever, headache, and pain that occurs during the 24 hours after initiating antibiotic treatment for syphilis and is caused by the release of fragments of the dead, infective microorganism into the bloodstream).¹</p> <p>The benefits associated with screening are substantial. Screening allows for early detection and treatment, prevention of complications that may occur in later stages of the disease, and prevention of neonatal transmission. Antibiotic treatment for syphilis is effective, and inexpensive. Therefore, the USPSTF concluded that the benefits of screening pregnant women for syphilis infection substantially outweigh the potential harms.¹</p>
<p>Initiation, Cessation, and Interval of Screening</p>	<p>All pregnant women should be screened for syphilis at their first prenatal care visit. For women in high-risk groups, repeat serologic testing may be necessary in the third trimester (28 weeks) and again at delivery.^{1,2} Follow-up serologic tests should be obtained to document successful treatment.¹</p>
<p>Intervention Process</p>	<p>A variety of syphilis tests are available and in development. Screening for syphilis typically involves the use of 2 different tests, a nontreponemal test and a treponemal-specific test, for screening and confirmation. For example, a nontreponemal blood test such as the venereal disease research laboratory (VDRL) or the rapid plasma reagin (RPR) may be performed. A second, different kind of test, such as the fluorescent treponemal antibody absorbed (FTA-ABS) or the <i>T. palladium</i> particle agglutination (TP-PA) may then be used to confirm the results of the nontreponemal test.^{1,4}</p> <p>Syphilis screening tests that are approved by the Food and Drug Administration (FDA) or are pending FDA approval include^{1,4}:</p> <ul style="list-style-type: none"> • Nontreponemal test such as the venereal disease research laboratory (VDRL) or the rapid plasma regain (RPR) on serum specimens followed by a fluorescent treponemal antibody absorbed (FTA-ABS) or <i>T. palladium</i> particle

agglutination (TP-PA) for confirmation.

- Immunochromatographic Strip (ICS) point-of-care test on blood specimen, when FDA approved.
- Line Immunoassay (LIA) point-of-care test on blood specimen, when FDA approved.
- Enzyme-linked Immunosorbent Assay (ELISA) for treponemal antibody in serum specimens.
- RPR point-of-care test for nontreponemal antibody in serum specimens.
- Dark field microscope examination of lesion specimens.

Follow-up tests should be performed using the same nontreponemal test initially used to document infection (e.g., VDRL or RPR) to ensure comparability.¹

Treatment Information

Syphilis should be treated with an antibiotic regimen appropriate for the woman's stage of disease. Some experts recommend additional therapy (e.g., a second dose of benzathine penicillin 2.4 million units IM) one week after the initial dose, particularly for those women in the third trimester of pregnancy and for women who have secondary syphilis during pregnancy.⁹

Infants should be treated for presumed congenital syphilis if they were born to mothers who, at delivery:

- Had untreated syphilis;
- Were treated with a non-recommended antibiotic regimen;
- Were treated less than one month prior to delivery; or
- Had evidence of relapse or reinfection after treatment.

Recommended treatment regimens for infants include aqueous crystalline penicillin G (administered every 12 hours during the first 7 days of life and every 8 hours thereafter) for 10 to 14 days or procaine penicillin G (administered daily in a single dose for 10 to 14 days). If more than one day of therapy is missed, the entire course should be restarted.¹⁰

Health benefits should include provisions for treatment services.

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Evidence-Based Research:

U.S. Preventive Services Task Force (USPSTF)

Strength of Evidence: A (Strongly Recommended/Good Evidence)

- The USPSTF found good evidence that screening pregnant women decreases the proportion of infants with clinical manifestations of syphilis infection and those with positive serologies. The USPSTF concludes that the benefits of screening substantially outweigh the potential harms.¹

Recommended Guidance:

Centers for Disease Control and Prevention (CDC)

Strength of Evidence: Not Specified

- The CDC recommends a serologic test for syphilis on all pregnant women at the first prenatal visit. Women who are at high risk for syphilis morbidity, are previously untested, or have a positive serology in the first trimester should be screened again early in the third trimester (28 weeks gestation) and at delivery. Infants should not be discharged from the hospital unless the syphilis serologic status of the mother has been determined at least one time during pregnancy and preferably again at delivery.²

