

## IV. CANCER OVERVIEW

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The cause of most cases of cancer is unknown. However, exposure to substances in the environment increase the likelihood that a person will develop cancer; certain behaviors can increase and other behaviors can decrease this chance. In addition, changes in some genes (called mutations) inherited (or passed on) from parent to child predispose a person to developing cancer. Exposure to substances in the environment, lifestyle behaviors, and the inherited genes combine to influence each individual's chance of developing cancer.

Oregon public health programs use cancer registry data in many ways:

- To identify substances in the environment that can cause cancer and decrease people's exposures to these substances.

- Encourage people to eliminate or reduce behaviors that increase the chance of cancer, for example smoking; and promote behaviors that decrease the chance of developing cancer, for example, getting plenty of exercise and eating a diet high in vegetables and fruit.
- Promote health screening to detect cancer early, while it is still treatable.

The Oregon Partnership for Cancer Control (OPCC) was formed in 2004 to develop and implement the first statewide cancer control plan for Oregon. The OPCC uses Oregon specific cancer data to monitor progress towards reducing the burden of cancer in Oregon. For more information about OPCC, its activities, and the Oregon Comprehensive Cancer Plan, visit [www.healthoregon.org/](http://www.healthoregon.org/) cancer or contact the program at 971-673-0984.

## A. CANCER RISKS

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The lifetime chance of developing cancer for males is about 46% and about 38% for females. Risk factors for cancer include biological predisposition, behaviors, and environmental exposures. While some biological risk factors are inherent and immutable (age, genes), many behavioral and environmental risk factors are modifiable. Behavioral factors that affect cancer risk include tobacco use, viral infections, diet, physical inactivity, and

alcohol intake. In addition, occupational or environmental exposures to radiation, asbestos, secondhand smoke, and other carcinogens contribute to cancers that are potentially preventable. In this section, we summarize the leading known risk factors for cancer. For additional information, please review the National Toxicology Program's *Report on Carcinogens* available at the following website <http://ntp.niehs.nih.gov/ntpweb>.

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### BIOLOGICAL PREDISPOSITION

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Alterations in genes, called mutations, cause the change of a normal cell to a cancer cell. Once a cell becomes cancerous, it multiplies, causing the descendants of the original cell to overgrow the surrounding tissue and eventually spread to other parts of the body. Mutations in multiple cells are almost always required for a cell to become cancerous. There is the potential for a mutation to occur each time a cell divides. Because cells continue to divide over a person's lifetime, mutations accumulate as a person ages. Thus, the risk of developing cancer increases with age. Overall, 75% of cancers in Oregon occur in people over the age of 55 years.

Most often, when more cases of cancer occur in a family than expected by chance alone, no single "cancer gene" can be found. This situation is termed "familial cancer" (as opposed to "inherited cancer"). Familial cancers may be a sign of common gene mutations, shared environment or lifestyles, or a combination of these factors.

Mutations can also be inherited from a parent. If a mutation is inherited, it is present in all of the cells of the body. Therefore, fewer

additional mutations are required in order for the person to develop cancer.

Most inherited mutations increase the chance of developing cancer by only a modest amount. A few increase a person's risk substantially. Two examples are BRCA1 and BRCA2 (short for breast cancer 1 and breast cancer 2). A woman with a mutation in the BRCA1 or BRCA2 gene has an approximately 36-85% chance of developing breast cancer over her lifetime compared to the population risk of about 13%. Lifetime risk estimates of ovarian cancer for women in the general population show that 1.7 percent will get ovarian cancer, compared with 16-60% of women with an altered BRCA1 or BRCA2 gene.

A third example is one of the genes predisposing to Hereditary Nonpolyposis Colon Cancer. A person who inherits a mutation in this gene has about an 80% lifetime risk of developing colon cancer compared to the general population lifetime risk of 2%. Also, the average age of colorectal cancer diagnosis in a person with a HNPCC gene mutation is twenty years earlier than for sporadic colorectal cancer (44 years vs. 64 years). Clues that a

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gene causing a significantly increased risk of cancer is present in a family include: multiple relatives with the same type of cancer, cancer diagnosed at an earlier than usual age, one individual with more than one primary cancer (of either the same type or different types), or very rare cancers.

Melanoma also appears to be influenced by genetics. About 10% of melanoma cases occur in individuals with a family history of melanoma. Individuals who have a first-degree relative with melanoma are eight

times more likely to develop the condition themselves compared to individuals without a family history.

