

# Lifestyle risk factors and the primary prevention of cancer

#### Created and released: June 2015

- 1. All needle biopsies performed as part of the BreastScreen Australia program should be reviewed and documented in the context of a multidisciplinary team meeting. [CBR<sup>1</sup>]
- It is recommended that needle biopsy be performed using image guidance (either ultrasound or mammography). As per the BreastScreen Australia data dictionary, the guidance method should be recorded.<sup>2</sup> [CBR<sup>1</sup>]

#### Core Biopsy

3. Core biopsy (including vacuum-assisted core biopsy) is the procedure of choice for the assessment of the majority of screen-detected breast abnormalities. Core biopsy provides histological confirmation of invasive status of malignant breast lesions, tumour subtype, and an indication of tumour grade in breast malignancies, which cannot be reliably obtained from FNA. In addition, it is recommended that assessment of receptor/biomarker status (ER/PR and HER2 status) be performed on core biopsy specimens (The Royal College of Pathologists of Australasia 2018). This information is important in guiding pre-operative treatment planning and informing patient decision-making. Core biopsy also aids in the definitive diagnosis of benign lesions and, in the context of a screening program, reduces the need for repeat procedures compared with FNA. [EBR<sup>3</sup>]

#### **FNA**

4. The use of FNA in the screening setting is appropriate for simple cysts, some complex cystic lesions, axillary lymph nodes<sup>4</sup> and rare situations where a core biopsy is not possible (for example in women with lesions close to a breast implant capsule or in some women on anticoagulation therapy). [CBR<sup>1</sup>]





# Table 23124: Circumstances where FNA and/or core biopsy are appropriate in the <u>BreastScreen Australia program</u> (see Guidance for further details and exceptional circumstances)<sup>5</sup>

Recommended pathological investigation <sup>6</sup>			
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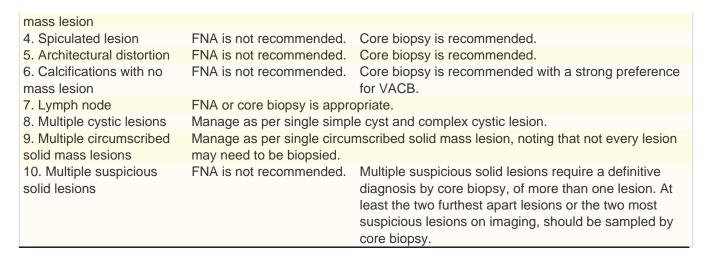




## Table 2: Summary of benefits and limitations of fine needle aspiration and core biopsy $\overset{*}{}$

Fine needle aspiration       Core biopsy         Sensitivity (95% Cl) <sup>3</sup> 74% (72-77) <sup>3</sup> 87% (84-89) <sup>3</sup> Specificity (95% Cl) <sup>3</sup> 96% (94-99) <sup>3</sup> 98% (96-99) <sup>3</sup> Specificity (95% Cl) <sup>3</sup> 96% (94-99) <sup>3</sup> 98% (96-99) <sup>3</sup> Procedural advantages and disadvantages       Low       High         Ability to distinguish between <i>in situ</i> and invasive       Low       Low to moderate         Degree of invasiveness of technique       Low       Low to moderate         Success rate (rate of sufficient sampling)       Moderate       Optional       Required         Success rate (rate of sufficient sampling)       Moderate       Low       Low         Use of local aneesthetic       Optional       Required       Noderate duration         Assessment of prognostic and predictive biomarkers       Moderate to High       Ability to assess HER2 and ER/PR receptors       Receptor testing is recommended on core biopsies of the primary ture         Lesion type on imaging       Recommended pathological investigation <sup>6</sup> Fine needle aspiration       Fine needle aspiration         Program)       Asymptomatic simple cyst is Core biopsy is not recommended. aspirated for diagnostic purposes, a sample of the fluid should be sent for confirmation of imaging indindings.       Findings.       Findings.         2. Complex cystic lesion       FNA is ap						
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<sup>1</sup> Consensus-based recommendation (CBR) – a recommendation formulated in the absence of systematically reviewed evidence, based on expert opinion and formulated via a deliberative process that sought to achieve consensus.

<sup>2</sup> Australian Institute of Health and Welfare 2015. BreastScreen Australia data dictionary: version 1.1. Cancer series no. 92. Cat. no. CAN 90. Canberra: AIHW

<sup>3</sup> Evidence-based recommendation (EBR) – a recommendation formulated after a systematic review of the evidence, with a clear linkage from the evidence base to the recommendation.

<sup>4</sup> Core biopsy may be appropriate, where technically feasible, for the investigation of axillary lymph nodes in situations where there is a large asymmetrical axillary lymph node and no known primary lesion in the breast.

<sup>5</sup> This Position Statement is not intended to provide guidance on the use of biopsy techniques outside of the BreastScreen Australia program and applies only to the assessment of screen-detected abnormalities.

<sup>6</sup> Needle biopsy is recommended to be performed under image guidance (either ultrasound or mammography). As per the BreastScreen Australia data dictionary, the guidance method should be recorded. Source: \*Willems 2012: Table 1, page 290; supplemented by Mitra 2016: Table 1, page 2.

<sup>7</sup> The sensitivity of a diagnostic test quantifies its ability to correctly identify subjects with the disease. It is the proportion of true positives that are correctly identified by the test.

<sup>8</sup> Wang 2017 – the limitations of this review are discussed within the text of the Position Statement including that Ultrasound guidance was used in 5 of the 12 studies included in Wang.

<sup>9</sup> The specificity of a diagnostic test is the ability of a test to correctly identify subjects without the disease. It is the proportion of true negatives that are correctly identified by the test.

<sup>10</sup> Using Nottingham histological score (Elston, CW; Ellis, IO. Pathologic prognostic factors in breast cancer. I. The value of histological grades in breast cancer. Experience from a large study with long-term follow-up. Histopathology 19(5):403–10. Republished Histopathology 41:154–161. 2002).

<sup>11</sup> Royal College of Pathologists of Australasia 2018 Abbreviations: ER, oestrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor;







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## Recommendations

It 123 a is estimated that at least one third of all cancer cases are preventable,<sup>1</sup> and that potentially more than half of all cancers could be avoided through a combination of healthy lifestyle and regular screening.<sup>2,3</sup> Prevention offers the most cost-effective long-term strategy for the control of cancer across the population.<sup>4</sup>

There are a number of modifiable lifestyle factors that can reduce risk of cancer, some of which have health benefits beyond cancer in the prevention of chronic diseases, such as cardiovascular diseases, chronic respiratory diseases and type 2 diabetes.