Authored by:

Choucair J, Lentine D, Campbell KP, Chattopadhyay S. Syphilis evidence-statement: screening. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Syphilis (Screening)

1. U.S. Preventive Services Task Force. Screening for syphilis infection. Summary of recommendations / Supporting documents. Rockville, MD: Agency for Healthcare Research and Quality; 2004.
2. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2006. MMWR 2006 ;55(No. RR 11).
3. Centers for Disease Control and Prevention. Congenital syphilis – United States, 2002. MMWR 2004; 50(No. RR-31): 716-719.
4. Nelson HD, Glass N, Huffman L, Villemeyer K, Hamilton A, Frame A, et al. Screening for syphilis: Brief update for the U.S. Preventive Services Task Force. AHRQ Publication No. 04-0545-B. Rockville, MD: Agency for Healthcare Research and Quality; 2004.
5. Bateman DA, Phibbs CS, Joyce T, Heagarty MC. The hospital cost of congenital syphilis. J Pediatr 1997; 130 (5): 752-8.
6. Blandford JM, Gift TL. The cost-effectiveness of single-dose azithromycin for treatment of incubating syphilis. Sex Transm Dis 2003;30(6):502-8.)
7. Thomson Medstat. Marketscan. 2004.
8. Schmid G. Economic and programmatic aspects of congenital syphilis prevention. Bull World Health Organ 2004; 82(6) 402-409.
9. New York State Department of Health. New York state addendum for congenital syphilis treatment guidelines. [cited 2006 Aug 22]. Available from: <http://www.health.state.ny.us/diseases/communicable/std/addendum.htm>.
10. Centers for Disease Control and Prevention. Congenital syphilis. Sexually transmitted diseases treatment guidelines. MMWR 2002 May 10;51(RR-6):26-8.

EVIDENCE-STATEMENT:**HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)****Tetanus (Immunization)****Clinical Preventive Service Recommendations**

U.S. Preventive Services Task Force Recommendation	Not Applicable – The U.S. Preventive Services Task Force defers to the Advisory Committee on Immunization Practices and the CDC on recommendations surrounding immunization.
CDC Recommendation	<p>The Advisory Committee on Immunization Practices (ACIP) recommends that all previously vaccinated pregnant women who have not been vaccinated against tetanus in the past 10 years receive a booster vaccination against tetanus.¹⁻² Pregnant women who have not completed a three-dose primary vaccination series against tetanus should complete the series.¹⁻² Pending guidance from ACIP, pregnant women should receive the Td vaccine in preference to the Tdap vaccine.³</p> <p>A summary of guidelines for the immunization of pregnant women can be found online (www.cdc.gov/nip/publications/preg_guide.htm).</p>
Evidence Rating:	Expert Consensus
Other Recommended Guidance American Academy of Family Physicians (AAFP)	The American Academy of Family Physicians (AAFP) supports the ACIP recommendation. ¹
Information Sources	<p>The recommendations and supporting information contained in this document came from several sources, including the:</p> <ul style="list-style-type: none"> • Advisory Committee on Immunizations (ACIP) • American Academy of Family Physicians (AAFP) • Centers for Disease Control and Prevention (CDC) • Peer-reviewed research <p>The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.</p>

Condition/Disease Specific Information**Epidemiology of Condition/Disease**

Tetanus is generally characterized by painful muscle rigidity and uncontrollable spasms. Between 1998 and 2000, 18% of persons in the United States who contracted tetanus died as a result of the disease.⁴ Neonatal tetanus is a severe and often fatal disease; it accounted for an estimated 200,000 deaths worldwide in 2000 but is extremely rare in the United States.⁵ Because nearly all neonatal tetanus occurs in infants born to mothers who are not adequately immunized against tetanus, it is important that all pregnant women be vaccinated against tetanus.⁴

EVIDENCE-STATEMENT: Healthy Pregnancy (Screening, Testing, Counseling, Immunization, and Preventive Medication)

