

EVIDENCE-STATEMENT:

BREAST CANCER (Screening, Counseling, Testing, Preventive Medication, and Treatment)

Why This Chapter is Important for Employers: An Overview

- Breast cancer is the most commonly diagnosed non-skin cancer and the second leading cause of cancer death among women in the United States.¹
- In 2005, 211,000 women are expected to be diagnosed with breast cancer and 40,000 women are expected to die as a result of breast cancer.¹
- Women aged 40 to 64 years accounted for 61% of *in situ* cases, 54% of invasive breast cancer cases, and 40% of breast cancer deaths in 2005.¹ The direct medical care costs for breast cancer treatment were estimated to exceed \$6 billion in 1996.²
- Breast cancer accounts for up to one-quarter of all cancer-related costs.³
- The risk of breast cancer increases with age.⁴ Population aging in the next three decades is expected to increase the number of breast cancer cases and the economic burden of the disease.
- Mammography screening is a valuable early detection tool because it can identify breast cancer at an early stage, usually before physical symptoms or complications develop, when treatment is more effective and less expensive.
- Women with certain specific family history patterns have an increased risk for developing breast or ovarian cancer associated with mutations in genes known as BRCA1 and BRCA2. Although these mutations are uncommon, public interest in testing is growing.⁵ Further, for women who are positive for a BRCA1 or BRCA2 genetic mutation, prophylactic surgery at a young age significantly improves survival and is cost-effective in comparison to other interventions.⁶
- For the minority of women with a clear, high risk for breast cancer, preventive medication can reduce the risk of certain types of breast cancer although such treatment can also produce serious side effects.⁷ For women at low or average risk for breast cancer, the potential harms of preventive medication may outweigh the potential benefits.

Clinical Preventive Service Recommendations

Breast Cancer (Screening)

U.S. Preventive Services Task Force Recommendation

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

The U.S. Preventive Services Task Force (USPSTF) recommends screening mammography, with or without clinical breast examination (CBE), every 1 to 2 years for women aged 40 and older.⁸

The USPSTF found fair evidence that screening for breast cancer every 12 to 33 months significantly reduces mortality from breast cancer and that the benefits of screening outweigh the associated risks, for women aged 40 and older.⁸

Breast Cancer: Genetic Risk Assessment and BRCA Mutation Testing (Counseling, Testing, and Preventive Treatment)

U.S. Preventive Services Task Force Recommendation

The U.S. Preventive Services Task Force (USPSTF) recommends that women whose family history is associated with an increased risk of deleterious mutations in BRCA1 or BRCA2 genes be referred for genetic counseling and evaluation for BRCA testing.⁹

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

The USPSTF found fair evidence that women with certain specific family history patterns (increased-risk family history) have an increased risk for developing breast or ovarian cancer associated with BRCA1 or BRCA2 mutations. The USPSTF determined that these women would benefit from genetic counseling that allows informed decision making about testing and further prophylactic treatment. This counseling should be done by suitably trained healthcare providers. There is fair evidence that prophylactic surgery significantly decreases breast and ovarian cancer incidence in women who test positive for deleterious BRCA1 or BRCA2 mutations, although there is insufficient evidence to determine other health-outcome benefits from intensive screening or preventive medication in such women.⁹

Note: The U.S. Preventive Services Task Force (USPSTF) recommends *against* routine referral for genetic counseling or routine breast cancer susceptibility gene (BRCA) testing for women whose family history is not associated with an increased risk for deleterious mutations in breast cancer susceptibility. The USPSTF concluded that the potential harms of routine referral for genetic counseling or BRCA testing in these women outweigh the benefits.⁹

Other Recommended Guidance American College of Medical Genetics (ACMG)

The American College of Medical Genetics (ACMG) recommends risk assessment and genetic counseling before testing for BRCA1/BRCA2 mutations in individuals at increased risk, based on a personal or family history of breast cancer, ovarian cancer or both.¹⁰ In a previous guideline published in 1996, the ACMG recommended testing for BRCA1 mutations in high-risk families and population screening of Ashkenazi Jews after discussion of test limitations and appropriate informed consent.¹¹