#### Recommendations for adults to reduce their risk of cancer and stay healthy

- **Don't smoke:** The greatest preventable cause of cancer is tobacco, which increases the risk of lung cancer and certain other cancers. Cancer Australia recommends not smoking and avoiding exposure to second-hand smoke to reduce cancer risk.
- Maintain a healthy weight: Overweight and obesity increase risk of certain cancers. Cancer Australia recommends achieving and maintaining a healthy body weight within a BMI range of 18.5 to 25 kg/m<sup>2</sup> to reduce cancer risk and a waist circumference below 94 cm for men and below 80 cm for women.
- **Be active:** Sedentary behaviour increases risk of weight gain, overweight and obesity, and may increase risk of certain cancers. Conversely, physical activity protects against certain cancers, as well as limiting weight gain. Cancer Australia recommends aiming for at least 30 minutes of moderate-intensity physical activity every day and limiting sedentary habits, such as watching television, to reduce cancer risk.
- Eat a balanced and nutritious diet: A balanced diet rich in plant-based foods, including fruit, vegetables and other foods containing dietary fibre, may protect against certain cancers. Cancer Australia recommends consuming adequate dietary fibre, including unprocessed cereals (grains) and pulses (legumes), and aiming for five servings of vegetables and two servings of fruit per day. Cancer Australia recommends limiting intake of red meat, processed meat and salt to reduce cancer risk.
- Limit alcohol consumption: Alcohol increases risk of certain cancers and interacts synergistically with smoking to increase risk of oesophageal and oral cancers. If alcoholic drinks are consumed, Cancer Australia recommends limiting daily alcohol intake to reduce cancer risk.
- **Be sun smart:** Ultraviolet (UV) radiation and UV-emitting solaria increase risk of melanoma and other types of skin cancer. Cancer Australia recommends avoiding excessive sun exposure and solaria, and wearing sunscreen and protective clothing to lower risk of skin cancer.
- Reduce risk and protect against infection: A range of infections, such as the human papillomavirus (HPV), or chronic infection with the hepatitis B or C viruses, increase risk of certain cancers. Cancer Australia recommends vaccination to protect against HPV and hepatitis B, and other protective behaviours, such as safe sex and safe injection and blood transfusion practices, to reduce risk of hepatitis C.







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## Methodology and scope

This position statement was developed by Cancer Australia, based on existing high level evidence and evidence reviews. Information was primarily sourced from: the 2012 International Agency for Research on Cancer (IARC) Monographs on tobacco, alcohol, UV radiation and infectious agents,<sup>5-7</sup> the 2007 World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR) report *Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective*,<sup>8</sup> and subsequent WCRF and AICR tumour-specific updates for breast, pancreatic, colorectal, endometrial, ovarian, prostate and liver cancers.<sup>9-15</sup> (Refer to Appendix 1 for more detail.) Evidence from additional systematic reviews, meta-analyses and studies, particularly those published after 2007, was also included where relevant. National and international leaders in cancer provided input through an external review of the position statement. Cancer Australia recommendations to reduce cancer risk have been developed, based on the available evidence from the IARC Monographs and the WCRF and AICR reports, with consideration of the Australian context and relevant Australian guidelines.

This position statement focuses on modifiable lifestyle factors where individual behavioural changes can reduce risk of cancers that are relevant to the Australian population. The scope of this position statement covers primary prevention of cancer through seven modifiable lifestyle factors, namely: tobacco, overweight and obesity, physical activity and sedentary behaviour, diet, alcohol, UV radiation and infections.

Outside this scope are occupational and environmental factors, which account for a lesser proportion of cancer than lifestyle factors.<sup>2</sup>,<sup>16</sup> Other factors, such as risk-reducing medication, family history of cancer and screening are not included in this position statement. Information about Australian screening programs is available from: www.cancerscreening.gov.au/

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### Impact of cancer

Cancer is a leading cause of death across the world and accounted for an estimated 8.2 million deaths worldwide in 2012.<sup>17</sup> The World Health Organization (WHO) has estimated that around 30% of cancer deaths are due to tobacco use, overweight and obesity, lack of physical exercise, diet and alcohol consumption.<sup>18</sup> The World Cancer Report 2014 estimates that by 2025, over 20 million new cancer cases will be diagnosed every year.<sup>17</sup>

In Australia, the most common cancer is non-melanoma skin cancer, with an estimated 474,000 new cases diagnosed in 2012.<sup>19</sup> However, two of the most common types of non-melanoma skin cancer, basal cell carcinoma and squamous cell carcinoma, are not required to be reported to cancer registries and national data are not routinely available.<sup>20</sup> Therefore, data in this position statement relate primarily to invasive cancers and exclude non-melanoma skin cancers (unless otherwise specified).

The number of new cancer cases each year is increasing and it is estimated that in 2020, there will be approximately 150,000 new cases diagnosed in Australia.<sup>21</sup> The most commonly diagnosed cancers in Australia are prostate, bowel, breast, melanoma of the skin and lung cancer, which together will account for an estimated 60% of all cases diagnosed in 2015.<sup>22</sup> In 2015, there will be nearly 46,600 deaths due to cancer, accounting for 3 out of every 10 deaths in Australia.<sup>22</sup> Lung, bowel, prostate, breast and pancreatic cancer will be the most common causes of cancer death, accounting for nearly half the total deaths due to cancer in 2015 in Australia.<sup>22</sup>

Cancer was estimated to be the leading cause of burden of disease in Australia in 2012 (see Appendix 2 for explanation).<sup>20</sup> Together, tobacco, physical inactivity, high body mass index (BMI), alcohol, occupational exposures and hazards, low fruit and vegetable consumption, air pollution and unsafe sex have been estimated to account for one third of the total burden of cancer in Australia – the majority of burden being due to tobacco.<sup>23</sup>

The Australian Institute of Health and Welfare (AIHW) has identified smoking, overweight and obesity, physical inactivity, alcohol consumption, diet and chronic infections as some of the risk factors relevant to cancer in Aboriginal and Torres Strait Islander peoples.<sup>24</sup> The AIHW report *Cancer in Australia: an overview, 2012* identified that people living in lower socioeconomic status areas are more likely to have higher levels of cancer and lifestyle risk factors, such as smoking, poor diet and physical inactivity.<sup>20</sup> Although cancer incidence varies across geographical regions for different cancers, people living in remote areas of Australia are more likely to have higher rates of risky health behaviours, such as smoking, heavy alcohol use and poor nutrition.<sup>20</sup>

Australian Government

## Primary prevention of cancer

Primary prevention reduces the likelihood that a disease or disorder will develop.<sup>25</sup> The aim of primary prevention is to limit the incidence of disease by controlling specific causes and risk factors.<sup>26</sup> Preventive steps to reduce risk factors for cancer, such as tobacco use, alcohol use, poor diet, physical inactivity, and overweight and obesity, also contribute to reducing risk of other chronic diseases, including cardiovascular diseases, type 2 diabetes and chronic respiratory diseases.<sup>4</sup> The Royal Australian College of General Practitioners (RACGP) <u>Guidelines for</u> <u>preventive activities in general practice</u>(the red book) provides recommendations for general practitioners, based on current, evidence-based guidelines for preventive activities.<sup>27</sup>