<p>Condition/Disease Risk Factors</p>	<p>All pregnant women who are not fully immunized are at risk of infection.</p>
<p>Value of Prevention</p>	
<p>Economic Burden of Condition/Disease</p>	<p>There are few economic data on the burden of tetanus disease and no data about the costs of neonatal tetanus in the United States. A recent economic evaluation of the 7-vaccine routine childhood immunization schedule in the United States estimated that, if there had not been a tetanus vaccination program in the United States, 153 cases of tetanus and 23 deaths from tetanus would have occurred at a total cost of \$29 million (direct and indirect costs in year 2001 dollars) based on a hypothetical 2001 birth cohort of 3.8 million infants that was followed from birth to death.⁶</p>
<p>Workplace Burden of Condition/Disease</p>	<p>Not Provided</p>
<p>Economic Benefit of Preventive Intervention</p>	<p>The averted mortality and morbidity costs due to prevented tetanus cases constitute the major economic benefit of immunization.</p>
<p>Estimated Cost of Preventive Intervention</p>	<p>In 2004, the private-sector cost of an adult tetanus vaccine (usually given as Td) averaged \$15; approximately 95% of all paid claims fell within the range of \$0 to \$28.⁷ The additional cost of vaccine administration averaged \$10 and 95% of paid claims fell within the range of \$0 to \$20.⁷</p>
<p>Estimated Cost of Treatment</p>	<p>Not Provided</p>
<p>Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention</p>	<p>In one analysis, it was estimated that administering tetanus booster immunizations every 10 years ('decennial' boosters) is associated with a cost of \$143,138 per year of life saved. Although decennial boosters are more expensive than once-in-a-lifetime booster immunizations, they also prevent more than twice the number of tetanus cases that would be prevented by a single lifetime booster.⁸</p>
<p>Preventive Intervention Information</p>	
<p>Preventive Intervention: Purpose of Immunization</p>	<p>Tetanus immunization offers long-term protection against tetanus for the vaccinated woman, and maternal vaccination confers significant protection to the fetus. In fact, field assessments have reported 70% to 100% effectiveness of the vaccine in preventing neonatal tetanus among the children of women receiving at least two doses of tetanus vaccine.⁹ Notably, in all three cases of neonatal tetanus that have occurred in the United States since 1989, the infant's mother was not fully immunized against tetanus.⁴</p>
<p>Benefits and Risks of Intervention</p>	<p>The benefits of tetanus immunization are substantial. Adverse reactions to tetanus vaccination can include local swelling or pain; extensive swelling and systemic reactions are rare, however.¹⁰ Although no evidence exists that tetanus immunization during pregnancy causes harm to the fetus, delaying needed</p>

Authored by:

Lindley MC, Bhatt A, Campbell KP, Chattopadhyay S. Tetanus immunization evidence-statement. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

References

Tetanus (Immunization)

1. Centers for Disease Control and Prevention. General recommendations on immunization: Recommendations of the Advisory Committee on Immunization Practices and the American Academy of Family Physicians. *MMWR* 2002; 51(RR-2):1-36.
2. Centers for Disease Control and Prevention. Diphtheria, tetanus, and pertussis: Recommendations for vaccine use and other preventive measures. Recommendations of the Immunization Practices Advisory Committee. *MMWR* 1991; 40(RR-10):1-28.
3. Centers for Disease Control and Prevention. Preventing tetanus, diphtheria, and pertussis among adolescents: Use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2006; 55(RR-03):1-34.
4. Centers for Disease Control and Prevention. Tetanus surveillance – United States, 1998-2000. *MMWR* 2003; 52(SS-3):1-8.
5. Vandelaer J, Birmingham M, Gasse F, Kurian M, Shaw C, Garnier S. Tetanus in developing countries: an update on the Maternal and Neonatal Tetanus Elimination Initiative. *Vaccine* 2003; 21:3442-3445.6. Zhou F, Santoli J, Messonnier ML, Yusuf HR, Shefer A, Chu SY, et al. Economic evaluation of the 7-vaccine routine childhood immunization schedule in the United States, 2001. *Arch Pediatr Adolesc Med* 2005;159:1136-1144.
7. Thomson Medstat. Marketscan. 2004.
8. Balestra DJ, Littenberg B. Should adult tetanus immunization be given as a single vaccination at age 65? *J Gen Intern Med* 1993; 8:405-412.
9. Wasilak SGE, Orenstein WA, Sutter RW. Chapter 18: Tetanus Toxoid. In Plotkin SA, Orenstein WA, eds. *Vaccines*, ed. 3. Philadelphia, PA: W.B. Saunders Company; 1999:441-474.
10. Centers for Disease Control and Prevention. Tetanus. In Atkinson W, Hamborsky J, McIntyre L, Wolfe S, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*, 9th ed. Washington D.C.: Public Health Foundation; 2006:69-78.
11. Centers for Disease Control and Prevention. Update: Vaccine side effects, adverse reactions, contraindications, and precautions. Recommendations of the Advisory Committee on Immunization Practices. *MMWR* 1996; 45(RR-12):1-35.

