Ontario
Cancer Care Ontario
Action Cancer Ontario

Cancer Risk Factors in Ontario

Tobacco Use

TOBACCO USE

Risk factor/exposure	Cancer	Direction of association	Magnitude of risk*	Strength of evidence[a]
Active smoking	Oral cavity and pharynx	↑	3.4–6.8[b]	Sufficient
	Nasopharynx, nasal cavity and paranasal sinuses	↑	2.0[b]	
	Esophagus	↑	2.5[b]	
	Stomach	↑	1.53–1.65[b,c]	
	Colon and rectum	↑	1.07–1.20[d,e,f,g]	
	Liver	↑	1.5–1.6[b,h]	
	Pancreas	↑	1.7[b]	
	Larynx	↑	7.0[b]	
	Lung	↑	9.0[b]	
	Cervix†	↑	1.8[b]	
	Ovary‡	↑	2.1[i]	
	Kidney, bladder, other urinary§	↑	1.5–2.8[b]	
	Leukemia, myeloid	↑	1.09[b]	
	Endometrium	↓	0.5–0.7[a]	
	Female breast	↑	…	Limited
Second-hand smoke	Lung	↑	1.2–1.4[j,k,l]	Sufficient
	Pharynx	↑	…	Limited
	Larynx	↑	…	
Preconception/ pregnancy exposure	Hepatoblastoma	↑	1.86–4.74[m]	Sufficient
	Childhood leukemia‖	↑	…	Limited
Smokeless tobacco	Oral cavity	↑	1.36–1.80[n,o]	Sufficient
	Esophagus	↑	1.13–1.60[n,o]	
	Pancreas	↑	1.07–1.60[n,o]	

Sources: [a]IARC, 2012; [b]Gandini et al., 2008 ; [c]Ladeiras-Lopes et al., 2008; [d]Botteri et al., 2008; [e]Tsoi et al., 2009 ; [f]Liang et al., 2009; [g]Huxley et al., 2009; [h]Lee et al., 2009; [i]Jordan et al., 2006 ; [j]IARC, 2004; [k]Taylor et al., 2007; [l]Stayner et al., 2007; [m]Pang et al 2003; [n]Boffetta et al., 2008; [o]Lee et al., 2008

*Relative risk (RR) comparing current cigarette smokers to (lifetime) never-smokers, never-smokers exposed to second-hand smoke to never-smokers not exposed to second-hand smoke, or ever-users of smokeless tobacco (oral use) to never-users.

… Magnitude of risk not shown in table if strength of evidence is "probable" or "limited."

† Tobacco acts as a co-factor with human papillomavirus (HPV) infection.

‡ Association is restricted to cancers with a mucinous morphology.

§ Tobacco is a cause of cancers of both the body and pelvis of the kidney; other urinary includes ureter.

‖ Association is most apparent for acute lymphocytic leukemia in offspring of parents who smoked during preconception and/or pregnancy.

ACTIVE SMOKING

Background

» Tobacco use is the largest cause of cancer worldwide.[1]

» Cigarettes (manufactured, hand-rolled, filtered, un-filtered, and flavoured) are the main form of tobacco smoked worldwide; other types of smoked tobacco products include cigars and pipes.[1]

» Tobacco smoke contains over 70 known carcinogens, including polycyclic aromatic hydrocarbons (PAHs), N-nitrosamines, aromatic amines, aldehydes, phenols, volatile hydrocarbons, other organics and inorganic compounds.[1]

- Tobacco smoke is a multi-organ carcinogen (Group 1). There is sufficient evidence that tobacco smoking causes cancers of the oral cavity and pharynx, nasopharynx, nasal cavity and paranasal sinuses, esophagus, stomach, colon and rectum, liver, pancreas, larynx, lung, cervix, ovary, kidney, bladder and other urinary (including ureter) and bone marrow (myeloid leukemia). Tobacco smoking is inversely related to endometrial cancer risk.[1]
- According to the International Agency for Research on Cancer (IARC), limited evidence suggests a causal association between active tobacco smoking and female breast cancer,[1] although several other consensus reviews have drawn different conclusions.[1–4]
- Tobacco smoking is most strongly related to cancers of the respiratory tract, particularly of the lung, larynx and upper digestive tract. A recent meta-analysis reported that current smokers have an approximately 7 times greater risk of laryngeal cancer and a 9 times greater risk of lung cancer than never-smokers,[5] although lung cancer risk has been estimated in some studies to be as much as 20 times greater among smokers than lifetime never-smokers.[6] The tobacco smoke-related risk of upper digestive tract cancers (i.e., oral cavity, nasopharynx, hypopharynx, pharynx, esophagus) associated with tobacco smoke is approximately 3.6 times greater among current smokers.[5] Tobacco smoking increases the risk of colorectal cancer by 7%–20%.[7–10]
- Most cancer sites show a strong positive dose-response relationship, with cancer risk increasing with both intensity (e.g., number of cigarettes per day) and duration of smoking.[1] For lung cancer, smoking duration appears to be a stronger determinant of risk than intensity.[6]
- Actively smoking cigars and pipes is also causally associated with higher risk of cancers of the lung, upper aerodigestive tract (i.e., oral cavity, pharynx, larynx), esophagus, pancreas, stomach and bladder.[6]
- Quitting smoking reduces the risk of tobacco-related cancers, compared to not quitting. Risk generally decreases with both increasing time since cessation and decreasing age at cessation. For some cancers, such as lung and laryngeal, risk declines rapidly,[11] while for others, such as esophageal cancer, risk reductions only occur many years after cessation.[12]
- For some cancers, particularly those of the oral cavity, pharynx, larynx and esophagus (squamous cell carcinoma),[1,13] there is a synergistic interaction between tobacco smoking and alcohol consumption, whereby the increased risk for these cancers associated with tobacco is greater in people who drink alcohol than in non-drinkers.