In addition to age and inherited mutations, a third biological factor affecting cancer risk is sex. Some cancers are clearly sex specific because of the involved organ, for example prostate cancer in men and uterine cancer in women. Other cancers are more common among persons of a particular sex. For example, lung cancer is more common in men, and breast cancer is more prevalent in women.

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## MODIFIABLE BEHAVIORS

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**Tobacco Use** – Tobacco use is the greatest preventable risk factor for cancer. Historically, tar has been considered the most important carcinogen in tobacco. However, recent evidence suggests that nicotine disrupts apoptosis, or programmed cell death, which can lead to tumor initiation, progression, or metastasis. Apoptosis is needed to destroy abnormal cells that are a threat to the body, such as cells with DNA damage due to age or an exposure, and is a central self-defense mechanism against cancer. This may explain the synergistic effect smoking has when combined with other exposures, such as sun exposure. Because of its overwhelming importance as a carcinogen, we have devoted an entire section of this report to the effects of smoking tobacco. (See *Tobacco and Cancer*.)

**Diet** – Dietary factors appear to increase the risk of developing many cancers. The varying incidence in different parts of the world suggests that diet plays an important role in the development of oral,

esophageal, and stomach cancers. Population studies suggest that persons who consume a high-fiber, low-fat diet have a lower risk of developing colorectal cancer. Comparative studies have shown that prostate cancer rates are generally higher in countries in which the population consumes more animal fat.

**Physical Activity** – Epidemiologic studies suggest that increased physical activity decreases risk of breast, colorectal, and pancreatic cancers. The association has been noted for occupational, transportation-related, and leisure time physical activity.

**Obesity** – People who are overweight are at increased risk of multiple cancers, including breast, colorectal, endometrial, kidney, pancreatic, oral, and esophageal cancers.

**Alcohol Use** – Heavy alcohol consumption is a risk factor for cancers of the oral cavity, pharynx, and larynx. Smoking and alcohol consumption result in a synergistic effect, producing a greater cancer risk than would be expected if their effects were merely additive.

These two behaviors account for approximately three-fourths of all oral cancers in the United States. In addition, heavy alcohol consumption increases the risk of developing esophageal and liver cancers and has been implicated in development of cancers at other sites.

**Reproductive Behavior** – Several epidemiological studies suggest that reproductive patterns influence breast cancer risk. Prolonged exposure to natural and therapeutic estrogen is believed to raise the risk of breast cancers slightly. The number of menstruating years for a woman is one risk factor; early menarche and late menopause increase a woman's risk. An early age at first pregnancy and a high number of full-term pregnancies are protective factors. The effect of lactation is still not clear; however, there is evidence of an increasing protective effect with the greater number of months a woman breastfeeds.

**Sexual Behavior** – The risk of cervical cancer is linked with the onset of sexual activity. The risk is higher among women who become sexually active at an early age and who have multiple sexual partners. This risk is related to the risk of exposure

to human papilloma viruses (HPV), which have been identified as a cause of cervical cancer. Several different types of HPV infect the genital tract. Some of these cause genital warts. Other types appear to cause cervical dysplasia and cervical cancer. Infection with HPV is the strongest risk factor for developing cervical cancer. HPV is spread primarily through sexual contact, and about 40 HPV variants have been linked to other cancers of the anus, vulva, vagina, penis, oropharynx, mouth, and skin. A vaccine for HPV was approved by the Food and Drug Administration (FDA) in the summer of 2006 and CDC's Advisory Committee on Immunization Practices recommends routine vaccination of females age 11-12. The HPV vaccine is effective against four strains of HPV that are estimated to cause 70% of cervical cancer.

Sexual activity may also be related to the development of prostate cancer. One study has shown greater sexual activity and frequency of venereal disease in prostate cancer cases compared to controls. This suggests the possibility that some cases of prostate cancer may also result from a sexually transmitted agent; however, no culprit has been identified.

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## ENVIRONMENTAL EXPOSURES

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**Environmental Contamination** – Exposure to carcinogens in the environment is a risk factor for cancers. However, assessing exposure to environmental contamination is particularly difficult due to the lag time between exposure and diagnosis, as well as the complexity of determining an individual's or community's exposure.

Currently, such exposures are thought to contribute to a relatively small proportion of all cancer diagnoses. However, there is sustained concern among the public about environmental hazards, and researchers are continually improving research techniques to address such issues.

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**Secondhand smoke** – Exposure to secondhand smoke increases the risk of lung cancer in a non-smoker. A non-smoking spouse of a heavy smoker will have double the risk of developing lung cancer compared to a non-smoking spouse of a non-smoker.