EVIDENCE-STATEMENT:

HEALTHY PREGNANCY (Screening, Testing, Counseling, Immunization, and Preventive Medication)

Tobacco Use Treatment (Screening and Counseling)

Clinical Preventive Service Recommendations

U.S. Preventive Services Task Force Recommendation

The U.S. Preventive Services Task Force (USPSTF) recommends that clinicians screen all pregnant women for tobacco use and provide augmented pregnancy-tailored counseling to those who smoke.¹

Evidence Rating: A (Strongly Recommended/ Good Evidence)

The USPSTF found good evidence that extended or augmented smoking cessation counseling (5 to 15 minutes) using messages and self-help materials tailored for pregnant smokers, compared with brief generic counseling interventions alone, substantially increases abstinence rates during pregnancy, and leads to increased birth weights. Although relapse rates are high in the postpartum period, the USPSTF concluded that reducing smoking during pregnancy is likely to have substantial health benefits for both the baby and the expectant mother. The USPSTF concluded that the benefits of smoking cessation counseling outweigh any potential harms.¹

The American Academy of Family Physicians (AAFP)², the American College of Preventive Medicine (ACPM)³, and the U.S. Surgeon General concur with the USPSTF recommendations.⁴

Other Evidence-Based Recommendations American Academy of Family Physicians (AAFP)

The American Academy of Family Physicians (AAFP) strongly recommends that clinicians counsel smoking parents with children in the house regarding the harmful effect of smoking and children's health.²

Evidence Rating: SR (Strongly Recommended)

Good quality evidence exists which demonstrates the substantial net benefit (compared with harm) of counseling to prevent exposure to secondhand smoke; the intervention is perceived to be cost-effective and acceptable to nearly all patients.²

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- American Academy of Family Physicians (AAFP)
- American College of Preventive Medicine (ACPM)
- Centers for Disease Control and Prevention (CDC)
- National Institutes of Health (NIH)
- Peer-reviewed research
- Smoke Free Families
- U.S. Public Health Service (USPHS)
- U.S. Surgeon General

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document

should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information

Epidemiology of Condition/Disease

Twenty-one percent (21%) of all childbearing-aged women in the United States smoke.⁴ Depending on demographic factors, between 11% and 20% of all pregnant women in the United States smoke.⁴

Tobacco use during pregnancy causes significant damage to the developing fetus, putting the future infant at risk for an array of severe short- and long-term health problems. Compared to non-smokers, women who smoke during their pregnancy are 83% more likely to deliver a low-birth-weight infant, 129% more likely to deliver an infant that will die of SIDS, 30% more likely to deliver an infant with respiratory distress syndrome, and 41% more likely to deliver an infant with a perinatal respiratory condition.⁵ And children whose mothers smoked during pregnancy and/or smoke in the home shortly after birth are at increased risk of asthma, impaired lung function, stunted growth, ear infections, and upper respiratory problems.⁶⁻⁷

Prenatal tobacco use is a known risk factor for low birth weight, which itself is a significant risk factor for neonatal morbidity and mortality. In 2003, 12.4% of all women, 13% of Hispanic women, and 20.2% of black women who smoked during pregnancy delivered a low-birth-weight infant.⁸