Evidence Rating:

Expert Opinion

American Society of Clinical Oncology (ASCO)

The American Society of Clinical Oncology (ASCO) recommends that genetic testing be offered when an individual has a personal or family history that suggests a genetic cancer susceptibility, the test can be adequately interpreted, and its results will influence diagnosis or management of the patient or family members at risk for hereditary cancer.¹²

Evidence Rating:

Not Specified

National Comprehensive Cancer Network

The National Comprehensive Cancer Network recommends offering genetic susceptibility testing (after risk assessment and counseling) to individuals who meet the criteria for hereditary breast or ovarian cancer or both.¹³

Evidence Rating:

Not Specified

U.S. Preventive Services Task Force Recommendation

Breast Cancer: (Counseling and Preventive Medication)

The U.S. Preventive Services Task Force (USPSTF) recommends that clinicians discuss preventive medication with women at high risk for breast cancer and at low risk for adverse effects of preventive medication use. Clinicians should inform patients of the potential benefits and harms of preventive medication.¹⁴

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

The USPSTF found fair evidence that treatment with tamoxifen can significantly reduce the risk of invasive estrogen-receptor-positive breast cancer in women at high risk for breast cancer and that the likelihood of benefit increases as the risk for breast cancer increases. Although raloxifene is not now FDA-approved for this use, the USPSTF found consistent, but less abundant, evidence for its benefit as well. The USPSTF found good evidence that estrogen antagonists (e.g., tamoxifen) increase the risk for thromboembolic events (for example, stroke, pulmonary embolism, and deep vein thrombosis) and symptomatic side effects (for example, hot flashes) and that tamoxifen increases the risk of endometrial cancer.¹⁴

The USPSTF concluded that the balance of benefits and harms may be favorable for some high-risk women but will depend on breast cancer risk, risk from potential harms and individual patient preferences.¹⁴

Note: The U.S. Preventive Services Task Force (USPSTF) recommends against routine use of tamoxifen or raloxifene for the primary prevention of breast cancer in women at low or average risk for breast cancer.¹⁴

Other Recommended Guidance American Society of Clinical Oncology (ASCO)

The American Society of Clinical Oncology (ASCO) suggests that women with sufficient risk, based on the Gail Index, be offered tamoxifen to reduce their risk of breast cancer.¹⁵ The Gail Index is a breast cancer risk tool developed by the National Cancer Institute, and is available online (<http://cancer.gov/bcrisktool/>) or by telephone (800-4-CANCER).

Evidence Rating:

Expert Opinion

Information Sources

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

- American Cancer Society (ACS)
- American College of Medical Genetics (ACMG)
- American Society of Clinical Oncology (ASCO)
- Centers for Disease Control and Prevention (CDC)
- International Agency for Research on Cancer (IARC)
- National Cancer Institute (NCI)
- National Committee for Quality Assurance (NCQA)
- National Comprehensive Cancer Network

- National Heart, Lung, and Blood Institute (NHLBI)
- 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

Breast cancer is the most commonly diagnosed non-skin cancer and the second leading cause of cancer death among women in the United States.¹ In 2005, 211,000 women are expected to be diagnosed with breast cancer and 40,000 women are expected to die as a result of breast cancer.¹

Condition/Disease Risk Factors

Risk factors for breast cancer (reported by the USPSTF) include¹⁶:

- A family history of breast cancer (especially a mother or sister with breast cancer)
- Atypical hyperplasia
- Having a first child after the age of 30
- Increasing age

Risk factors reported by other organizations include¹⁷⁻¹⁹:

- Early age at menarche
- Late age at menopause
- Overweight/obesity
- Physical inactivity
- Hormone replacement therapy
- Exposure to radiation

Another risk factor for breast cancer is the presence of genetic markers for the BRCA1 or BRCA2 genes.¹⁹ However, only a *small* proportion of breast cancer cases are attributable to genetic susceptibility. Approximately 2% of adult women in the United States have a family history indicating they are at increased risk of a deleterious mutation in the BRCA1 or BRCA2 gene, and about 1 in 10 women with these histories (2 to 3 per 1,000 adult US women) actually have a mutation.⁵ Among women with a deleterious BRCA1 or BRCA2 mutation, 35% to 84% may develop breast cancer by age 70.⁵