**Ionizing Radiation** – Sources of exposure to ionizing radiation include medical imaging and treatment (x-rays, radiotherapy), radioactive elements in the soil and air (uranium, radon gas), nuclear weapons, and occupational exposure (such as that occurring among nuclear shipyard workers). Ionizing radiation has been related to an increased risk of several cancers, including leukemia, thyroid, breast, and lung cancers.

**Occupational Exposures** – Many occupational exposures have been associated with increased risk of developing certain cancers. For instance, workers exposed to aniline dyes and certain solvents are at increased risk for bladder cancer. Miners exposed to radon gas have an increased risk of developing lung cancer. Asbestos exposure is the primary risk factor for developing mesothelioma, and workers exposed to vinyl chloride are at increased risk for developing angiosarcoma of the liver.

**Sun Exposure** – Epidemiologic studies have identified a strong relationship between being sunburned as a child or adolescent and developing melanoma as an adult. Exposure to sun also increases the risk of developing basal and squamous cell carcinomas for the skin. While the use of sunscreen is recommended for general skin health, there is limited evidence that sunscreen use can prevent skin cancers. Therefore, using sunscreen is not a substitute for avoidance of sun exposure.

**Viral Infections** – In addition to HPV and its contributory role in developing cervical, vulvar, and penile cancers (*See Sexual Behavior*), several other viruses have been associated with cancers. These include Epstein-Barr virus, which has been associated with Burkitts lymphoma, nasopharyngeal carcinoma, and Hodgkin lymphoma; hepatitis B and C virus, which increase the risk of hepatocellular carcinoma; HTLV-1 virus, which causes adult T-cell leukemia, and the human immunodeficiency virus (HIV), which has been associated with non-Hodgkin lymphoma and Kaposi sarcomas.

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## UNKNOWN FACTORS

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The causes of many cancers are still unknown. For instance, most breast cancers (80%) occur in women with no identifiable risk factors other than being female and post-menopausal. Colorectal cancers frequently occur in individuals without any known risk factors other than

age. This emphasizes the importance of population-based preventive screening so that these cancers can be identified early at the most treatable stage. (*See Cancer Screening and Prevention* for recommendations on preventive screenings.)

## B. TOBACCO AND CANCER

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Smoking contributes to about one in every five deaths in the US and is one of the most important modifiable risk factors leading to premature death. Cigarette smoking resulted in over one million years of potential life lost (YPLL) before age 65 in 1990 alone. More than 6,000 Oregonians die annually from tobacco-related disease. Tobacco annually claims more lives than AIDS, drug and alcohol abuse, motor vehicle crashes, murders, and fires combined. In 2003, more than 500,000 Oregon adults smoked

cigarettes, and nearly 100,000 adults chewed tobacco. For most smokers, addiction to tobacco began in their youth. Despite gains in preventing Oregon youth from starting to smoke, 10% of 8<sup>th</sup> graders and 19% of 11<sup>th</sup> graders still smoke, and 5% of 11<sup>th</sup> grade males chew tobacco.

Although lung cancer is perhaps the most well-known and well-publicized disease linked to tobacco use, a variety of other illnesses and cancers are associated with tobacco exposure.

### TOBACCO-ASSOCIATED SITES

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**Lung cancer** continues to receive enormous amounts of media attention, and its association with tobacco use is a source of numerous recent and pending lawsuits. It is estimated that 85% of all lung cancers are etiologically related to smoking, and smoking confers 12 to 22 times the risk of dying from lung cancer. Other factors, such as occupational and environmental exposures, play a much lesser role in the development of lung cancer. Non-smokers exposed to second-hand smoke have twice the risk of developing lung cancer compared to non-smokers without passive tobacco smoke exposure.

Most people who develop lung cancer die from the disease, and smoking prevention and cessation remain the best hope for reducing mortality from this cancer. After ten years of smoking cessation, the risk of developing lung cancer falls to about 50% of that of a continuing smoker. At 20 years, the risk approaches that of a non-smoker.

**Oral cancers** include those of the tongue, gums, inner cheeks, lips, tonsils, and palate, and are highly associated with tobacco and heavy alcohol use. These behaviors have a

synergistic effect on oral cancer risk. Although oral cancers only account for about 3% of all Oregon invasive malignancies, they are highly preventable because the use of tobacco and alcohol accounts for approximately 75% of these cancers. Preventive measures for these cancers include discouraging the initiation of tobacco use, encouraging the cessation of smoking and smokeless tobacco, and decreasing alcohol use. There is good evidence that oral cancer risk declines quickly with cessation of smoking or smokeless tobacco use. In fact, little or no elevation in risk was found among those who had quit smoking for ten or more years.