Table 1.0 Infant Deaths Resulting from Tobacco Use

Health Problem	Percent of Cases Caused by Smoking	No. of Infants who Died as a Result of a Smoking Induced Health Problem (2001)	Years of Potential Life Lost due to Smoking Induced Health Problem	Estimated Cost per Case
Low birth weight (LBW)	9.1%	400	20,732	\$32,000-\$90,000*
Sudden infant death syndrome (SIDS)	13.4%	299	22,909	
Respiratory distress syndrome	3.5%	35	2,686	\$8,500 per day of intensive care**
Other respiratory problem	4.7%	71	5,444	

Source: Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion: Division of Reproductive Health. MCH health outcomes report. Maternal and Child Health Smoking-Attributable Mortality, Morbidity, and Economic Costs. Atlanta, GA: Centers for Disease Control and Prevention; 2005.

* March of Dimes. Perinatal statistics. [cited 2005 Jul 8]. Available from: http://www.marchofdimes.com/aboutus/680_2203.asp.

**Discovery labs (distributors of surfactant, a medicine used to treat RDS in infants. [cited 2005 Jul 8]. Available from: <http://www.discoverylabs.com/2002pr/071802-PR.pdf>.

Condition/Disease Risk Factors	<p>Women who smoke during pregnancy are likely to be young (18 to 24 years of age), have low levels of education, and be from racial or ethnic minorities. Level of education is highly correlated with prenatal smoking. For example, while only 2% of college-educated non-Hispanic white women smoke during pregnancy, 42.7% of non-Hispanic white women with only 9 to 11 years of education smoke during one or more of their pregnancies.⁹</p>
Value of Prevention	
Economic Burden of Condition/Disease	<p>The economic burden of prenatal tobacco use is substantial. In 1996, maternal smoking accounted for 2.3% of all neonatal medical expenditures.¹⁰ Each pregnant smoker incurs an additional \$704 in healthcare costs (in year 1996 dollars)⁵ and, annually, smoking-attributable neonatal costs (defined as all costs related to labor /delivery and the care of infants within the first few months of life) are estimated to meet or exceed \$367 million in the United States.¹⁰⁻¹¹</p> <p>The direct costs of care for mothers and their children exposed to environmental tobacco smoke (ETS) (also known as secondhand smoke) also add to the overall cost of smoking, although exact cost figures are not known.</p>
Workplace Burden of Condition/Disease	<p>Smoking-attributable neonatal costs impose a heavy burden on employer-sponsored health insurance spending. Moreover, working parents are required to take additional time off from work to attend to the health care needs of children affected by neonatal smoke exposure. This results in productivity losses in the workplace.</p>
Economic Benefit of Preventive Intervention	<p>A smoking cessation program that could achieve an annual drop of 1 percentage point in smoking prevalence has been estimated to produce an economic benefit of \$21 million in (in year 1995 dollars) direct medical costs solely by reducing the number of low-birth-weight live births. In 7 years, the cumulative undiscounted saving in direct medical costs would become \$572 million through the prevention of 57,200 low-birth-weight infants.¹²</p>
Estimated Cost of Preventive Intervention	<p>In 2004, the private-sector cost of tobacco risk assessment and prevention counseling averaged \$62; approximately 95% of all paid claims fell within the range of \$0 to \$139.¹³ In 2004, the private-sector cost (per pregnant smoker) for tobacco use treatment averaged \$39 and approximately 95% of all paid claims fell within the range of \$0 to \$134.¹³</p>
Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention	<p>Tobacco cessation treatment for pregnant women is considered one of the most cost-saving preventive services.^{4,14} Clinical trials have shown that \$6 are saved in healthcare costs for every \$1 invested in smoking cessation programs for pregnant women.¹⁵</p>

Preventive Intervention Information

**Preventive Intervention:
Purpose of Screening
and Counseling**

Screening allows clinicians to identify smokers and offer them cessation services in order to improve their chances of quitting. Quitting smoking reduces the risk of serious smoking-related health problems for the individual and — with regards to pregnant smokers — reduces the fetus’s risk of smoking-related health problems such as pre-term birth, low birth weight, and SIDS.

