POSITION STATEMENT

Beta-carotene and cancer risk

Key messages

- Beta-carotene (β-carotene) is a type of carotenoid, an important precursor to vitamin A. Vitamin A is essential for biochemical and physiological processes in the body including vision, reproduction, cellular differentiation and immunity.

- β-carotene can be obtained from dark-green leafy vegetables and some (not all) yellow and orange coloured vegetables and fruits, as well as dietary supplements.

- There appears to be a marked interaction between β-carotene, smoking and genotype. Studies have shown there is a *convincing* association between β-carotene supplements and an **increased** risk of lung cancer in current smokers. β-carotene supplements are *unlikely* to have a substantial effect on the risk of prostate and non-melanoma skin cancers.

- However, foods containing carotenoids are associated with a *probable* **reduced** risk of lung, mouth, pharynx, and larynx cancer. Dietary β-carotene *probably* **reduces** the risk of oesophageal cancer and is *unlikely* to have a substantial effect on the risk of prostate and non-melanoma skin cancers.

- Cancer Council recommends people obtain their nutritional requirements from whole foods, rather than individual nutrients in a supplement form, and **avoid taking high doses (>18 mg) of β-carotene supplements**, especially if they smoke.

- Cancer Council supports the Australian Dietary Guidelines that recommend eating plenty of fruit and vegetables, and the population recommendation of at least two serves of fruit and five serves of vegetables daily. People should eat a wide variety of fruit and vegetables, including a range of different coloured fruit and vegetables, to obtain maximum benefits.

Background

β-carotene is the most potent carotenoid precursor to vitamin A.[1] Vitamin A is essential for biochemical and physiological processes in the body including vision, reproduction, cellular differentiation, gene expression, immunity and growth.[1,2]

Carotenoids are pigments in plants that are usually yellow or red.[1] The main dietary sources of β-carotene include dark-green leafy vegetables and some (not all) orange and yellow coloured vegetables and fruits such as carrots and dried apricots (Table 1).[1] Red palm oil is also rich in β-carotene, but is not often consumed in Australia.[1]

Table 1. Dietary sources of beta-carotene (β-carotene).[3]

Food	β-carotene (mg)*	Food	β-carotene (mg)*	Food	β-carotene (mg)*
Chilli powder	17.8	Sundried tomato	2.9	Cos lettuce	1.2
Carrot	7.9	Apricot, dried	2.5	Tabasco sauce	1.1
Sweet potato	6.8	Chives	2.3	Paw paw	0.9
Parsley	5.0	Mango	2.2	Rockmelon	0.9
Basil	3.2	English spinach	2.0	Persimmon	0.8
Butternut pumpkin	2.9	Red capsicum	1.3	Passionfruit	0.8

* β-carotene equivalents per 100g edible portion

Carotenes are not absorbed as well as other forms of vitamin A, such as retinol.[1] Carotenoids in the cells of dark-green leafy vegetables and carrots are not readily released in the body.[1] However carotenoids in the cell walls of fruits are more readily absorbed.[1]

In the western diet, vitamin A is mainly obtained from animal products rich in retinol such as milk, butter, cheese, egg yolk, liver and some fatty fish.[1] However carotenes, particularly β-carotene, are the main source of vitamin A in countries where animal product consumption is low.

β-carotene may also be obtained from dietary supplement preparations.

Rationale

Nutritional factors can play a role in the prevention of cancer. Epidemiological studies have shown that the intake of foods such as fruit and vegetables, which are rich in an array of phytochemicals and certain nutrients like carotenoids, are associated with a modest reduced risk of certain cancers. This evidence has encouraged research on individual nutrients and their association with cancer.

Vitamin A was one of the first nutrients to be evaluated, and β-carotene was initially believed to reduce the risk of lung cancer.[4] However in the 1990's two large randomised controlled trials (RCTs)[5,6] investigating high doses (≥20 mg/day of β-carotene) of β-carotene from supplements challenged this finding and prompted an intense review of β-carotene and its association with cancer.

The trials highlighted the need for further research, particularly into the mechanisms involved for individual nutrients. They also highlighted the potential dangers of dietary supplements, particularly when administered at doses not naturally found in foods.

Cancer Council has an important role to play in determining the association between different nutritional factors and cancer, and promoting advice to the community about how to reduce cancer risk. The purpose of this position statement is to evaluate and summarise the evidence linking β-carotene with cancer prevention.

