

IV. Cancer Overview

A. *Cancer Risks*

Risk factors for cancers include biological predisposition (genetics), individual behaviors, and environmental exposures. While some risk factors are inherent and immutable (age, sex, genes), other factors are modifiable and preventable (tobacco use, diet, environmental exposures). No single factor can determine whether or not a person will get cancer; genetic, lifestyle, and environmental factors together influence the risk of developing cancer.

Fifteen percent of all cancers have a recognized familial basis (in other words, 85% of cancers occur in people without a family history of cancer). Familial cancers may reflect both shared genes and shared environments. It is estimated that 80% of all cancers are due to environmental and lifestyle factors which means they are potentially preventable. Internationally, cancer incidence varies widely by country for many cancers. Studies have shown that immigrants gradually acquire the cancer rates of their adopted countries as they become acculturated. This illustrates the considerable influence of environmental and lifestyle factors on cancer incidence.

Environmental and lifestyle factors that affect cancer risk include tobacco use, viral infections, radiation, diet, physical inactivity, and alcohol intake. In addition, occupational or environmental exposures to asbestos, second-hand smoke, and other carcinogens contribute to cancers that are potentially preventable. These exposures are likely to interact with genetic factors to determine an individual's risk of developing cancer. In this section, we summarize the leading known risk factors for cancer.

Biological Predisposition

As an individual ages, his or her risk of developing cancer increases. Overall, 75% of cancers in Oregon occur in people over the age of 55 years. A person's sex also affects his or her risk of developing cancer. Certain cancers are clearly sex specific (cervical in women, prostate in men). Other cancers may be more common, but are not limited to, among persons of a particular sex (such as breast cancer among women).

Genetic predisposition appears to play an important role in many cancers, as demonstrated by clustering of cancer in some families. A woman's risk of breast cancer is doubled if her mother or sister has had breast cancer. If both the woman's mother and sister have had breast cancer, the risk is increased about four times. Risk is further in-

creased when the relative was diagnosed before age 50. Two genes have been identified as “breast cancer genes”: BRCA1 and BRCA2. Together, they account for 5% - 10% of all breast cancers.

Melanoma also appears to have a genetic component. In general, the lighter one’s skin, the higher one’s risk of developing melanoma. The susceptibility to develop melanoma is related to the propensity for sunburn, which is inherited. About 10% of melanoma cases occur in individuals with a family history of melanoma. Individuals who have one affected relative have a two-fold increased risk of melanoma; those with two affected relatives have a five-fold increased risk. Researchers have identified several genes that may mediate this familial risk.

There are two recognized forms of hereditary colorectal cancer: familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer (HNPCC). In addition to these well-described hereditary cancers, a family history of colorectal cancer may increase a person’s risk of colon cancer two to four fold. Twenty percent of colorectal cancer cases have a recognized familial component. Individuals with first-degree relatives who have had colorectal cancer are at increased risk for developing this cancer, especially if the relative was diagnosed before age 45. If several first-degree relatives have a history of colorectal cancer, the risk is even greater.

Modifiable Behaviors

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 use of 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 both occupational, transportation, and leisure time physical activity.

Obesity – People who are overweight are at increased risk of several 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 in those who do both 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 cancer 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, and two of the HPV types 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.

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.

Environmental Exposures

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.

Environmental Tobacco Smoke (ETS) – Better known as second-hand smoke, ETS increases the risk of lung cancer in non-smokers. Spouses of heavy smokers have about double the risk of lung cancer compared to spouses of non-smokers.

Ionizing Radiation – Sources of exposure and ionizing radiation include medical imaging and treatment (x-rays, radiotherapy), radioactive elements in the soil and air (uranium, radon gas), nuclear weapons, and occupational exposures (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 getting sunburned as a child or adolescent and developing melanoma as an adult. Exposure to the sun also increases the risk of developing basal and squamous cell carcinomas of the skin. Using sunscreen reduces the risk of basal and squamous cell carcinoma but has not been shown to reduce the risk of melanoma. 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 cancer (see *Sexual Behavior*), several other viruses have been associated with cancers. These include Epstein-Barr virus, which causes Burkitts lymphoma; nasopharyngeal carcinoma; Hodgkin lymphoma; hepatitis B (and possibly C) virus, which increase the risk of hepatocellular carcinoma; and HTLV-1 virus, which causes adult T-cell leukemia.

Unknown Factors

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 cancer also frequently occurs 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.)

Causes of other types of cancers are also chiefly unknown, and there is continuing public concern about environmental contamination and industrialization possibly contributing to increasing cancer rates. However, it may not be prudent to use cancer incidence as a rationale for environmental action. Cancers diagnosed today represent

exposures that occurred many years ago. To improve public health, environmental and other exposures that place citizens' health at risk should be addressed before they lead to increased cancer incidence. Such primary prevention is particularly important for cancer sites that have no early detection methods or viable treatment regimens.

B. Tobacco and Cancer

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, and over five million total YPLL 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 2002, 500,000 Oregon adults smoked, and 60,000 adults chewed tobacco. For most smokers, addiction to tobacco began in their youth. Despite gains in preventing youth from starting to smoke, 50,000 Oregon youth still smoke and 17,000 chew tobacco.