Recommendations by the WCRF and AICR on food, nutrition and physical activity<sup>8</sup> to reduce risk of cancer have recently been assessed through analysis of participants in the large European Prospective Investigation into Cancer (EPIC) study. Concordance with the WCRF and AICR recommendations was significantly associated with decreased risk of cancer, risk of death, and risk of death from cancer, circulatory disease and respiratory disease.<sup>28</sup>,<sup>29</sup>

WHO estimates that at least one third of all cancer cases are preventable.<sup>1</sup> Other estimates suggest that more than half of all cancers could be prevented through a combination of healthy lifestyle and regular screening.<sup>2,3</sup>

Changes in lifestyle have the potential to reduce the number of cancer cases. The WCRF and AICR estimate that 21-24% of cancers in high-income countries could be prevented through changes to food, nutrition, physical activity and body fatness.<sup>30</sup> Using WCRF and AICR estimates, improvements in diet and physical activity, and their impact on obesity, could prevent an estimated 43,000 cancers in Australia in 2025.<sup>31</sup>

Estimates on the percentage of cancers caused by modifiable risk factors vary depending on the population and the approach used to estimate the magnitude of association of individual risk factors.<sup>3</sup> This position statement includes estimates from Australia and, when Australian estimates are not available, estimates from other developed regions, such as the United States and Europe, to indicate the proportion of preventable or avoidable cancer attributable to specific risk factors.

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## Lifestyle risk factors

A risk factor is any factor associated with an increased likelihood of a person developing a health disorder or condition, such as cancer. Having one or more risk factors does not mean a person will develop cancer. Many people have at least one cancer risk factor but will never get cancer, while others with cancer may have had no known risk factors.<sup>20</sup>

However, there are a number of modifiable lifestyle factors that can reduce risk of cancer.

- <u>Tobacco</u>
- Overweight and obesity
- Physical activity and sedentary behaviour
- Diet
- <u>Alcohol</u>
- UV radiation
- Infections



## Tobacco



Tobacco is the **greatest preventable cause of cancer**.<sup>2,3</sup> The estimated percentage of cancer cases attributable to tobacco ranges from 15.5–24% using European estimates<sup>16</sup> to 29-33% in the United States.<sup>2,3</sup> WHO identifies tobacco use as the single greatest avoidable risk factor for cancer mortality worldwide, and estimates tobacco use to cause up to 1.5 million cancer deaths each year.<sup>1</sup>

#### Tobacco in Australia

In Australia, the percentage of daily smokers has been steadily declining, from 22.4% of adults in 2001 to 16.1% in 2011–12. $\frac{32}{2}$  This equates to 2.8 million adults who were daily smokers in 2011–12. $\frac{32}{2}$ 

Tobacco smoking has been estimated to be the greatest contributor to the health burden of Indigenous people, at 12% of the total Indigenous health burden.<sup>33</sup> While the proportion of current smokers amongst Indigenous people has decreased from 51% in 2002 to 47% in 2008,<sup>34</sup> Indigenous Australians were 2.2 times as likely to smoke tobacco compared to non-Indigenous Australians.<sup>19</sup>

#### Tobacco and cancer

The IARC has identified tobacco consumption as the single largest cause of cancer in the world and tobacco smoking as the single largest cause of lung cancer.<sup>5</sup> About 90% of lung cancer in Australian men and 65% of lung cancer in Australian women is estimated to be a result of tobacco smoking.<sup>35</sup> A 2012 IARC Monograph on tobacco smoking reviewed the evidence and classified **tobacco smoking as a Group 1 carcinogen** (see Appendix 1 for explanation of IARC classifications).<sup>5</sup> The IARC identified that tobacco smoking also causes cancers of the oral cavity, pharynx, nasal cavity and accessory sinuses, larynx, oesophagus, stomach, pancreas, colorectum, liver, kidney (body and pelvis), ureter, urinary bladder, uterine cervix and ovary (mucinous), and myeloid leukaemia.<sup>5</sup> A positive association between tobacco smoking and female breast cancer was also reported by the IARC<sup>5</sup> and was supported by a recent meta-analysis of nearly 32,000 breast cancer cases.<sup>36</sup>

The IARC Monograph identified that both the duration of smoking and total tobacco consumption increase the risk of lung and many other cancers.<sup>5</sup> Alcohol consumption also interacts synergistically with tobacco smoking to increase the incidence of cancers of the upper aero-digestive tract (i.e. oral cavity, pharyngeal, laryngeal and oesophageal cancers) beyond the single additive effects of tobacco smoking or alcohol (See Appendix 2 for explanation).<sup>5</sup>

#### Second-hand smoke and cancer

Tobacco smoke has an effect on the wider population beyond smokers, through exposure to second-hand tobacco smoke or the chemicals in tobacco smoke (also known as passive smoking and environmental smoke). The IARC Monograph classified **second-hand smoke as a Group 1 carcinogen**, which causes lung cancer and is associated with pharyngeal and laryngeal cancers.<sup>5</sup>

#### Reducing individual risk of cancer and staying healthy

Quitting smoking reduces the risk of lung and other major cancers.<sup>37</sup>,<sup>38</sup> Five years after quitting smoking, risk of





mouth, throat, oesophageal and bladder cancers are halved, and the risk for dying from lung cancer drops by half after 10 years.<sup>39</sup> Quitting smoking can also contribute to both short and long-term improvements in health,<sup>40-42</sup> including: a dramatic drop in blood levels of carbon monoxide, a drop in heart rate and blood pressure, improved circulation and lung function, decreased coughing and shortness of breath, and reduced risk of coronary heart disease and stroke.<sup>43</sup> WHO reports that people of all ages can still benefit from quitting, including those who have already developed smoking-related health problems.<sup>43</sup>

The Australian National Tobacco Campaign encourages individuals to stop smoking and provides support through the <u>Quitline.</u>

#### Cancer Australia recommendations for individuals

Cancer Australia recommends not smoking and avoiding exposure to second-hand smoke to reduce cancer risk.

#### Table 1: Summary of evidence for tobacco and cancer sites

Risk factor	Source	Evidence	Cancer site
Tobacco smoking	cco smoking IARC 2012 <sup>5</sup>		Lung, oral cavity, pharynx, nasal cavity and accessory sinuses, larynx, oesophagus, stomach, pancreas, colorectum, liver, kidney (body and pelvis), ureter, urinary bladder, uterine cervix and ovary (mucinous), myeloid leukaemia
		Limited evidence (positive association)	Female breast
Second-hand smoke	IARC 2012 <sup>5</sup>	Sufficient evidence (highest IARC classification for carcinogenicity)	Lung
		Limited evidence (positive association)	Pharynx, larynx

See <u>Appendix 1</u> for explanation of evidence.



