Ontario
Cancer Care Ontario
Action Cancer Ontario

Cancer Risk Factors in Ontario

Appendix A

APPENDIX A

CRITERIA FOR ASSESSING STRENGTH OF EVIDENCE

a. Criteria used by the World Cancer Research Fund/American Institute for Cancer Research

The terms "convincing" and "probable," used to classify the strength of evidence for the relationship between a risk factor or exposure to an agent and a specific cancer type, were based on the following criteria:

Convincing

These criteria are for evidence strong enough to support a judgement of a convincing causal relationship, which justifies goals and recommendations designed to reduce the incidence of cancer. A convincing relationship should be robust enough to be highly unlikely to be modified in the foreseeable future as new evidence accumulates. All of the following are generally required:

- evidence from more than one study type
- evidence from at least two independent cohort studies
- no substantial unexplained heterogeneity within or between study types or in different populations relating to the presence or absence of an association or direction of effect
- good-quality studies to exclude with confidence the possibility that the observed association results from random or systematic error, including confounding, measurement error and selection bias
- presence of a plausible biological gradient ("dose-response") in the association—such a gradient need not be linear or even in the same direction across the different levels of exposure, so long as this can be explained plausibly
- strong and plausible experimental evidence, either from human studies or relevant animal models, that typical human exposures can lead to relevant cancer outcomes

Probable

These criteria are for evidence strong enough to support a judgement of a probable causal relationship, which would generally justify goals and recommendations designed to reduce the incidence of cancer. All of the following are generally required:

- evidence from at least two independent cohort studies or at least five case-control studies
- no substantial unexplained heterogeneity between or within study types in the presence or absence of an association or direction of effect
- good quality studies to exclude with confidence the possibility that the observed association results from random or systematic error and selection bias
- evidence for biological plausibility

Source:
World Cancer Research Fund/American Institute for Cancer Research. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington DC: AICR, 2007. Page 60.

b. Criteria used by the International Agency for Research on Cancer (IARC):
The terms "sufficient" and "limited," used to classify the strength of evidence for the relationship between a risk factor or exposure to an agent and a specific cancer type, were assigned based on the following general criteria:

Sufficient evidence of carcinogenicity in humans

The IARC Working Group uses the term "sufficient evidence" when a causal relationship has been established between exposure to the agent and human cancer at the target organ(s) or tissue(s). That is, when a positive relationship has been observed between the exposure and cancer at the target organ(s) or tissue(s) in studies in which chance, bias and confounding could be ruled out with reasonable confidence. Identification of a specific target organ or tissue does not preclude the possibility that the agent may cause cancer at other sites.

Limited evidence of carcinogenicity in humans

The term "limited evidence" is used when a positive association is observed between exposure to the agent and cancer at the target organ(s) or tissues(s) in humans and a causal relationship is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.

In addition to classifying a relationship between exposure to the agent and human cancer at a specific target organ or tissue, IARC classifies the strength of the evidence for carcinogenicity in experimental animals and also considers mechanistic and other relevant data. The body of evidence is then considered as a whole to provide an overall evaluation of the carcinogenicity of the agent itself. Agents with Group 1 or Group 2A classifications are included in this report. The criteria for these classifications are as follows:

Group 1: the agent is carcinogenic to humans

This category is used when there is *sufficient evidence of carcinogenicity* in humans (for at least one target organ or tissue). Exceptionally, an agent may be placed in this category when evidence of carcinogenicity in humans is less than sufficient but there is *sufficient evidence of carcinogenicity* in experimental animals and strong evidence in exposed humans that the agent acts through a relevant mechanism.

Group 2A: the agent is probably carcinogenic to humans

This category is used when there is *limited evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals. In some cases, an agent may be classified in this category when there is *inadequate evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans.

Exceptionally, an agent may be classified in this category solely on the basis of *limited evidence of carcinogenicity* in humans. An agent may be assigned to this category if it clearly belongs, based on mechanistic considerations, to a class of agents for which one or more members have been classified in Group 1 or Group 2A.

Source:
A review of human carcinogens. Part E: Personal habits and indoor combustions / IARC Working Group on the Evaluation of Carcinogenic Risks to Humans (2009: Lyon, France). Pages 29–30.