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

Lung Cancer

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 - 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 "secondhand smoke", or ETS, 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

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 chewing 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

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, and the risk increases with the quantity smoked. Heavy smokers have bladder cancer risks up to five times those of non-smokers.

Cervical Cancer

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

Smoking is also 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. Because symptoms are frequently vague, pancreatic cancer is often diagnosed at later stages when it is difficult to treat. Therefore, eliminating any modifiable risk factor, specifically smoking, is important to reduce the burden of this disease.

Cancers of the Gastrointestinal Tract

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 large bowel polyps. Smokers also have a risk of anal cancer eight times higher than 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.

Tobacco Use Cessation

Tobacco 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.

Tobacco Prevention Efforts

Prevention efforts in Oregon have resulted in a dramatic drop in youth and adult smoking. 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 smoking prevention program in 1997. The program includes passage of smokefree workplace ordinances, community education activities, smoking cessation programs, school-based anti-smoking programs, anti-smoking commercials, and billboard advertising. Compared to 1996, there are 75,000 fewer adult and 25,000 fewer youth smokers in Oregon, and 60,000 fewer adults are using smokeless tobacco in 2002. In 2002, there were 1.5 billion fewer cigarettes sold in Oregon compared to 1996. In addition, 2,200 fewer pregnant women smoked, which resulted in 57 fewer low birth weight babies born in 2002 than in 1996. Besides health benefits, reduced tobacco use results in monetary savings in Oregon. The reduction in low birth weight babies saved over \$1 million in neonatal medical costs for 2002. Overall, the 2002 reduction in smoking saved nearly \$40 million a year in direct medical costs of which one fourth of the savings were in the Oregon Health Plan.

Data from 2003 showed Oregonian's tobacco use declining more rapidly than the rest of the nation, particularly for youth who chew and pregnant women who smoke. Unfortunately, the Oregon State Legislature reallocated the Measure 44 funding and dismantled the Tobacco Prevention and Education Program (TPEP) to address existing budget constraints. Recently, TPEP was reinstated at about 30% of past funding. As a result, the Oregon Tobacco Quit Line is currently available again for Oregonians wanting to quit smoking or chewing tobacco. Since its inception in 1998, the quit line has helped more than 60,000 Oregonians who called seeking help. Follow up surveys indicate that 20% of those callers (12,000) were tobaccofree 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

In addition to 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 of effectiveness and develops recommendations for clinical preventive services for both acute and chronic disease.

The USPSTF recommends the following tests 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>.

Recommendations

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. Mammography 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. A high false-positive rate 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. Although there is still considerable debate on this subject, these recommendations now 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.

According to the USPSTF, there is no clear evidence of an ideal interval for mammography screening among women in the 40-49 age group. The USPSTF states, “The absolute benefit is smaller because the incidence of breast cancer is lower among women in their 40s than it is among older women. The USPSTF concluded that the evidence is also generalizable to women aged 70 and older (who face a higher absolute risk for breast cancer) if their life expectancy is not compromised by comorbid disease. The absolute probability of benefits of regular mammography increases along a continuum with age, whereas the likelihood of harms from screening (false-positive results and unnecessary anxiety, biopsies, and cost) diminish from ages 40-70. The balance of benefits and potential harms, therefore, grows more favorable as women age. The precise age at which the potential benefits of mammography justify the possible harms is a subjective choice.” This decision can be made between a woman and her provider after a discussion of the benefits and risks of mammography and subsequent workup.

Pap Smear – The Papanicolaou (PAP) test can detect both precancerous conditions and cervical cancer. The Pap test has been credited with the decline in cervical cancer diagnoses and deaths seen in the United States over the past few decades. The USPSTF states that direct evidence to determine the optimal starting and stopping age and interval for screening is limited. But the ACS, CDC, and the USPSTF recommend beginning screening within three years of onset of sexual activity or age twenty-one (whichever comes first) and screening at least every three years. The CDC also has national guidelines that recommend that, after a woman has a Pap test each year for three years in a row, and test results show there are no problems, she can then get the Pap test once every two to three years.

This test should be considered for all women with a cervix—not just women of childbearing age. Efforts need to be increased to ensure that women aged sixty and over are also receiving this test. Routine Pap testing is certainly appropriate for post-menopausal women, although the USPSTF recommends against screening women over age 65 if they have a recent history of normal screening and are not otherwise at high risk for cervical cancer. It is important that women seek the advice of their physician about when to begin screening, how often to be screened, and when they can 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 – 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 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 are another means of detecting cancer early, particularly for breast and oral cancers. A rough, whitish plaque or a 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 Counseling and Testing – Though not appropriate for routine screening, in the general population, individuals with a strong family history for certain cancers (e.g., breast, ovarian, colorectal cancer) may benefit from targeted, more frequent screening beginning at an earlier age. Genetic testing can also be done to determine if they carry one of the known high-risk genes for cancer (such as BRCA1 or BRCA2). Referral to a genetic counselor for in-depth evaluation of family history and discussion of the risks and benefits of genetic testing may be appropriate.