Value of Prevention	
Economic Burden of Condition/Disease	<p>The direct medical care costs for breast cancer treatment were estimated to exceed \$6 billion in 1996.² The total economic burden of breast cancer would be much higher if breast cancer related mortality and morbidity costs were included in this figure. In 2004, for example, the overall cost of cancer (including direct and indirect costs) was estimated to be almost \$190 billion²⁰, and breast cancer could account for up to one-quarter of this total.³ A small proportion of the economic burden of breast cancer is attributable to genetically-related breast cancers.</p> <p>The risk of breast cancer increases with age.⁴ Population aging in the coming decades is expected to increase the number of breast cancer cases and the economic burden of the disease.</p>
Workplace Burden of Condition/Disease	<p>Women aged 40 to 64 years accounted for 61% of <i>in situ</i> cases, 54% of invasive breast cancer cases, and 40% of breast cancer deaths in 2005.¹ The breast cancer medical care costs, productivity losses, and mortality costs among working women in this group is substantial.</p>
Economic Benefit of Preventive Intervention Screening	<p>Screening may reduce breast cancer treatment costs by identifying tumors in their earliest stages when treatment is more successful and less expensive. For example, a study that examined the cancer-care costs among members of a health maintenance organization (HMO) found that the net cost of initial care for breast cancer was \$7,093 when the cancer was identified at the carcinoma <i>in situ</i> stage and to \$10,900 when it was identified at the regional stage (both figures in year 1992 dollars).²¹</p>
Counseling, Testing, and Preventive Treatment	<p>The recognition of BRCA mutations through testing allows for early intervention and treatment. This is important because women who receive early treatment generally have better outcomes. For example, in one research model, a 30-year-old BRCA1 and 2 positive woman could prolong her life by about 1 year by having bilateral oophorectomy, 3.4 years by having bilateral mastectomy, and 4.3 years by having both procedures instead of surveillance alone.⁷</p>
Preventive Medication	<p>The use of preventive medication in carefully-selected, high-risk women can reduce their risk of breast cancer or delay the onset of breast and ovarian cancers. It is estimated that for every 100 women treated with tamoxifen for 5 years, 1.665 expected cancers are delayed or prevented. If breast cancer death is fully prevented by this strategy, then the use of preventive medication (compared to no intervention) would cost \$8,479 per year of life gained.²²</p>
Estimated Cost of Preventive Intervention Screening	<p>In 2004, the private-sector cost of a screening mammography averaged \$51 (range \$0 to \$122).²³ A diagnosis of breast cancer is more costly (\$451 to \$2,520 in year 2002 dollars) as it requires additional tests, interpretations, and office visits.⁴</p>

EVIDENCE-STATEMENT: Breast Cancer (Screening, Counseling, Testing, Preventive Medication, and Treatment)

Counseling, Testing, and Preventive Treatment

In 2004, the private-sector cost of BRCA mutation testing averaged \$53 per test; approximately 95% of all paid claims fell within the range of \$12 to \$201 per test.²³ The cost of genetic counseling averaged \$39 per session; approximately 95% of all paid claims fell within the range of \$0 to \$129 per session.²³ The cost of a preventive mastectomy or oophorectomy varies by location and facility type.

Preventive Medication

The average wholesale price (AWP) of a 1-month supply of tamoxifen citrate is between \$58.38 (generic) and \$128.62 (brand — Nolvadex®).²⁴

Estimated Cost of Treatment

The cost of breast cancer treatment depends on the stage of disease at diagnosis and the procedures or treatments selected. Treatment costs have been reported to range from \$21,287 to \$45,220 per patient. However, terminal care costs for Medicare patients were reported to be as high as \$63,455 (all figures in year 2002 dollars).⁴