Evidence from major reviews of epidemiological literature

Dietary β-carotene

The World Cancer Research Fund (WCRF) released a comprehensive report on food and the prevention of cancer in 2007 which found that foods containing carotenoids were *probably* protective against lung, mouth, pharynx, and larynx cancer.[7] Dietary β-carotene was associated with a *probable* reduced risk of oesophageal cancer, but was *unlikely* to have a substantial effect on the risk of prostate and non-melanoma skin cancers.[7]

In 2003 an expert report by the World Health Organization (WHO) observed that there was *possible/insufficient* evidence that carotenoids decreased the risk of cancer.[8] However the report did not distinguish between dietary and supplemental sources of carotenoids.

The International Agency for Research on Cancer (IARC) published a review of the evidence on carotenoids and cancer in 1998.[9] The review found there was *inadequate* evidence for the cancer preventive activity of β-carotene at usual dietary levels.[9] However the incidence of lung, oral and pharyngeal cancer tended to be inversely related to dietary β-carotene intake.[9]

β-carotene from supplements

In 2007, the WCRF found that β-carotene supplements were *convincingly* associated with an increased risk of lung cancer.[7] This evidence was derived from studies using high-dose supplements (≥ 20mg/day of β-carotene) in smokers (Figure 1).[7]

Trial name	Number of participants	Intervention	Length of intervention	Length of follow-up
Physicians' Health Study (PHS) Cook 2000	22 071	50 mg beta-carotene taken on alternate days	13 years	–
Women's Health Study (WHS) Lee 1999	39 876	50 mg of beta-carotene taken on alternate days	2 years	4 years
ATBC study (male smokers) Virtamo 2003 Albanes 1996	29 133	20 mg of beta-carotene only or with 50 mg of alpha-tocopherol	5–8 years	6–8 years
Western Perth asbestos workers de Klerk 1998	1024	30 mg/day beta-carotene or 25 000 IU/day retinol	Up to 5 years	–
Beta-Carotene and Retinol Efficacy Trial (CARET) Goodman 2004 Omenn 1996	18 314 at high risk of developing lung cancer	30 mg beta-carotene and 25 000 IU retinyl palmitate	4 years (trial ended early)	5 years

Figure 1. Trials identified by the World Cancer Research Fund investigating beta-carotene and lung cancer risk.[7]

The report noted that there was a marked interaction between β-carotene, smoking and genotype.[7] People who lack the carcinogen-detoxifying enzymes glutathione-*S* transferase 1 and 2, due to genetic variation, had a higher risk of lung cancer, particularly if they were smokers.[7] In addition, the risk of lung cancer among smokers taking higher does of β-carotene was greater than in smokers taking lower doses, despite adjustment for smoking habits and age.[7]

The WCRF concluded that β-carotene supplements were *unlikely* to have a substantial effect on the risk of prostate and non-melanoma skin cancers.[7]

In 2003 an expert report by the World Health Organization (WHO) observed that there was *possible/insufficient* evidence that carotenoids decreased the risk of cancer.[8]

The IARC review concluded in 1998 that the evidence *suggested* that β-carotene lacked cancer preventative activity when used as a supplement at high doses (≥15 mg/day of β-carotene).[9] In fact it was

noted that there was evidence of an increased risk of lung cancer among smokers and asbestos workers taking high doses of β-carotene supplements.[9]

Evidence from epidemiological studies for β-carotene as a supplement

Lung cancer

An RCT published in 2009 found that β-carotene (50 mg on alternative days) was not significantly associated with the risk of lung cancer in 8,171 women at high risk of cardiovascular disease (relative risk (RR)= 1.26, 95% confidence interval (CI)= 0.80-1.99).[10]

Another RCT, the Women's Health Study, did not find any significant association between β-carotene (50 mg on alternative days) and lung cancer risk in 39,876 female health professionals.[11] There was also no significant difference for smokers taking β-carotene supplements.[11]

Similarly, the Physicians' Health Study RCT found that β-carotene (50 mg on alternative days) did not significantly affect the risk of lung cancer in 22,071 male physicians (RR= 0.9, 95% CI= 0.7-1.2, p= 0.54).[12] When stratified by smoking status, there was no significant effect (p for trend= 0.88) of beta-carotene on lung cancer risk in both former (RR= 0.9, 95% CI= 0.8-1.0) and current smokers (RR= 1.0, 95% CI= 0.9-1.2).[12]

However, other trials do not support these results. An RCT published in 1998 showed that among 1,024 former asbestos workers, those taking retinol (7.5 mg/day) were significantly less likely to have malignant mesothelioma than those taking β-carotene (30 mg/day) (RR= 0.24, 95% CI= 0.07-0.86) (note this trial did not include a placebo arm).[13]

Therefore while β-carotene supplements do not appear to provide any benefit for cancer prevention, they may be harmful.