**Benefits and Risks
of Intervention**

The benefits of tobacco use screening and counseling are substantial. Tailored tobacco cessation programs that feature patient education and support have been proven to be effective in reducing the number of women who smoke during pregnancy. For example, one health plan’s tobacco cessation program saw a massive reduction in smoking among participants; 81% of participants reported that they stopped smoking altogether or cut the number of cigarettes they smoked each day in half. Women in the program who stopped smoking completely had fewer preterm deliveries and fewer low-birth-weight babies compared to the pregnant smokers who did not participate in the program.¹⁶

Counseling interventions (as compared to printed self-help materials) are especially effective for smokers at high risk of complications from smoking, such as pregnant women. Notably, 21% of pregnant women who receive physician counseling successfully quit, which is double the quit rate of their nonpregnant counterparts.³

There are no documented risks to screening pregnant women for tobacco use. Risks of tobacco cessation counseling are few but include the possibility of a negative self-perception and perceived feelings of discrimination.

The benefits of screening and counseling, including early identification and early treatment, far outweigh the risks associated with screening and counseling.

**Initiation, Cessation,
and Interval of
Screening and
Counseling**

All adults, including pregnant women, should be screened for tobacco use at every preventive care visit or as deemed appropriate by the clinician.^{1,3} Pregnant women who screen positive for tobacco use should be advised to quit at every medical encounter and referred to 1-800-Quit-Now, the national portal number that refers callers to their state’s quitline service. All pregnant women who screen positive for tobacco use should be counseled.

**Intervention Process
Screening**

The USPSTF recommends the use of the “5-A” behavioral counseling framework for tobacco screening and counseling. This framework is composed of 5 steps aimed at engaging the patient in a discussion about their tobacco use and their intention to quit:

- Ask about tobacco use
- Advise to quit through clear and personalized messages
- Assess the patient’s willingness to quit
- Assist to quit
- Arrange for follow-up and support services

Counseling

The USPSTF further recommends that clinicians provide problem-solving guidance for smokers to develop a quit plan and to overcome common barriers to quitting. Practices that complement the “5-A” framework include motivational interviewing or other methods of intensive counseling, referral for quitters that may need extra help, and referral to quitlines for adjunct counseling.^{1,5}

Effective counseling interventions for pregnant smokers include individual face-to-face, group, and telephone counseling.¹⁷ The most effective type of smoking cessation interventions for pregnant women are multi-component programs that feature: 1) healthcare provider reinforcement, 2) printed self-help materials, and 3) follow-up in-person or telephone counseling.¹¹ Physician counseling has been shown to increase quit rates among patients in primary care. The more intensive the counseling is (as measured by length of counseling session) the higher the quit rate. For example, 10.5% of patients who receive less than 3 minutes of physician counseling quit smoking, 12.1% of patients who receive 3 to 10 minutes quit, and 18.7% of patients who receive over 10 minutes of counseling quit.³

Pharmacologic therapy can enhance the effectiveness of tobacco-cessation interventions and can be used when the physician and patient concur that medication use would be beneficial. Because there have not been adequate studies to ensure the safety of tobacco cessation medications among pregnant women, patient education and provider counseling remain the primary methods of tobacco use treatment. Postpartum women who are not breastfeeding may want to consider using medication to enhance their likelihood of a successful quit attempt.¹⁷

Treatment Information

Please refer to the “Intervention Process” section.

Strength of Evidence for the Clinical Preventive Service

The level of evidence supporting the recommendations contained in this section is described below.

Evidence-Based Research:

The U.S. Preventive Services Task Force (USPSTF)

Strength of Evidence: A (Strongly Recommended/Good Evidence)

- The USPSTF found good evidence that extended or augmented smoking cessation counseling (5 to 15 minutes) using messages and self-help materials tailored for pregnant smokers, compared with brief generic counseling interventions alone, substantially increases abstinence rates during pregnancy, and leads to increased birth weights.¹

This recommendation is supported by the:

- American Academy of Family Physicians (AAFP)
- American College of Preventive Medicine (ACPM)
- The U.S. Surgeon General

- U.S. Public Health Service (USPHS)