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

The cost-effectiveness of breast cancer screening depends on the age of the population screened. Many cost-effectiveness analyses have shown that screening for breast cancer in women 65 years of age and younger reduces mortality at a reasonable cost.¹ A systematic review of cost-effectiveness analyses performed for the USPSTF noted that biennial screening after the age of 65 also reduces mortality at a reasonable cost. However, screening becomes more costly in women with significant comorbidities, such as dementia, or comorbidities that limit life expectancy. For example, the incremental costs per life-year saved for screening beyond age 65 were found to range from \$34,000 to \$88,000 in year 2002 dollars⁴, which compare favorably with most other preventive interventions and to commonly accepted cost-effectiveness benchmarks.¹

Counseling, Testing, and Preventive Treatment

One study, using modeling techniques, concluded that BRCA1 and BRCA2 testing is cost-effective only if women who screen positive proceed with prophylactic surgery.²⁵ The model further suggested that, per life-year saved, combined surgery cost \$20,717, mastectomy cost \$29,970, and oophorectomy cost \$72,780 (all figures in year 1995 dollars).²⁵ Another study, which also used modeling techniques, concluded that for women who are positive for a BRCA1 or BRCA2 genetic mutation, prophylactic surgery at a young age significantly improves survival and is cost-effective in comparison to other interventions.⁸

Preventive Medication

Tamoxifen is cost-effective for women aged 40 to 50 years who are at significant risk for breast cancer.²⁶ Tamoxifen costs \$46,619 per life-year saved for women who begin taking the medication at age 35. For women over the age of 50, the intervention costs more than \$50,000 per life-year saved.²⁷

Preventive Intervention Information

Preventive Intervention: Purpose of Screening

Mammography screening is a valuable early detection tool because it can identify breast cancer at an early stage, usually before physical symptoms or complications develop, and when treatment is more effective and less expensive.

Purpose of Counseling, Testing, and Preventive Treatment

The purpose of family history assessment, counseling, and BRCA mutation-testing is to identify women with certain specific family history patterns that are associated with an increased risk for deleterious mutations in the BRCA1 or BRCA2 gene and an increased risk of breast or ovarian cancer. With the assistance of genetic counseling, women at risk can make an informed decision on testing and treatment options.

Purpose of Counseling and Preventive Medication

The purpose of preventive medication counseling is to educate women at high risk of breast cancer on the benefits and risks associated with tamoxifen.

Benefits and Risks of Intervention Screening

Screening allows for the early detection of breast cancer. Screening is estimated to reduce breast cancer mortality by 20% to 25% during the 10-year period following screening.⁸ The risk of breast cancer increases with age. Therefore, the absolute benefit of screening also increases as a woman ages, at least from age 40 through age 70.¹⁶ Because the risk of breast cancer is higher after age 70, mammography may offer important benefits to older women. However, these benefits may be offset by the fact that many older women, especially the very old and those with other illnesses, will die from other causes before they experience the benefits of early cancer detection.¹⁶ Risks associated with screening include false-positive test results, which may cause undue anxiety, and the inconvenience, occasional complications, and costs associated with biopsies. False-positive test results are common among all types of cancer screening, including mammography; 80% to 90% of abnormal mammogram or clinical breast exam results are false-positive.¹⁶

Counseling, Testing, and Preventive Treatment

The USPSTF determined that women with certain specific family history patterns benefit from genetic counseling that allows informed decision making about testing and preventive treatment (e.g., removal of the breasts and/or ovaries).⁹ The USPSTF found fair evidence that prophylactic surgery significantly decreases the incidence of breast and ovarian cancer among women with a BRCA mutation. Thus, the potential benefits of referral and discussion of testing and prophylactic treatment for these women may be substantial. The inherent risk associated with preventive treatment and surgery, such as patient anxiety and medical errors, may be substantial for some individuals.