In 1996 the Beta-Carotene and Retinol Efficacy Trial (CARET) was stopped prematurely after it was found that in 18,314 smokers, former smokers and workers exposed to asbestos, the effects of a combination of β-carotene (30 mg/day) and vitamin A (7.5 mg/day of retinol in the form of retinyl palmitate) led to a significantly increased risk of lung cancer (RR= 1.28, 95% CI= 1.04-1.57, p= 0.02).[5] This effect was greatest in the heavy smokers who were smoking at the time of randomisation (RR= 1.42 95% CI= 1.07-1.87, p= 0.02).[5]

The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) trial was also stopped early after it was found that in 29,133 male smokers, lung cancer incidence was 18% higher in those receiving β-carotene supplements (20 mg/day) compared to those in the control group (95% CI= 3-36%).[6] The risk of lung cancer was higher in men who were heavy smokers and those with a higher alcohol intake.[14]

Therefore evidence suggests that β-carotene supplements may be associated with an increased risk of lung cancer in current smokers.[7]

Other cancers

Epidemiological studies do not show any strong association between β-carotene supplementation and the risk other cancers. Tables 2 and 3 show the evidence for cancers of the digestive tract and other sites respectively.

Potential mechanisms of action

Dietary carotenoids, including β-carotene, may lower cancer risk by:[9,15]

- Acting as an anti-oxidant, which inhibits oxidative or free radical induced damage to cells

- Stimulating gap-junctional communication between cells, which may prevent the malignant transformation and proliferation of cells
- Enhancing cellular defence systems, possibly involving tumour-specific antigens
- Formulating retinoic acid (particularly in those with low preformed retinol intake), which plays a role in gene regulation.

Cigarette smoke is highly oxidative and has been shown to destroy carotenoids in plasma.[16] Therefore β-carotene in the lungs of smokers may be susceptible to oxidative attack, leading to a pro-oxidant state which may promote cancer.[16]

The protective effect seen for dietary β-carotene and cancer may also not be due to β-carotene specifically, but possibly another carotenoid or mix of compounds in the diet.[7,9]

It is also possible that the protective effect of β-carotene at dietary intake amounts is lost or reversed with dietary supplementation and the higher levels that this can supply.[7] While excessive cellular oxidants can induce damage to cells, they are needed in moderate concentrations for several protective reactions, including apoptosis, phagocytosis and detoxification reactions provided by cytochrome P-450 complexes.[17] High doses of antioxidants can inactivate more cellular oxidants than necessary and interfere with these protective functions.[17]

Table 2. Summary of epidemiological studies on β-carotene supplements and risk of gastrointestinal cancers

Cancer Type	Author	Trial name	β-carotene Dose	Key Results
Gastrointestinal	Bjelakovic et al.[18]	Cochrane review	n/a	β-carotene supplements given singly (RR= 1.04, 95% CI= 0.80-1.35) or in combination with vitamin A (RR= 1.10, 95% CI= 0.91-1.32) or vitamin E (RR= 1.18, 95% CI= 0.98-1.41) did not significantly influence gastrointestinal cancer risk. β-carotene dose significantly associated with the estimated intervention effect on the occurrence of gastrointestinal cancers in a univariate meta-regression analysis (RR= 1.01, 95% CI= 1.002-1.02, p= 0.012), however the level of increased risk was very small.
Oral, Pharyngeal & Laryngeal	Wright et al.[19]	ATBC	20 mg/day	β-carotene supplement not significantly associated with the risk of oral/pharyngeal (RR= 0.97, 95% CI= 0.60-1.58) and laryngeal (RR= 0.65, 95% CI= 0.38-1.11) cancers in male smokers. Subgroup analysis suggests β-carotene supplement may have a protective effect on early stage laryngeal cancer (RR= 0.28, 95% CI= 0.10-0.75).
Oesophageal	Bjelakovic et al.[18]	Cochrane review	n/a	β-carotene supplements given singly (RR= 0.75, 95% CI= 0.25-2.30) or in combination with vitamin A (RR= 1.43, 95% CI= 0.90-2.29) or vitamin E (RR= 1.23, 95% CI= 0.59-2.56) did not significantly influence oesophageal cancer risk
	Wright et al.[19]	ATBC	20 mg/day	β-carotene supplement not significantly associated with the risk of oesophageal cancer in male smokers (RR= 0.85, 95% CI= 0.38-1.90)
Stomach	Bjelakovic et al.[18]	Cochrane review	n/a	β-carotene supplements given singly (RR= 1.12, 95% CI= 0.79-1.59) or in combination with vitamin A (RR= 0.89, 95% CI= 0.46-1.73) or vitamin E (RR= 1.40, 95% CI= 0.98-2.01) did not significantly influence stomach cancer risk