## Overweight and obesity

Overweight is defined by WHO as having a body mass index (BMI) of 25 kg/m<sup>2</sup> or more and obesity as a BMI of 30 kg/m<sup>2</sup> or more.<sup>44</sup> Waist circumference is considered to be a measure of abdominal fatness. The WHO reference values for waist circumferences of 94 cm in men and 80 cm in women (on a population basis) are based on their rough equivalence to a BMI of around 25.<sup>8</sup> Estimates on the percentage of cancer attributable to overweight and obesity range from 4.5% of cancer cases in Europe<sup>16</sup> to 20% in the United States.<sup>3</sup> Globally, it is estimated that 3.6% of all new cancers in adults are attributable to excess bodyweight, representing a total of 481,000 cases.<sup>45</sup>

#### Overweight and obesity in Australia

The prevalence of overweight and obesity continues to rise in Australia, from 56.3% of adults in 1995 to 62.8% in  $2011-12.\frac{46}{2}$  Around a quarter of children aged 2 to 17 years in Australia were overweight or obese in  $2011-12.\frac{46}{2}$ 

#### Overweight and obesity and cancer

Based on systematic literature reviews, the 2007 WCRF and AICR report *Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective* and subsequent tumour-specific updates identified convincing evidence that **greater body fatness increased the risk of various cancers**, namely colorectal, oesophageal (adenocarcinoma), endometrial, pancreatic, kidney, postmenopausal breast and liver cancers (see Appendix 1 for explanation of WCRF & AICR categories of evidence).<sup>8-15</sup> Greater body fatness was identified as a probable cause of gallbladder, advanced prostate and ovarian cancers.<sup>8-15</sup>

A large UK population-based cohort study of 5.24 million adults published in 2014 investigated the association between BMI and the most common site-specific cancers.<sup>47</sup> Each 5 kg/m<sup>2</sup> increase in BMI was linearly associated with a large increase in risk of uterine, gallbladder, kidney, cervical, thyroid cancers, and leukaemia.<sup>47</sup> Overall positive associations with higher BMI, while non-linear or modified by individual level factors, were also reported for liver, colon, ovarian, and postmenopausal breast cancers.<sup>47</sup> An earlier (2008) large systematic review and meta-analysis examined the association between BMI and different cancers and investigated differences in the association between men and women.<sup>48</sup> It was reported that a 5 kg/m<sup>2</sup> increase in BMI was strongly associated with oesophageal (adenocarcinoma), thyroid, colon and renal cancers in men, and endometrial, gallbladder, oesophageal (adenocarcinoma) and renal cancers in women.<sup>48</sup> Weaker positive associations were observed with leukaemia, multiple myeloma and non-Hodgkin lymphoma for both genders, rectal cancer and malignant melanoma in men, and postmenopausal breast, pancreatic, thyroid and colon cancers in women.<sup>48</sup>

The 2007 WCRF and AICR report and subsequent updates identified convincing evidence that **abdominal fatness (i.e. wider girth) increased risk** of colorectal cancer and endometrial cancer, and was a probable cause of pancreatic cancer and postmenopausal breast cancer.<sup>8-15</sup> **Adult weight gain** was identified as a further probable cause of postmenopausal breast cancer.<sup>8-15</sup>

#### Reducing individual risk of cancer and staying healthy

The 2002 IARC Handbook of Cancer Prevention reviewed the evidence on weight control and indicated obesity as a cause of 39% of endometrial cancer cases, 37% of oesophageal cancer cases, 25% of kidney cancer cases, 11% of colon cancer cases and 9% of postmenopausal breast cancer cases.<sup>49</sup> The Handbook identified that



#### avoiding weight gain had a preventive effect for these cancers.<sup>49</sup>

Few data are available regarding the **preventive effect of intentional weight loss** on cancer. A 2011 review indicated that limited information from observational studies suggests a reduced risk of breast cancer and potentially other cancers due to intentional weight loss.<sup>50</sup> Further research is required to determine the degree of weight loss and timeframe to reduce cancer risk.

The WCRF and AICR report states that, while obesity is a cause of some cancers and other diseases, it is also a marker for dietary and physical activity patterns that independently lead to poor health.<sup>8</sup> Maintaining a healthy weight throughout life has clear health benefits and may have an important protective effect against cancer.<sup>8</sup> Results from recent analyses of the large EPIC study indicated a significant association between higher BMI and risk of cancer and risk of death.<sup>28</sup>,<sup>29</sup>

The WCRF and AICR report recommends being as lean as possible within the normal range of body weight in order to reduce cancer risk.<sup>8</sup> Avoiding weight gain and increases in waist circumference throughout adulthood is also recommended to reduce risk of cancer.<sup>8</sup> Cut-off points for healthy waist circumferences were specified as 94 cm (37 inches) for men and 80 cm (31.5 inches) for women, based on general equivalence to a BMI of 25 kg/m<sup>2</sup>.<sup>8</sup>

The rough a healthy weight (BMI of 18.5–24.9 kg/m

#### Cancer Australia recommendations for individuals

Cancer Australia recommends achieving and maintaining a healthy body weight within a BMI range of 18.5 to 25 kg/m<sup>2</sup> to reduce cancer risk and a waist circumference below 94 cm for men and below 80 cm for women.

#### Table 2: Summary of evidence for overweight and obesity and cancer sites

Risk factor	Source	Evidence	Cancer site
Greater body fatness WCRF/AICR 2007–2015 <sup>8-15</sup>		Convincing	Colorectum, oesophagus (adenocarcinoma), endometrium, pancreas, kidney, postmenopausal breast, liver
		Probable	Gallbladder, ovary, advanced prostate
Abdominal (central)		Convincing	Colorectum, endometrium
fatness 2007–2015 <sup>8-15</sup>	Probable	Pancreas, postmenopausal breast	
Adult weight gain	WCRF/AICR 2007–2015 <sup>8-15</sup>	Probable	Postmenopausal breast
Protective factor	Source	Evidence	Cancer site
Avoiding weight gain	IARC 2002 <sup>49</sup>	Sufficient evidence (highest IARC classification for carcinogenicity)	Colon, postmenopausal breast, endometrium, kidney (renal-cell), oesophagus (adenocarcinoma)





See <u>Appendix 1</u> for explanation of evidence.