**Bladder cancer** is strongly linked to smoking. Carcinogens in the smoke are absorbed into the bloodstream and partially excreted in the urine. Since the bladder collects and holds urine, the lining of the bladder wall is exposed to carcinogenic tobacco by-products for long periods of time. Cigarette smokers develop bladder cancer two to three times more often than non-smokers do, and the risk increases with the quantity smoked. Heavy smokers have bladder cancer risks up to five times those of non-smokers.

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**Cervical cancer** is most strongly associated with the presence of the human papilloma virus (HPV); however, smoking is also associated with elevated risk for cervical cancer. Studies that controlled for other factors, such as age at first intercourse and number of sexual partners, have found this association with smoking to persist. The Pap smear is a useful screening test to detect early stage and precancerous lesions. Safe sexual practices and abstinence from tobacco are the most effective primary prevention strategies.

**Pancreatic Cancer** is often diagnosed at later stages when it is difficult to treat because symptoms are frequently vague. Smoking is a significant risk factor for pancreatic cancer. Increased smoking increases the risk of developing pancreatic cancers in a dose-dependent fashion up to two times the baseline risk. Eliminating any

modifiable risk factor, specifically smoking, is important to reduce the burden of this disease.

**Gastrointestinal cancers** have also been linked to smoking. The strength of the relationship between tobacco and these cancers declines with progression from the esophagus downward to the rectum. Heavy smokers have about five times the risk of developing esophageal cancer, and between one and three times the risk of developing stomach cancer. Recently, several studies have suggested that smoking may be related to adenocarcinoma of the bowel after a long latent period, and other studies have suggested a link between smoking and colon polyps. Smokers also have a risk of anal cancer eight times that of non-smokers. Although the anus is at the distal end of the gastrointestinal tract, the anal canal is lined with squamous epithelium, which may be a factor in the stronger association between tobacco smoke and anal cancer.

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## TOBACCO USE CESSATION

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Tobacco use cessation is always advisable because the risk of developing tobacco-related cancers is correlated with the amount of tobacco exposure. Cutting back or, ideally, quitting smoking altogether not only reduces the risk of the aforementioned cancers, but also decreases the morbidity

associated with a variety of other illnesses including chronic bronchitis, emphysema, heart disease, asthma, and stroke. The evidence is clear that quitting use of tobacco early can play a significant role in an individual's health and well-being.

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## TOBACCO PREVENTION EFFORTS

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Prevention efforts in Oregon have resulted in a dramatic drop in youth and adult tobacco use. Much of this decrease can be attributed to Oregon's statewide campaign against tobacco use. In November 1996,

Oregon voters passed Measure 44, an initiative that raised taxes on tobacco and dedicated 10% of the new revenue to tobacco prevention and education. Oregon started a comprehensive tobacco prevention program in 1997. The

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program included passage of smokefree workplace ordinances, community education activities, tobacco cessation programs, school-based anti-tobacco programs, anti-tobacco commercials, and billboard advertising. In 2003, there were 2 billion fewer cigarettes sold in Oregon compared to 1996. An additional 2,700 infants were born without fetal exposure to tobacco smoke, because of the decrease in the percentage of mothers who smoked during pregnancy between 1996 and 2003. Besides improved health among Oregonians, reduced tobacco use results in monetary savings in Oregon. In 2002, tobacco use cost Oregonians more than \$1.0 billion in medical care for those made ill by tobacco, and another \$1.0 billion in lost productivity. The reduction in low birth weight babies saved an estimated \$2 million in neonatal medical costs for 2002.

Since 1996, Oregonians' tobacco use has declined more rapidly than the rest of the nation. However, in 2003, the Oregon State Legislature reallocated the Measure 44 funding and dismantled the Tobacco Prevention and Education Program (TPEP) to address existing budget constraints. Funding for TPEP was subsequently reinstated but at less than half the level that voters approved with Ballot Measure 44. Nonetheless, tobacco prevention activities are taking place in several communities around the state. The Oregon Tobacco Quit Line (1-877-270-STOP) is also currently available for Oregonians wanting to quit smoking or chewing tobacco. Since its inception in 1998, the quit line has helped more than 30,000 Oregonians who called seeking help. Follow-up surveys indicate that 20% of those callers were tobacco-free six months after the telephone counseling; this is twice the rate seen among those attempting to quit without quit line support.