Cancer Type	Author	Trial name	β-carotene Dose	Key Results
	Lee et al.[11]	Women's Health Study	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of stomach cancer in female health professionals *
	Cook et al.[12]	Physicians' Health Study	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of stomach cancer in male physicians (RR= 0.9, 95% CI= 0.5-1.8, p= 0.87)
	Malila et al.[20]	ATBC	20 mg/day	β-carotene supplement not significantly associated with the risk of stomach cancer in male smokers (RR= 1.26, 95% CI= 0.88-1.80)
Colorectal	Bjelakovic et al.[18]	Cochrane review	n/a	β-carotene supplements given singly (RR= 1.09, 95% CI= 0.79-1.51) or in combination with vitamin A (RR= 0.97, 95% CI= 0.76-1.25) or vitamin E (RR= 1.20, 95% CI= 0.89-1.63) did not significantly influence colorectal cancer risk
	Lin et al.[10]	n/a	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of colorectal cancer in women at high risk of cardiovascular disease (RR= 1.32, 95% CI= 0.73-2.39)
	Lee et al.[11]	Women's Health Study	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of colon or rectal cancer in female health professionals *
	Cook et al.[12]	Physicians' Health Study	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of colon (RR= 0.9, 95% CI= 0.7-1.2, p= 0.48) or rectal (RR= 1.1, 95% CI= 0.7-1.8, p= 0.58) cancer in male physicians
	Albanes et al.[21]	ATBC	20 mg/day	β-carotene supplement not significantly associated with colorectal cancer incidence in male smokers (RR= 1.05, 95% CI= 0.75-1.47)

* Relative risk not reported.

Table 3. Summary of epidemiological studies on β-carotene supplements and risk of other cancers

Cancer Type	Author	Trial name	β-carotene Dose	Key Results
Breast	Lin et al.[10]	n/a	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of breast cancer in women at high risk of cardiovascular disease (RR= 1.01, 95% CI= 0.79-1.30)
	Lee et al.[11]	Women's Health Study	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of breast cancer in female health professionals *
Endometrial	Lin et al.[10]	n/a	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of uterine cancer in women at high risk of cardiovascular disease (RR= 1.27, 95% CI= 0.73-2.23)
	Lee et al.[11]	Women's Health Study	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of uterine cancer in female health professionals *
Ovarian	Lin et al.[10]	n/a	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of ovarian cancer in women at high risk of cardiovascular disease (RR= 1.20, 95% CI= 0.52-2.78)
	Lee et al.[11]	Women's Health Study	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of ovarian cancer in female health professionals *
Prostate	Cook et al.[12]	Physicians' Health	50 mg on alternative	β-carotene supplement not significantly associated with the risk of prostate cancer in male physicians (RR=