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## Physical activity and sedentary behaviour

It is estimated that 5% of cancers in the United States are linked to lack of regular exercise<sup>3</sup> or sedentary lifestyle.<sup>2</sup> Globally, it has been estimated that 135,000 deaths from cancer each year are attributable to physical inactivity.<sup>52</sup>

#### Physical activity and sedentary behaviour in Australia

Data from the 2011-12 Australian Health Survey indicate that 60% of Australian adults do less than 30 minutes of exercise per day.<sup>53</sup> Around 30% of the adult population reported more than 5 hours of sedentary leisure activity each day.<sup>53</sup>

#### Physical activity

The 2007 WCRF and AICR report and tumour-specific updates identified that **physical activity protects against certain cancers** and also limits weight gain, itself a cause of some cancers.<sup>8-15</sup> There was convincing evidence for the protective effect of physical activity against colon cancer and probable evidence for postmenopausal breast cancer and endometrial cancer.<sup>8-15</sup> Limited suggestive evidence supports a protective effect against premenopausal breast, lung and liver cancers.<sup>8-15</sup> To reduce risk of cancer, the report recommends being physically active as part of everyday life, including at least 30–60 minutes daily, and limiting sedentary habits, such as watching television.<sup>8</sup>

<u>Australia's Physical Activity and Sedentary Behaviour Guidelines</u> recommend that adults should accumulate 150 to 300 minutes of moderate intensity physical activity or 75 to 150 minutes of vigorous intensity physical activity, or an equivalent combination of both moderate and vigorous activities, each week.<sup>54</sup> Activity at the upper end of the scale (i.e. 300 minutes of moderate / 150 minutes of vigorous) is required for the prevention of unhealthy weight gain and some cancers.<sup>54</sup> The guidelines also recommend minimising the amount of time spent in prolonged sitting and to break up long periods of sitting as often as possible.<sup>54</sup>

#### Sedentary behaviour and cancer

The WCRF and AICR report indicated that there is convincing evidence that sedentary behaviour increases risk of weight gain, overweight and obesity.<sup>8</sup> Two 2014 meta-analyses reported an association between **sedentary behaviour** and **increased risk of some cancers**, including colorectal, endometrial and lung cancers.<sup>55, 56</sup> There was inconsistency with results for breast cancer.<sup>55, 56</sup>

The 2002 IARC Handbook of Cancer Prevention linked decreasing levels of physical activity to increases in overweight and obesity.<sup>49</sup> The Handbook reported that adiposity (obesity) and inactivity appeared to be the most important, avoidable causes of postmenopausal breast cancer, endometrial cancer, renal-cell cancer, and oesophageal adenocarcinoma, and among the most important avoidable causes of colon cancer.<sup>49</sup>

#### Cancer Australia recommendations for individuals

Cancer Australia recommends aiming for at least 30 minutes of moderate-intensity physical activity every day and limiting sedentary habits, such as watching television, to reduce cancer risk.





#### Table 3: Summary of evidence for physical activity and cancer sites

Protective factor	Source	Evidence	Cancer site
Physical activity	vsical activity WCRF/AICR 2007–2015 <sup>8-15</sup>	Convincing	Colon
		Probable	Postmenopausal breast, endometrium
		Limited	Premenopausal breast, lung, liver

See <u>Appendix 1</u> for explanation of evidence.



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## Diet

Estimates for the percentage of cancer cases attributable to diet range from 5% of all cancer cases in the United States<sup>3</sup> to 30% of cancer cases in European men.<sup>16</sup>,<sup>57</sup> Worldwide, it has been estimated that 374,000 cancer deaths each year can be attributed to low fruit and vegetable intake.<sup>52</sup>

#### Diet in Australia

Many Australians do not include sufficient vegetables and fruits in their daily diets. Data from the 2011-12 Australian Health Survey indicate that only 5.5% of Australian adults had an adequate usual daily intake of fruit and vegetables.<sup>58</sup> While 48.5% of Australian adults reported that they usually met the guideline for daily fruit intake (2 serves per day), only 8.2% met the guideline for daily vegetable intake (5 serves per day).<sup>58</sup>

#### Dietary fibre

Foods containing **dietary fibre**, such as vegetables, fruits, pulses (legumes) and cereals, are identified by the 2007 WCRF and AICR report and updates as having convincing evidence for a **protective effect** against colorectal cancer, with limited suggestive evidence for oesophageal cancer.<sup>8-15</sup> A recent meta-analysis of around 580,000 subjects indicated a protective association between dietary fibre and risk of gastric cancer.<sup>59</sup> The WCRF and AICR report recommends consuming at least 400 g of a variety of non-starchy vegetables and fruits every day, as well as including relatively unprocessed cereals (grains) and/or pulses (legumes) with each meal to reduce risk of cancer.<sup>8</sup>

#### Plant-based foods

The WCRF and AICR report and updates identified that the evidence for the protective effect of plant-based foods is less compelling than in the mid-1990s, when the previous WCRF and AICR report was published.<sup>8</sup> The report and updates identified probable evidence that a **diet rich in plant-based foods**, such as fruit, vegetables and unprocessed cereals, **reduces the risk** of various cancers and likely protects against weight gain due to the low energy density of such foods.<sup>8-15</sup> Fruits and vegetables (particularly non-starchy vegetables) probably protect against mouth, pharyngeal, laryngeal, oesophageal and stomach cancers, and lung cancer (fruits only).<sup>8-15</sup> Limited suggestive evidence supports a protective effect of non-starchy vegetables and fruits for nasopharyngeal and colorectal cancers.<sup>8-15</sup> The WCRF and AICR also identified limited evidence suggesting that vegetables protect against lung cancer.<sup>8-15</sup> Data from the large EPIC study indicated a modest association between increased intake of total fruits and vegetables, notably intake of vegetables, and reduced overall cancer risk.<sup>60</sup>

#### Overnutrition and weight gain

Overnutrition, i.e. overconsumption of calories and the weight gain it causes, has been identified as contributing greatly to cancer burden.<sup>2</sup> Consumption of additional calories from any source contributes to weight gain and increasing cancer risk.<sup>61</sup> The WCRF and AICR report identified that increasing consumption of energy-dense foods and sugary drinks is probably contributing to the rise in overweight and obesity, which increases risk of certain types of cancer.<sup>8</sup> The report recommends limiting energy-dense foods and fast foods, and avoiding sugary drinks to prevent and control weight gain, overweight and obesity.<sup>8</sup>



#### Red meat, processed meat and cancer

Data on meat consumption indicate that Australian males and females eat around 200 g and 120 g respectively of meat, poultry and game each day.<sup>51</sup> The WCRF and AICR report and updates identified convincing evidence that increased consumption of **red meat and processed meat increased risk of colorectal cancer**, and limited evidence suggests increased risk of oesophageal, lung, pancreatic and stomach cancers.<sup>8-15</sup> Dose response meta-analyses have indicated a 17% increase in colorectal cancer risk for each 100 g increase per day in red meat, and an 18% increase in colorectal cancer risk for each 50 g increase per day in processed meat.<sup>10</sup> The WCRF and AICR report recommends limiting consumption of red meat to less than 500 g per week, very little if any to be processed meat.<sup>8</sup>

#### Salt and cancer

The WCRF and AICR report identified evidence that **salt** (from salty foods, processed foods, and added salt) **is a probable cause of stomach cancer**.<sup>8</sup> As processed foods are a major source of salt, the WCRF and AICR report recommends that individuals limit consumption of processed foods with added salt to ensure an intake of less than 6 g of salt per day<sup>8</sup> (equivalent to approximately 2,300 mg sodium). The *Nutrient Reference Values for Australia and New Zealand* recommend an adequate intake of 460-920 mg of sodium per day for the adult population, and an intake of 2,300 mg of sodium per day is considered the upper level of intake that should not be exceeded.<sup>62</sup>