## C. CANCER SCREENING AND PREVENTION

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In addition to engaging in preventive behaviors, people can reduce their cancer burden by receiving appropriate screening tests. Many cancers, if diagnosed at an early stage, are curable.

The US Preventive Services Task Force (USPSTF) is an independent panel of experts in primary care and prevention that systematically reviews the evidence for the effectiveness of clinical preventive services and develops recommendations for their use.

This section lists the USPSTF recommendations for people at average risk for cancer. Individuals with a personal or family history of cancer or other risk factors that increase their personal cancer risk should consult their physician for individualized recommendations.

The complete USPSTF recommendations are available on the web at: <http://www.ahcpr.gov/clinic/uspstfix.htm>.

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### RECOMMENDATIONS

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**Mammography** – The data are clear that screening women 50-69 years of age every one to two years is of benefit in detecting early stage breast cancer. Estimates of mammography sensitivity in detecting breast cancer range between 75% and 88%. In numerous studies, regular mammography reduced breast cancer mortality in women older than 50 years of age by 20-30%.

The data are less compelling for routine mammography among women 40-49 years of age. Screening in this age group may be less effective due to the greater density of the premenopausal breast. Routine population-based mammography for younger women results in a higher false-positive rate than for post-menopausal women, which can lead to undue patient anxiety and potentially unnecessary diagnostic tests.

Beginning September 2002, the USPSTF began recommending screening mammography, with or without clinical breast examination (CBE), every one to two years for women aged 40 and older. These recommendations correlate with Centers for Disease Control and Prevention (CDC),

National Cancer Institute (NCI), American Cancer Society (ACS), American College of Surgeons (ACoS), and American College of Radiologists (ACR) recommendations.

**Pap Smear** –The Papanicolaou (Pap) test can detect both precancerous conditions and cervical cancer and has been credited with the decline in cervical cancer diagnoses and deaths seen in the United States over the past few decades. The USPSTF recommends beginning Pap screening within three (3) years of onset of sexual activity or age twenty-one (whichever comes first) and screening at least every three years. The task force recommends against routine screening of women older than 65 if they have had three recent normal Paps and are not otherwise at high risk for cervical cancer. ACS and American College of Obstetricians and Gynecologists (ACOG) recommend annual screenings until a woman is age 30 or older. ACS and ACOG recommend screening every 2-3 years for women over 30 with three (3) negative Pap tests. ACS recommends stopping screening for women over 70 with three recent, consecutive negative tests and no abnormal tests in

three recent, consecutive negative tests and no abnormal tests in 10 years. ACOG does not recommend an upper age-limit for screening cessation.

This test should be considered for all women with a cervix—not just women of childbearing age. Efforts need to be increased to ensure post-menopausal women are receiving this test. It is important that women seek the advice of a physician about when to begin, how often, and when to discontinue cervical screenings—especially if they are at higher-than-average risk of cervical cancer.

#### **Fecal Occult Blood Tests (FOBT), Sigmoidoscopy, Colonoscopy, & Double-Contrast Barium Enema**

Routine screening for colorectal cancer is recommended for persons 50 and older. Screening methods include FOBT (a chemical test for blood in stool), sigmoidoscopy (direct visualization of the lower one-third of the bowel using a flexible fiberoptic endoscope), colonoscopy (visualization of the entire colon with a flexible scope), and barium enema (a series of x-rays). The USPSTF does not specify a particular combination of these methods or frequency of screening. However, annual FOBT and sigmoidoscopy every 3-5 years has been advocated by the ACS and other organizations starting at age 50. New data suggest that a full colonoscopy every ten

years may be a suitable alternative screening strategy to improve the sensitivity of colorectal cancer detection.

**Regular Physical Exams** – Clinical exams detect cancer early, particularly breast and oral cancers. A rough, whitish plaque or reddish patch on the mucous membrane frequently precedes oral cancers and can be identified during a regular physical exam. Periodic examination for and treatment of these precancerous conditions could nearly eliminate oral cancers.

**Genetic Testing and Genetic Counseling** - Individuals with multiple relatives with the same type of cancer, cancer diagnosed at an earlier than usual age, one individual with more than one primary cancer (of either the same type or different types) may benefit from genetic testing for a known cancer gene. Individuals considering a genetic test should first receive genetic counseling for an in-depth family history evaluation and discussion of the risks and benefits of genetic testing.

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

Screening the general population for mutations in genes that increase the risk for cancer is not recommended.