The USPSTF concluded that for women whose family history is not associated with an increased risk of deleterious mutations, the harms of routine referral for counseling and testing outweigh the benefits.⁹

Counseling and Preventive Medication

Among women at high risk for breast cancer, an estrogen antagonist (i.e., tamoxifen) has been found to reduce the incidence of invasive breast cancer by approximately one-half.^{14, 28} Estrogen antagonists increased survival by 1.6 years (range 1.0 to 2.1 years) and 2.2 years (range 1.3 to 2.8 years), respectively. Research shows that preventive medication yields more quality-adjusted life years than does prophylactic surgery, even when treatment is delayed to age 40 or 50 years.⁹

Estrogen antagonists are associated with an increased risk of venous thromboembolic disease (deep vein thrombosis and pulmonary embolism); tamoxifen is also associated with an increased risk of endometrial cancer.^{14, 28}

The balance between benefits and harms varies among subgroups of women, depending on age, predicted risk of breast cancer, and hysterectomy status. In general, the balance of benefits and harms of preventive medication is more favorable for women in their 40s who are at increased risk for breast cancer and have no predisposition to thromboembolic events or women in their 50s who are at increased risk for breast cancer, have no predisposition to thromboembolic events, and do not have a uterus. Women are at lower risk for adverse effects from preventive medication if they are younger; have no predisposition to thromboembolic events such as stroke, pulmonary embolism, or deep venous thrombosis; or do not have a uterus.

The USPSTF concluded that routine use of estrogen antagonists for the primary prevention of breast cancer in women at low or average risk for breast cancer would cause more harm than benefit.¹⁴

Initiation, Cessation, and Interval Screening

According to the USPSTF women aged 40 and above should be screened for breast cancer with mammography, with or without CBE (clinical breast examination), every 1 to 2 years.¹⁶ The USPSTF notes that the precise age is not known when the benefits of breast cancer screening first outweigh the associated risks and costs; thus, the specific ages at which screening should begin and cease should consider patient preferences.¹⁶

Counseling, Testing, and Preventive Treatment

Patients identified as high-risk through a clinician risk assessment should be referred for genetic counseling and, if appropriate, follow-up genetic mutation testing. The initiation, cessation, and frequency of counseling is left to the discretion of the clinician. A onetime BRCA test should be administered to at-risk patients who request testing. Preventive treatment including mastectomy and/or oophorectomy should be conducted, as medically necessary, at the discretion of the clinician.

Note: The USPSTF realizes that clinical decisions about patients involve more complex considerations than the evidence alone; clinicians should always understand the evidence but individualize decision making to the specific patient and situation.

Counseling and Preventive Medication

The initiation and cessation of preventive medication therapy with an estrogen antagonist is left to the discretion of the clinician (in discussion with the patient). In general, preventive medication is more favorable for women in their 40s who are at increased risk for breast cancer and have no predisposition to thromboembolic events or women in their 50s who are at increased risk for breast cancer, have no predisposition to thromboembolic events, and do not have a uterus.¹⁴ Women younger than 40 years of age have a lower risk for breast cancer, and thus will not experience as large an absolute benefit from breast cancer preventive medication as older women.¹⁴ Women 60 years of age and older, who have the highest risk for breast cancer also have the highest risk for complications

from preventive medication/chemoprevention with a less favorable balance of benefits and harms.¹⁴

The standard course of preventive medication with tamoxifen in clinical trials is 5 years.²⁹

**Intervention Process
Screening**

Approved screening methods for breast cancer include mammography and, as an adjunct, a clinical breast exam. CBE is a low-cost screening method that provides an opportunity for health professionals to discuss breast health with women.³⁰ Although CBE is not explicitly recommended by the USPSTF, many experts encourage routine CBE.³⁰ However, clinicians who perform routine CBE should understand that there is currently insufficient evidence to determine whether CBE affects breast cancer mortality and that they are likely to increase the incidence of clinical assessments and biopsies.¹⁶ Coverage should also include diagnostic follow-up. Coverage should also include diagnostic follow-up (e.g., biopsies).

**Counseling, Testing,
and Preventive
Treatment**

The clinician should assess the patient's family history of breast cancer to determine the likelihood that the patient has a deleterious BRCA mutation.⁹ If the assessment is positive, the woman should be referred for genetic counseling to help determine if she wishes to have genetic testing. Women may require further counseling after test results are received. A positive test for a deleterious mutation may result in a decision to have the surgical removal of her breasts and/or ovaries. Coverage should include clinician time to evaluate family history for possible referral to a genetic counselor, counseling on the harms and benefits of genetic testing by a qualified practitioner, and preventive treatment (e.g., complete mastectomy with or without reconstructive surgery, oophorectomy).