#### Reducing individual risk of cancer and staying healthy

Some studies suggest that a diet with greater fruit and vegetable consumption may reduce the risk of becoming obese.<sup>63-65</sup> To reduce risk of cancer, the 2007 WCRF and AICR report recommends: limiting consumption of energy-dense foods and avoiding sugary drinks, eating mainly foods of plant origin, limiting intake of red meat and avoiding processed meat, and limiting consumption of salt and processed foods with added salt.<sup>8</sup> The WCRF and AICR report indicates that dietary supplements are not recommended for cancer prevention.<sup>8</sup> The report judges that food and drinks, rather than dietary supplements, are the best source of nourishment for the general population, and recommends aiming to meet nutritional needs through diet alone.<sup>8</sup>

The <u>Australian Dietary Guidelines</u> recommend a **varied diet of nutritious foods**, including vegetables, fruits, grains, dairy products, lean meat, fish and water, and limiting intake of foods with saturated fat, added salt and added sugars.<sup>51</sup> The guidelines recommend consuming five servings of vegetables and two servings of fruit per day, and limiting meat consumption to 455 g of lean meat per week (i.e. up to 65 g per day).<sup>51</sup>

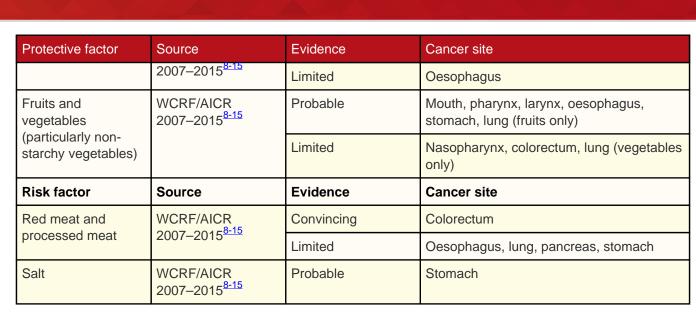
#### Cancer Australia recommendations for individuals

Cancer Australia recommends consuming adequate dietary fibre, including unprocessed cereals (grains) and pulses (legumes), and aiming for five servings of vegetables and two servings of fruit per day. Cancer Australia recommends limiting intake of red meat to less than 500 g per week and avoiding processed meat to reduce cancer risk. Cancer Australia recommends limiting intake of salt and processed foods with added salt to reduce cancer risk.

#### Table 4: Summary of evidence for diet and cancer sites

Protective factor	Source	Evidence	Cancer site
Dietary fibre in food	WCRF/AICR	Convincing	Colorectum





See <u>Appendix 1</u> for explanation of evidence.



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## Alcohol

It is estimated that 5.6% of cancer cases in Australia each year are attributable to long-term chronic use of alcohol.<sup>66</sup> Recent data from eight European countries in the EPIC study indicated that 10% of cancers in men and 3% of cancers in women were attributable to current and former alcohol consumption, a substantial proportion of which was associated with consumption above recommended upper limits.<sup>67</sup> The increased risk of cancer commenced at a low level and increased with higher levels of alcohol consumption.<sup>67</sup> WHO has estimated that excess alcohol consumption is responsible for 351,000 cancer deaths internationally each year.<sup>4</sup>

#### Alcohol consumption in Australia

Around one fifth of Australian adults consumed more than two standard drinks daily in 2011–12 and 44.7% consumed in excess of four standard drinks at least once a year.<sup>68</sup> Alcohol is the second greatest preventable cause of drug-related death and hospitalisation in Australia following tobacco.<sup>69</sup>

#### Alcohol and cancer

A 2012 IARC Monograph on alcohol reviewed the evidence and concluded that **alcohol is a Group 1 carcinogen**, which causes oral cavity, pharyngeal, laryngeal, oesophageal, colorectal, liver (hepatocellular carcinoma) and female breast cancers.<sup>5</sup> A positive association between alcohol and pancreatic cancer was also identified.<sup>5</sup> A recent meta-analysis including 572 studies has confirmed that alcohol increases the risk of these cancers.<sup>70</sup>

The IARC Monograph and WCRF and AICR report both reported that total alcohol consumption affects the risk of cancer, independent of the type of alcohol.<sup>5,8</sup> The IARC Monograph also classified both ethanol and acetaldehyde associated with alcohol consumption as Group 1 carcinogens.<sup>5</sup> The WCRF and AICR 2007 report recommends **limiting alcohol consumption**, based on the evidence that even small amounts of alcohol increase cancer risk.<sup>8</sup> The WCRF and AICR report recommends if alcoholic drinks are consumed, limiting consumption to no more than two drinks a day for men and one drink a day for women.<sup>8</sup>

Together, **tobacco smoking and alcohol consumption interact synergistically** to increase the incidence of cancers of the upper aerodigestive tract (i.e. oral cavity, pharyngeal, laryngeal and oesophageal cancers) beyond the single effects of tobacco smoking or alcohol (see Appendix 2 for explanation).<sup>5</sup> Alcohol consumption also contributes to greater energy intake, and the *Australian Dietary Guidelines* suggest limiting alcohol intake (and therefore energy intake) in the context of growing levels of obesity.<sup>51</sup>

#### Reducing individual risk of cancer and staying healthy

The <u>Australian Guidelines to Reduce Health Risks from Drinking Alcohol</u> provide the following guideline on reducing the risk of alcohol-related harm over a lifetime<sup>69</sup>:

- The lifetime risk of harm from drinking alcohol increases with the amount consumed.
- For healthy men and women, drinking no more than two standard drinks on any day reduces the lifetime risk of harm from alcohol-related disease or injury.

There are few studies on the effects of cessation of alcohol consumption on cancer risk. The available data



suggest that former drinkers have lower risks than current drinkers after 5-10 years' cessation for certain cancers, including oesophageal, oral and pharyngeal cancers. $^{5}$ 

#### Cancer Australia recommendations for individuals

The lifetime risk of harm from drinking alcohol increases with the amount consumed.<sup>69</sup>

For healthy men and women, drinking no more than two standard drinks on any day reduces the lifetime risk of harm from alcohol-related disease or injury.<sup>69</sup>

On the basis of international evidence specific to cancer,<sup>8</sup> it is recommended that if alcoholic drinks are consumed, women further limit alcohol consumption to one standard drink, to reduce cancer risk.

#### Table 5: Summary of evidence for alcohol and cancer sites

Risk factor	Source	Evidence	Cancer site
Alcohol consumption	IARC 2012 <sup>5</sup>	Sufficient evidence (highest IARC classification of carcinogenicity)	Oral cavity, pharynx, larynx, oesophagus, colorectum, liver (hepatocellular carcinoma), female breast
		Limited evidence (positive association)	Pancreas

See <u>Appendix 1</u> for explanation of evidence.



