

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This recommendation is considered out of date and has been archived.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

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 of¹⁵:</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.

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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.

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