The American Academy of Family Physicians (AAFP)
Strength of Evidence: SR (Strongly Recommended)

- AAFP strongly recommends that clinicians counsel smoking parents with children in the house regarding the harmful effect of smoking and children's health.² Good quality evidence exists which demonstrates the substantial net benefit of counseling to prevent exposure to secondhand smoke; the intervention is perceived to be cost-effective and acceptable to nearly all patients.²

Authored by:

Campbell KP, Rosenthal AC, Chattopadhyay S. Tobacco use treatment during pregnancy evidence-statement: screening and counseling. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

Tobacco Use Treatment (Screening and Counseling)

1. U.S. Preventive Services Task Force. Counseling to prevent tobacco use. Rockville, MD; Agency for Healthcare Research and Quality: 2003 [cited 2006 Aug 22]. Available from: <http://www.ahrq.gov/clinic/uspstf/uspstbac.htm>.
2. American Academy of Family Physicians. Summary of policy recommendations for periodic health examinations. AAFP Policy Action. Revision 6.0; August 2005.
3. Kattapong VJ, Locher TL, Secker-Walker RH, Bell TA. Tobacco-cessation patient counseling. American College of Preventive Medicine Practice Policy Statement. *Am J Prev Med* 1998; 15(2): 160-162.
4. U.S. Public Health Service. Treating tobacco use and dependence: A systems approach. Rockville, MD: Office of the U.S. Surgeon General; U.S. Public Health Service; U.S. Department of Health and Human Services; 2000.
5. Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion: Division of Reproductive Health. Smoking-attributable neonatal expenditures: Maternal and child health smoking-attributable mortality, morbidity, and economic costs. Atlanta, GA: Centers for Disease Control and Prevention; 2004.
6. Smoke Free Families: Smoking and pregnancy: The real risks for mothers and their babies. [cited 2005 July 8]. Available from: www.smokefreefamilies.org.
7. U.S. Surgeon General. Women and Smoking: A Report of the Surgeon General. Rockville, MD: Office of the U.S. Surgeon General; U.S. Public Health Service; U.S. Department of Health and Human Services; 2001.
8. National Center for Healthcare Statistics. Final Birth Data, 2003. From Table 32. Percentage low birth weight by smoking status, age, and race and Hispanic origin of mother: Total of 47 reporting States and the District of Columbia, 2003. Atlanta, GA: Centers for Disease Control and Prevention; 2004.
9. Smoke Free Families: Cigarette smoking during pregnancy, by age, ethnicity, and education. [cited 2005 July 8]. Available from: www.smokefreefamilies.org.
10. Centers for Disease Control and Prevention. Annual smoking-attributable mortality, years of potential life lost, and economic Costs — United States, 1995–1999. *MMWR* 2002; 51(14): 300-303.
11. Adams KE, Miller VP, Ernst C, Nishimura BK, Melvin C, Merritt R. Determinants of health: Neonatal health care costs related to smoking during pregnancy. *Health Econ* 2002; 11(3): 193-206.

12. Lightwood JM, Phibbs, CS, and Glantz SA. Short-term health and economic benefits of smoking cessation: Low birth weight. *Pediatrics* 1999; 104:1312-1320.
13. Thomson Medstat. MarketScan. 2004.
14. Maciosek MV, Coffield AB, Edwards NM, Goodman MJ, Flottemesch TJ, Solberg LI. Priorities among effective clinical preventive services: results of a systematic review and analysis. *Am J Prev Med* 2006; 31(1):52-61. Table reprinted from *Am J Prev Med* 2006; 31(1):52-61 with permission from the American Journal of Preventive Medicine.
15. Marks JS, Koplan JP, Hogue CJR, et al. A cost-benefit/cost-effectiveness analysis of smoking cessation for pregnant women. *Am J Prev Med* 1990;6:282-291.
16. Smoke Free Families. Helping pregnant smokers quit: Model programs. [cited 2005 July 8]. Available from: www.smokefreefamilies.org.
17. Ibrahim JK, Schauffler HH, Barker DC, Orleans CT. Coverage of tobacco dependence treatments for pregnant women and for children and their parents. *Am J Public Health* 2002; 92(12): 1940-1942.