## UV radiation



Internationally, estimates of the percentage of cancer caused by ultraviolet (UV)/ionising radiation range from 2% in the United States<sup>2,3</sup> to 8–10% of cancer cases in European men.<sup>16,57</sup> According to WHO, there were 65,000 melanoma-related deaths internationally in 2000.<sup>1</sup>

#### UV radiation and cancer in Australia

International statistics likely underestimate the effect of UV radiation in Australia, which has the highest rate of skin cancer in the world.<sup>20</sup> The age-standardised incidence rate of melanoma in Australia in 2008 was more than 12 times than the average global rate.<sup>20</sup> Sun exposure has been estimated to cause around 95% of melanoma cases in areas of high exposure, such as Australia,<sup>71</sup> and around 99% of non-melanoma skin cancers in Australia.<sup>72</sup> Non-melanoma skin cancer (including basal cell carcinoma and squamous cell carcinoma) is the largest cause of hospitalisation from cancer in Australia<sup>73</sup> and around two in three Australians acquire at least one non-melanoma skin cancer by the age of 70 years.<sup>74</sup> Exposure to UV radiation, particularly during childhood and adolescence, is identified as the greatest risk factor for non-melanoma skin cancer.<sup>73</sup>

The National Sun Protection Survey 2010–11 indicates improvements in Australian attitudes regarding skin cancer prevention and protective behaviours.<sup>75</sup> Of those surveyed, 13% of adults and 21% of adolescents were sunburnt on a typical summer weekend, compared to the 2003–04 survey results of 18% and 25% respectively.<sup>75</sup> In the 2010–11 survey, 36% of adults and 37% of adolescents reported using sunscreen while outdoors.<sup>75</sup>

#### UV radiation and cancer

A 2012 IARC Monograph on radiation classified **UV radiation as a Group 1 carcinogen, which causes melanoma and other types of skin cancer**, including basal cell carcinoma and squamous cell carcinoma.<sup>6</sup> The IARC Monograph identified a positive association with lip cancer and cancer of the eye (conjunctival squamous cell carcinoma and ocular melanoma).<sup>6</sup> A systematic review in 2001 reported that melanoma risk may increase with cumulative sun exposure, and especially repeat burning and blistering.<sup>76</sup>

#### UV-emitting solaria and cancer

UV-emitting tanning devices (solaria) have also been classified as **Group 1 carcinogens** by the IARC, with evidence that these devices cause melanoma of the skin and eye, and are positively associated with squamous cell skin carcinoma.<sup>6</sup> An increased melanoma risk is associated with solaria use before the age of  $30.^{6}$ 

All Australian jurisdictions, except the Northern Territory and Western Australia, have introduced legislation to ban commercial solaria tanning units from 1 January 2015.<sup>78</sup> There are no solaria currently operating in the Northern Territory, <sup>78</sup> and Western Australia is reported to be committed to banning the commercial use of solaria.<sup>79</sup>

#### Reducing individual risk of cancer and staying healthy

Australian programs to reduce UV exposure and promote use of sunscreen and protective attire have changed attitudes regarding tanning and increasing protective behaviours,  $\frac{3}{7}$ ,  $\frac{75}{80}$  and there has been a decrease in sunburn amongst both adolescents and adults.  $\frac{75}{7}$ ,  $\frac{81}{7}$ 





Five sun protection behaviours are advised for Australians: to seek shade, wear sun protective clothing, put on a broad-brimmed hat, wear wrap-around sunglasses and to apply SPF30+ or higher sunscreen. It is also advised that sunbeds and solaria also emit UV radiation, so to be aware of the risks associated with tanning.

#### Cancer Australia recommendations for individuals

Cancer Australia recommends avoiding excessive sun exposure and solaria, and wearing sunscreen and protective clothing to lower risk of skin cancer.

#### Table 6: Summary of evidence for UV radiation and cancer sites

Risk factor	Source	Evidence	Cancer site
UV radiation	IARC 2012 <sup>6</sup>	Sufficient evidence (highest IARC classification of carcinogenicity)	Melanoma, basal cell carcinoma of the skin, squamous cell carcinoma of the skin
		Limited evidence (positive association)	Lip, conjunctival squamous cell carcinoma, ocular melanoma
UV-emitting tanning devices	IARC 2012 <sup>6</sup>	Sufficient evidence (highest IARC classification of carcinogenicity)	Melanoma of the skin and eye
		Limited evidence (positive association)	Squamous cell skin carcinoma

See <u>Appendix 1</u> for explanation of evidence.



## Infections

An estimated 3.3% of cancer cases in Australia and New Zealand are attributable to infections.<sup>82</sup> Globally, an estimated 16.1% of new cancers are attributed to infections, however estimates vary greatly between regions.<sup>82</sup>

A 2012 IARC Monograph on biological agents identified a number of different agents that cause cancers.<sup>7</sup> Human papillomavirus, *Helicobacter pylori*, and hepatitis B and C viruses were identified as the principal infectious agents in the World Cancer Report 2008, accounting internationally for 6.1%, 5.4% and 4.3% of all cancer cases respectively<sup>83</sup> and 1.9 million cancer cases worldwide.<sup>82</sup>

#### Human papillomavirus and cancer

Human papillomavirus (HPV) is a sexually transmitted virus. WHO has reported that HPV is responsible for 235,000 cancer deaths each year.<sup>4</sup> The IARC Monograph on biological agents classified **certain types of HPV as Group 1 carcinogens**, and reported that certain types of the virus cause cervical cancer, vulval cancer, vaginal cancer, penile cancer, anal cancer, oral cavity cancer, oropharyngeal cancer and tonsil cancer.<sup>7</sup> HPV is estimated to cause 100% of cervical cancer cases, 90% of anal cancers and 40% of external genitalia cancers.<sup>84</sup> The IARC evidence also supports an association between HPV and laryngeal cancer.<sup>7</sup>

#### Hepatitis B, hepatitis C and cancer

Hepatitis B and C viruses (HBV and HCV) are infections of the liver, transmitted via contact with blood or body fluids.<sup>85,86</sup> The majority of liver cancers are caused by chronic HBV and HCV infections, which have been estimated to be responsible for nearly 340,000 and 124,000 deaths worldwide per year respectively.<sup>4</sup> The IARC Monograph identified **chronic infection with HBV or HCV as Group 1 carcinogens**, and that chronic HBV or HCV infections cause hepatocellular (liver) carcinoma and non-Hodgkin lymphoma (HCV only).<sup>7</sup> The evidence also supports a positive association between these infections and cholangiocarcinoma (bile duct cancer) and non-Hodgkin lymphoma (HBV only).<sup>7</sup>

#### Other infections and cancer

Other infectious agents identified in the IARC Monograph cause cancers, including gastric cancer, lymphoma, nasopharyngeal cancer, cervical cancer, anal cancer, conjunctival cancer, Kaposi sarcoma, adult T-cell leukaemia/lymphoma, cholangiocarcinoma (bile duct cancer) and urinary bladder cancer.<sup>Z</sup>

#### Reducing individual risk of cancer and staying healthy

**Vaccination** protects against some infections, such as HPV and HBV.<sup>87</sup>,<sup>88</sup> A national Australian vaccination program to protect against HPV provides free school-based vaccination to boys and girls aged 12-13, with a catchup program during 2013-2014 for boys aged 14-15.<sup>89</sup> Vaccination against HBV is recommended for children as part of the National Immunisation Program.<sup>87</sup> More information about vaccination is available from the Immunise Australia Program.