**Preventive
Medication**

Clinicians should assess a patient's risk for breast cancer and the risk for adverse preventive medication effects when identifying women who may be candidates for preventive medication therapy. Clinicians can assess a patient's risk of developing breast cancer within the next 5 years using risk-factor information from the National Cancer Institute Breast Cancer Risk Tool (the "Gail Index"). Clinicians should discuss the results of the risk assessment, inform the patient of the risks associated with breast cancer, and counsel about the benefits and risks associated with the use of preventive treatment. Clinicians should counsel on the harms and benefits of preventive medication use and prescribe an FDA-approved preventive medication to eligible women who choose to use preventive medication. Coverage should include clinician time to monitor the potential harms/adverse effects associated with preventive medication use and the cost of the preventive medication approved for use by the FDA.

**Treatment
Information**

Health benefits should include provisions for diagnostic and treatment services.

Strength of Evidence for the Clinical Preventive Service Breast Cancer (Screening)

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 fair evidence to recommend screening mammography, with or without clinical breast examination (CBE), every 1 to 2 years for women aged 40 and older.⁸

Strength of Evidence for the Clinical Preventive Service Breast Cancer Genetic Risk Assessment and BRCA Mutation Testing (Counseling, Testing and Preventive Treatment)

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 fair evidence that women with certain specific family history patterns (increased risk family history) have an increased risk for developing breast or ovarian cancer associated with BRCA1 or BRCA2 mutations.⁹

Note: The USPSTF recommended against routine referral for genetic counseling or gene testing for women whose family history is not associated with an increased risk of deleterious mutations as the USPSTF concluded that the potential harms of routine referral for genetic counseling or BRCA testing in these women outweigh the benefits.⁹

Recommended Guidance:

The American College of Medical Genetics (ACMG)

Strength of Evidence: Expert Opinion

- The ACMG recommends risk assessment and genetic counseling before testing for BRCA1/BRCA2 mutations in individuals at increased risk, based on a personal or family history of breast cancer, ovarian cancer or both.¹⁰ In a previous guideline published in 1996, the ACMG recommended testing for BRCA1 mutations in high risk families and population screening of Ashkenazi Jewish individuals after discussion of test limitations and appropriate informed consent.¹¹

The American Society of Clinical Oncology (ASCO)

Strength of Evidence: Not Specified

- The American Society of Clinical Oncology recommends that genetic testing be offered when: an individual has a personal or family history that suggests a genetic cancer susceptibility and the test can be adequately interpreted and its

results will influence diagnosis or management of the patient or family members at risk for hereditary cancer.¹²

The National Comprehensive Cancer Network

Strength of Evidence: Not Specified

- The National Comprehensive Cancer Network recommends offering genetic susceptibility testing (after risk assessment and counseling) to individuals who meet the criteria for hereditary breast or ovarian cancer or both.¹³

Strength of Evidence for the Clinical Preventive Service Breast Cancer (Counseling and Preventive Medication)

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)

B (Recommended/At Least Fair Evidence);

- The USPSTF recommends that clinicians discuss preventive medication with women at high risk for breast cancer and at low risk for adverse effects of chemoprevention. Clinicians should inform patients of the potential benefits and harms of chemoprevention.¹⁴

Note: The USPSTF recommends against routine use of tamoxifen for the primary prevention of breast cancer in women at low or average risk for breast cancer.¹⁴

Recommended Guidance:

American Society of Clinical Oncology (ASCO)

Strength of Evidence: Expert Opinion

- The American Society of Clinical Oncology suggests that women with sufficient risk, based on the Gail Index, be offered tamoxifen to reduce their risk of breast cancer.¹⁶

Authored by:

Campbell KP, Coates RJ, Lanza A, Chattopadhyay S. Breast cancer evidence-statement: screening, counseling, testing, preventive medication, and preventive 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.

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