

## Risk Factor Summary for Bladder Cancer

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### How to Use this Factsheet

This risk factor summary was developed to serve as a general fact sheet. It is an overview and should not be considered exhaustive. For more information on other possible risk factors and health effects being researched, please see the References section.

A risk factor is anything that increases a person's chance of developing cancer. Some risk factors can be controlled while others cannot. Risk factors can include *hereditary conditions, medical conditions or treatments, infections, lifestyle factors, or environmental exposures*. Although risk factors can influence the development of cancer, most do not directly cause cancer. An individual's risk for developing cancer may change over time due to many factors, and it is likely that multiple risk factors influence the development of most cancers. Knowing the risk factors that apply to specific concerns and discussing them with your health care provider can help to make more informed lifestyle and health care decisions.

For those cancer types with environmentally-related risk factors, an important factor in evaluating cancer risk is the route of exposure. This is particularly relevant when considering exposures to chemicals in the environment. For example, a particular chemical may have the potential to cause cancer if it is inhaled, but that same chemical may not increase the risk of cancer through skin contact. In addition, the dose and duration of time one might be exposed to an environmental agent is important in considering whether an adverse health effect could occur.

Gene-environment interactions are another important area of cancer research. An individual's risk of developing cancer may depend on a complex interaction between their genetic makeup and exposure to an environmental agent (for example, a virus or a chemical contaminant). This may explain why some individuals have a fairly low risk of developing cancer as a result of an environmental factor or exposure, while others may be more vulnerable.

### Key Statistics

The American Cancer Society estimates that bladder cancer will affect 74,000 people in the U.S (56,320 men and 17,680 women) in 2015, accounting for 6.6% of all cancers among men and 2.2% among women.<sup>1, 2</sup> In Massachusetts, bladder cancer is expected to account for approximately 5.3% of all cancers diagnosed among males and females combined.<sup>1</sup>

Males are three to four times more likely to develop bladder cancer than females, and whites are twice as likely to develop the disease as blacks.<sup>2, 6</sup> The risk of bladder cancer increases with age and nearly 90% of people with this cancer are over the age of 55 at the time of diagnosis.<sup>2</sup>

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### Types of Bladder Cancer

The term "cancer" is used to describe a variety of diseases associated with abnormal cell and tissue growth. Cancers are classified by the location in the body where the disease originated (the primary site) and the tissue or cell type of the cancer (histology).

Transitional cell carcinoma, also called urothelial carcinoma, is the most common type of bladder cancer, accounting for over 90% of all bladder cancers.<sup>2, 6</sup> These tumors can further be subdivided into two types: papillary tumors and flat carcinomas.

Papillary tumors have slender finger-like projections that grow from the inner surface of the bladder toward the hollow center. Papillary tumors often grow toward the center of the bladder without growing into the deeper bladder layers. These tumors are called noninvasive papillary cancers although they can become invasive if they penetrate deeper into the bladder wall.<sup>2</sup>

Flat carcinomas may only involve the layer of cells in the bladder lining. This type of tumor is known as a noninvasive flat transitional cell carcinoma or a flat carcinoma in situ (CIS). Some flat carcinomas can go on to grow into the deeper layers of the bladder, even into the muscle layer. These are then called invasive transitional cell carcinomas.<sup>2</sup>

Other less common subtypes of bladder cancer include squamous cell carcinomas, which account for approximately 1-2% of all bladder cancers, and adenocarcinomas, which account for approximately another 1%. Small cell carcinomas are rare as they account for less than 1% of bladder cancers. Although rare, sarcomas are cancers that start in the muscle tissue of the bladder and are not covered in this risk factor summary.<sup>2</sup>

### Established Risk Factors

#### *Hereditary Conditions*

People with a family history of bladder cancer are at increased risk.<sup>2,10</sup> For a small number of people, this is because they inherited a genetic syndrome. For example:

- A mutation of the retinoblastoma (Rb1) gene can cause cancer of the eye in infants, and also increases the risk of bladder cancer.
- Cowden disease, caused by mutations in a gene called PTEN, is linked to cancers of the breast, thyroid and bladder.
- Hereditary nonpolyposis colorectal cancer (HNPCC) syndrome (also known as Lynch syndrome) is mainly linked to colon and endometrial cancer. People with this syndrome also have an increased risk of bladder cancer.
- Mutations in the GST or NAT genes, which slow the body's ability to break down toxins, may increase risk of bladder cancer.<sup>2</sup>

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### *Medical Conditions and Treatments*