Additional protective behaviours, such as practising safe sex and avoiding blood exposure through safe injection and blood transfusion practices, are suggested to lower risk of cancer due to infection.<sup>2</sup>,<sup>82</sup>



#### Cancer Australia recommendations for individuals

Cancer Australia recommends vaccination to protect against HPV and hepatitis B, and other protective behaviours, such as safe sex and safe injection and blood transfusion practices, to reduce risk of hepatitis C.

#### Table 7: Summary of evidence for infections and cancer sites

Risk factor	Source	Evidence	Cancer site
HPV	IARC 2012 <sup>Z</sup>	Sufficient evidence (highest IARC classification of carcinogenicity)	Cervix, vulva, vagina, penis, anus, oral cavity, oropharynx, tonsil
		Limited evidence (positive association)	Larynx
HBV and HCV	IARC 2012 <sup>Z</sup>	Sufficient evidence (highest IARC classification of carcinogenicity)	Hepatocellular (liver) carcinoma, non- Hodgkin lymphoma (HCV only)
		Limited evidence (positive association)	Cholangiocarcinoma (bile duct cancer), non- Hodgkin lymphoma (HBV only)

See <u>Appendix 1</u> for explanation of evidence.

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## Conclusion



At least one third<sup>1</sup> and potentially more than half of all cancers could be prevented through a combination of healthy lifestyle and regular screening.<sup>2,3</sup> This position statement summarises the evidence on cancer risk for seven modifiable lifestyle factors: tobacco, overweight and obesity, physical activity and sedentary behaviour, diet, alcohol, UV radiation and infections.

Based on the available evidence, Cancer Australia recommends seven behaviours for adults to reduce their risk of cancer:

- Don't smoke
- · Maintain a healthy weight
- Be active
- Eat a balanced and nutritious diet
- Limit alcohol consumption
- Be sun smart
- Reduce risk and protect against infection.

A number of these behaviours also have health benefits beyond cancer, in reducing risk of disease and death from other chronic diseases, such as cardiovascular disease and chronic respiratory disease. $\frac{4}{29}$ 



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## Appendix 1



#### International Agency for Research on Cancer (IARC)

The <u>IARC Monographs</u> identify factors that can increase the risk of human cancer, including lifestyle factors.<sup>5-7</sup> Interdisciplinary working groups of expert scientists review the published studies and evaluate the weight of the evidence that an agent can increase risk of cancer. Agents are then categorised as carcinogenic, probably or possibly carcinogenic, or not carcinogenic to humans, based on the strength of the evidence.

The evidence relevant to carcinogenicity of agents from studies in humans is classified into four categories by the IARC Working Group:<sup>90</sup>

- Sufficient evidence of carcinogenicity (highest IARC classification for carcinogenicity): The Working Group considers that a causal relationship has been established between exposure to the agent and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence.
- Limited evidence of carcinogenicity (positive association): A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.
- **Inadequate evidence of carcinogenicity**: The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between exposure and cancer, or no data on cancer in humans are available.
- Evidence suggesting lack of carcinogenicity: There are several adequate studies covering the full range of levels of exposure that humans are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure.

The IARC Working Group also considers the body of evidence as a whole, in order to reach an overall evaluation of the carcinogenicity of the agent to humans. The categorisation of an agent into one of the following four groups is a matter of scientific judgement that reflects the strength of the evidence derived from studies in humans and in experimental animals and from mechanistic and other relevant data:<sup>90</sup>

- Group 1 carcinogen: The agent is carcinogenic to humans. This category is used when there is sufficient evidence of carcinogenicity in humans.
- Group 2: Group 2A (probably carcinogenic to humans) or Group 2B (possibly carcinogenic to humans). This category includes agents for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost sufficient, as well as those for which, at the other extreme, there are no human data but for which there is evidence of carcinogenicity in experimental animals.
- Group 3: The agent is not classifiable as to its carcinogenicity to humans. This category is used most commonly for agents for which the evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals.
- Group 4: The agent is probably not carcinogenic to humans. This category is used for agents for which there is evidence suggesting lack of carcinogenicity in humans and in experimental animals.

Note – this position statement does not include agents with *inadequate evidence of carcinogenicity* or *evidence suggesting lack of carcinogenicity*, or agents which have been categorised lower than Group 1 by the IARC





Working Group.

## World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR)

The 2007 WCRF and AICR *Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective* report and subsequent tumour-specific updates are based on systematic reviews of the scientific literature for food, nutrition and physical activity.<sup>8-15</sup> An expert Panel judged and graded the evidence as convincing, probable, limited or unlikely to affect cancer risk, and developed recommendations to reduce the incidence of cancer.

The WCRF and AICR Panel made judgements on causation of disease based on assessment of independently conducted systematic reviews of the literature. The WCRF and AICR Panel graded the evidence into five categories:<sup>8</sup>

- **Convincing evidence**: This is the highest level attributed by the WCRF & AICR Panel, 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.
- **Probable evidence**: This is the second-highest level attributed by the WCRF & AICR Panel, 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.
- Limited suggestive evidence: These criteria are for evidence that is too limited to permit a probable or convincing causal judgement, but where there is evidence suggestive of a direction of effect.
- Limited no conclusion: Evidence is so limited that no firm conclusion can be made. This category is intended to allow any exposure for which there are sufficient data to warrant Panel consideration, but where insufficient evidence exists to permit a more definitive grading.
- **Substantial effect on risk unlikely**: Evidence is strong enough to support a judgement that a particular food, nutrition, or physical activity exposure is unlikely to have a substantial causal relation to a cancer outcome.

Note – this position statement does not include agents where the Panel has judged the evidence to be *limited* – *no conclusion* or *substantial effect on risk is unlikely*.



## Appendix 2

**Burden of disease** – a measure used to assess and compare the relative impact of different diseases and injuries on populations. It quantifies health loss due to disease and injury that remains after treatment, rehabilitation or prevention efforts of the health system and society generally.<sup>91</sup>

**Synergistic** – the interaction of two or more agents (or drugs) such that their combined effect is greater than the sum of the individual effects alone.  $\frac{92}{2}$ 



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