Cancer Type	Author	Trial name	β-carotene Dose	Key Results
		Study	days	1.0, 95% CI= 0.9-1.1, p= 0.62)
	Heinonen et al.[22]	ATBC	20 mg/day	Prostate cancer incidence 23% higher among male smokers receiving β-carotene supplements compared to those who did not; however difference not statistically significant
Pancreatic	Bjelakovic et al.[18]	Cochrane review	n/a	β-carotene supplements given singly (RR= 1.02, 95% CI= 0.54-1.90) or in combination with vitamin A (RR= 1.33, 95% CI= 0.84-2.09) or vitamin E (RR= 0.93, 95% CI= 0.65-1.35) did not significantly influence pancreatic cancer risk
	Lin et al.[10]	n/a	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of pancreatic cancer in women at high risk of cardiovascular disease (RR= 1.24, 95% CI= 0.51-2.99)
	Lee et al.[11]	Women's Health Study	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of pancreatic cancer in female health professionals *
	Cook et al.[12]	Physicians' Health Study	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of pancreatic cancer in male physicians (RR= 1.4, 95% CI= 0.8-2.6, p= 0.20)
	Rautalahti et al.[23]	ATBC	20 mg/day	Pancreatic cancer incidence 25% lower among male smokers receiving β-carotene supplements compared to those who did not, although the difference was not statistically significant
Liver	Bjelakovic et al.[18]	Cochrane review	n/a	β-carotene supplements given singly (RR= 1.92, 95% CI= 0.96-3.85) or in combination with vitamin A (RR= 1.35, 95% CI= 0.51-3.54) or vitamin E (RR= 1.25, 95% CI= 0.59-2.67) did not significantly influence liver cancer risk
Urinary tract	Lee et al.[11]	Women's Health Study	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of bladder cancer in female health professionals *
	Cook et al.[12]	Physicians' Health Study	50 mg on alternative days	β-carotene supplement significantly associated with the increased risk of bladder cancer in male physicians (RR= 1.5, 95% CI= 1.0-2.2, p= 0.04)
	Virtamo et al.[24]	ATBC	20 mg/day	β-carotene supplement not significantly associated with urothelial (bladder, renal pelvis and ureter) (RR= 1.0, 95% CI= 0.7-1.3) or kidney cancer (RR= 0.8, 95% CI= 0.6-1.3) in male smokers
Non-melanoma skin cancer	Frieling & Muntwyler[25]	Physicians' Health Study	50 mg on alternative days	β-carotene supplement not significantly associated with the risk of non-melanoma skin cancer (RR= 0.98, 95% CI= 0.92-1.05) in male physicians. No significant association when stratified by smoking status.

* Relative risk not reported.

Toxicity and recommended dietary intake

Vitamin A intakes are generally expressed as retinol equivalents (RE), where 6 mg of β-carotene gives rise to 1mg RE.[1,2] The recommended dietary intake (RDI) for vitamin A (RE) in the Nutrient Reference Values for Australia and New Zealand (NRVs) is 0.9 mg/day for men and 0.7 mg/day, with an upper level of intake (UL) of 3 mg/day (Table 4).[2]

Table 4. Estimated average requirements (EAR), recommended dietary intakes (RDI) and upper level of intake (UL) of vitamin A (as retinol equivalents).[2]

Age group & gender		Retinol equivalents (mg/day)		
		EAR	RDI	UL
Men	≥19 years	0.625	0.9	3.0*
Women	≥19 years	0.5	0.7	3.0*
Pregnancy	14-18 years	0.53	0.7	2.8
	19-50 years	0.55	0.8	3.0
Lactation	14-18 years	0.78	1.1	2.8
	19-50 years	0.8		3.0

* While no UL has been set for β-carotene specifically, 3 mg RE is equivalent to 18 mg β-carotene, which is less than the dose used in the ATBC study (20 mg) and CARET (30 mg).

Vitamin A is fat soluble and can be acutely toxic in adults at doses greater than 200 mg.[1] Chronic toxicity can occur after consuming at least 10 times the recommended daily allowance for a month or more.[1] Vitamin A toxicity can cause headache, visual impairment, skin disorders and death.[1]

Despite being a precursor of vitamin A, the toxicity of carotenoids is low.[1,2] Large amounts of β-carotene from foods can cause hypercarotenaemia (increased plasma carotene) and yellow colouration of the skin, particularly on the palms of the hand and soles of the foot.[1,2]

An UL for β-carotene from foods is not needed due to the lack of adverse effects.[2] However the UL for β-carotene for dietary supplement use has not been able to be established due to the lack of dose-response information in the literature.[2]

Current level of intake in Australia

The last National Nutrition Survey showed that men had a mean intake of 1.4 mg of vitamin A (RE) per day and women 1.1 mg per day.[26]

The Blue Mountains Eye Study showed that the mean intake of β-carotene in Australian women aged 55 years or over was 7.6 mg/day, and in men 6.9 mg/day.[27] However these values may be overestimates due to the use of a food frequency questionnaire for measuring intake.[27] Carrots and pumpkin contributed the most to dietary β-carotene intake in this population.[27]

Data on the use of specific dietary supplements (such as type and dose) is currently limited. Studies in the US have shown that dietary supplement use has increased over the past two decades.[28] Most people taking supplements are generally seeking health benefits, which could also be achieved by eating a healthy, well balanced diet.