Certain bladder birth defects may increase the risk of bladder cancer. Before birth, there is a connection between the belly button and the bladder called the urachus. This connection normally disappears before birth but if part of this connection remains after birth, it could become cancerous. Cancers starting in this way are rare, causing less than half of 1% of bladder cancers. However, it does represent about one third of the adenocarcinomas of the bladder, which are also rare.<sup>2</sup>

Another rare birth defect, called exstrophy, greatly increases a person's risk of developing bladder cancer. In this case, tissues of the bladder fail to close completely, leaving a defect in the wall of the abdomen. Exstrophy leaves the bladder exposed to chronic infection and may eventually lead to adenocarcinoma of the bladder.<sup>2</sup>

Having a previous cancer diagnosis in any part of the urinary tract lining puts a person at higher risk of developing another tumor.<sup>2</sup>

People who have taken the chemotherapy drugs cyclophosphamide (Cytoxan) or ifosfamide (Ifex) have a higher risk of developing bladder cancer. People who are treated with radiation to the pelvis are also more likely to develop bladder cancer.<sup>2</sup>

### *Environmental Exposures*

Arsenic in drinking water has been associated with an increased risk of bladder cancer. The chance of being exposed to arsenic in drinking water depends on where you live and the source of your drinking water.<sup>2</sup> Arsenic levels tend to be higher in drinking water that comes from groundwater sources, such as wells, as opposed to surface water sources, such as lakes or reservoirs.<sup>3</sup>

### *Lifestyle*

Cigarette smoking is a well-established risk factor for bladder cancer. Smokers are at least three times as likely to develop bladder cancer compared to nonsmokers.<sup>2</sup> The risk of developing bladder cancer increases with the number of packs smoked per day and with duration of smoking. Further, the risk of bladder cancer may be higher in women than in men who smoke comparable numbers of cigarettes. Smoking cessation has been found to reduce the risk of developing bladder cancer by 30% to 60%.<sup>11</sup> If you would like information about quitting smoking, contact the Massachusetts DPH Tobacco Cessation and Prevention Program at 1-800-Quit-Now or 1-800-784-8669.

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### Possible Risk Factors

#### *Medical Conditions*

Urinary infections, kidney and bladder stones, and other causes of chronic bladder irritation have been linked with bladder cancer (especially squamous cell carcinoma of the bladder), but they do not necessarily cause bladder cancer.<sup>2, 6</sup>

#### *Infections*

Infection with *Schistosoma haematobium* (a parasite found in Africa and other parts of the world) is thought to be associated with the development of bladder cancer, although this is rare in the U.S.<sup>2, 11</sup>

#### *Environmental Exposures*

Workplace exposure to certain industrial chemicals, such as benzidine and beta-naphthylamine, increases the risk of bladder cancer.<sup>2, 11</sup> A higher risk of bladder cancer has been observed among aromatic amine manufacturing workers as well as among workers in the dye, rubber, leather, textiles, metal, printing, and paint products industries. Studies also suggest that hairdressers, machinists, and truck drivers may be at increased risk of bladder cancer.<sup>10, 11</sup> Further, the risk of bladder cancer from occupational exposures may be higher among smokers.<sup>11</sup>

#### *Lifestyle*

People who do not drink enough liquids on a regular basis may have a higher risk of bladder cancer.<sup>2, 11</sup>

### Other Risk Factors That Have Been Investigated

Though animal studies suggested a possible relationship, epidemiologic studies in people have not substantiated a relationship between artificial sweeteners, such as saccharin, and bladder cancer. Coffee consumption was once suggested as a risk factor for bladder cancer, but studies have not found a clear association.<sup>11</sup>

Initial occupational studies of hairdressers pointed to a possible association between hair dye exposure and bladder cancer but more recent population-based studies of hair dye use have not found an elevated risk.<sup>4, 11</sup> In 2012, the International Agency for Research on Cancer (IARC) found limited evidence of an association between exposure to diesel exhaust and bladder cancer.<sup>7</sup>

Concerns have been raised about chlorine by-products in drinking water and bladder cancer risk, but several decades of research have not shown a clear association.<sup>8</sup> The

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health risks associated with disinfection by-products in drinking water are extremely small compared to the risks associated with disease due to inadequate disinfection. It is important, therefore, that disinfection not be compromised in an attempt to decrease such by-products.

### Bladder Cancer in Children

Bladder cancer is a cancer of older people and rarely occurs in individuals younger than age 40. Nearly 90% of people with this cancer are over the age of 55.<sup>2</sup>

### For More Information / References

*Much of the information contained in this summary has been taken directly from the following sources. This material is provided for informational purposes only and should not be considered as medical advice. Persons with questions regarding a specific medical problem or condition should consult their physician.*

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