- Tobacco smoking also interacts synergistically with radon exposure to influence lung cancer risk; the increased risk of lung cancer among smokers is substantially higher among those who smoke and are exposed to radon than those without radon exposure.[1,14]
- In addition, an interaction between tobacco smoking and infectious agents is likely. A recent meta-analysis concluded that tobacco smoke seems to interact with both hepatitis B and C infections to influence liver cancer risk, with risk particularly high among smokers.[15] For cervical cancer, tobacco smoke acts as a co-factor with human papillomavirus (HPV) infection.[1]
- Potential gene-tobacco smoke interactions that could influence susceptibility to tobacco-related cancers remain largely unclear. The strongest evidence of an interaction is for a variant of the N-acetyltransferase gene (NAT2) in bladder and breast cancer risk and for the GTSM1 gene variant alone or in combination with the CYP1A1 variant in lung cancer.[1]

SECOND-HAND SMOKE

Background

» Second-hand smoke (also known as involuntary or passive smoking, or environmental tobacco smoke) consists of sidestream smoke (released from the burning tip of a cigarette between puffs) and mainstream smoke (released from the mouth end of a cigarette during smoking) exhaled by the smoker.[1]

» Second-hand smoke has a similar composition as mainstream smoke that is actively inhaled, but the concentration of individual chemicals and compounds differs.[1]

» Second-hand smoke exposure can occur in all places where smoking is present (e.g., the home, workplace, bars, restaurants, public buildings and other public spaces).

- There is sufficient evidence that second-hand smoke exposure causes lung cancer.[1] Limited evidence also suggests an association between second-hand smoke and cancers of the larynx and pharynx.[1]
- Several meta-analyses have demonstrated a 20%–40% increased risk of lung cancer among non-smoking adults exposed to second-hand smoke at home or work.[6,16,17] Emerging evidence suggests that exposure to second-hand smoke during childhood may also increase the risk of lung cancer in adulthood.[1]
- For lung cancer, evidence of a positive dose-response exists for both duration and intensity of exposure to second-hand tobacco smoke.[6]
- Few studies have examined the possible association between second-hand smoke exposure and cancers of the upper aerodigestive tract but the risk of laryngeal and pharyngeal cancer may be increased in response to long duration (>15 years) of exposure to second-hand smoke at home and/or work.[18]

PRECONCEPTION/PREGNANCY EXPOSURE

- There is now sufficient evidence that parental tobacco smoking (by the father and/or mother during the preconception period and during pregnancy) causes hepatoblastoma, a rare embryonic cancer.[1,19] Parental tobacco smoking has also been associated with increased risk of childhood leukemia (particularly acute lymphocytic leukemia).[1]

SMOKELESS TOBACCO

Background

» Smokeless tobacco products are tobacco products that are consumed without burning, including products intended for oral use that are placed in the mouth and are sucked (dipped), chewed, gargled or applied to the gums or teeth, and products inhaled through the nasal passages.[1]

» Smokeless tobacco products most commonly used in North America include chewing tobacco and snuff.[20]

» Smokeless tobacco products contain multiple carcinogens, including tobacco-specific N-nitrosamines, N-nitrosamino acids, volatile N-nitrosamines, polycyclic aromatic hydrocarbons (PAHs), formaldehyde and acetaldehyde.[1]

- Smokeless tobacco (e.g., chewing tobacco, snuff, snus) causes cancer of the oral cavity, esophagus and pancreas.[1]
- Smokeless tobacco increases the risk of oral cancer by approximately 36%–80%[20,21] after adjusting for tobacco smoking. Smokeless tobacco-related oral cancers generally appear to occur more frequently in areas directly in contact with tobacco, including the gums and buccal mucosa.[22]

BIOLOGIC MECHANISMS

- Tobacco smoke may induce cancer through several mechanisms when ingested (either directly through tobacco smoke or indirectly by dissolving in saliva):[23]
  - Tobacco carcinogens can form DNA adducts, which can lead to DNA damage.
  - Nicotine and tobacco-specific nitrosamines (e.g., 4-[methylnitrosamino]-1-[3-pyridyl]-1-butanone [NNK]) may activate signal transduction pathways and allow damaged epithelial cells, which would normally die, to survive.
  - Co-carcinogens and tumour promoters in tobacco smoke can lead to methylation of key tumour suppressor genes, interfering with mechanisms that regulate normal cell growth.
- Smokeless tobacco may induce cancer through tobacco-specific nitrosamines such as *N*'-nitrosonornicotine (NNN) and NNK, which are considered "carcinogenic to humans." Once ingested by smokeless tobacco users, these may form DNA adducts and/or interfere with signal transduction pathways.[22]