Just under half (43%) of Australians aged 65-98 years reported using some form of dietary supplement in 2006.[29] Supplement use was significantly associated with gender (females) and conditions such as arthritis and osteoporosis, although the latter reason was likely to be representative of the population demographics in this particular study group.[29]

In 2003, a similar number (49%) of American adolescents aged 11-18 years from a single co-educational government school consumed vitamin and mineral tablets.[30] Commonly cited reasons for use included

health benefits, prevention of illness, sports performance, parental control, energy, poor diet and to do something positive for self.[31]

Interestingly, studies have shown that dietary supplement use is similar between cancer survivors and cancer-free controls.[32,33]

β-carotene supplements available in Australia

Increasingly complex mixtures of ingredients, which often contain other herbal and botanical compounds with anti-oxidant properties, are available in the market.[34] Consumers have access to numerous brands and formulations, including those available on the internet.

In Australia, dietary supplements are sold at places such as supermarkets, chemists and health food stores. β-carotene is available as an individual supplement or as part of a multi-vitamin preparation. Vitamin A preparations usually contain retinyl palmitate as the active ingredient.

As an indication at the time of writing this position statement, supplements available in Australia contained between 1 to 6.6 mg of β-carotene per tablet. Common brands recommended taking 1 to 3 tablets per day, making the maximum dose of β-carotene from any supplement 9 mg if taken according to the supplement instructions. Therefore amounts greater than the equivalent UL of 18 mg β-carotene in the NRVs (Table 4) may be obtained if tablets are taken in excess of the recommended dosage.

Recommendations

The NRVs do not contain an UL for β-carotene intake for dietary supplement use due to a lack of dose-response information in the literature.[2] β-carotene is of low toxicity and until recently was thought to only cause yellowing of the skin after sustained high intake.[1,2]

However recent epidemiological evidence shows that high doses of β-carotene supplements might increase the risk of lung cancer, particularly in smokers.

Therefore Cancer Council recommends people:

- Obtain their nutritional requirements from whole foods, such as fruits and vegetables, rather than individual nutrients in a supplement form
- **Avoid taking high doses (>18 mg) of β-carotene supplements**, especially if they smoke. Trials have shown that adverse consequences may result from doses of 20 mg.

Cancer Council supports the Australian Dietary Guidelines that recommend eating plenty of fruit and vegetables, and the population recommendation of at least two serves of fruit and five serves of vegetables daily (Table 6).[35,36] Cancer Council recommends that people eat a **variety** of fruit and vegetables, including a range of different coloured fruit and vegetables, to obtain maximum benefits.

Table 6. Sample fruit and vegetable serving sizes in The Australian Guide to Healthy Eating.[36]

Fruit	1 serve equals: • 1 medium piece (150g) of fruit (apple, banana, orange, pear) • 2 small pieces (150g) of fruit (apricots, kiwifruit, plums) • 1 cup (150g) diced pieces or canned fruit • 1½ tablespoons sultanas, 4 dried apricot halves • ½ cup (125mL) fruit juice
Vegetables	1 serve equals: • ½ cup (75g) cooked vegetables • ½ cup (75g) cooked dried beans, peas or lentils • 1 cup salad vegetable • 1 small potato

Cancer Council also:

- Supports that β-carotene supplements sold in Australia should include a **warning** with regard to the increased risk of cancer from high doses, especially for smokers
- Supports the **development of an UL** for beta-carotene in the NRVs due to the increased risk of cancer from high doses, especially for smokers.

Future research

In the future, there is a need for more studies that investigate:

- The dose-response relationship for β-carotene and lung cancer risk so that a safe upper limit can be established. Although an RCT with high doses may not be ethically feasible, other study designs may be able to provide further guidance on this issue.
- The mechanisms of action for β-carotene and cancer risk in order to determine if there is any difference between natural and synthetic β-carotene i.e. β-carotene from foods versus pharmacological supplements.

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References

1. West CE. Vitamin A and carotenoids. In: Essentials of Human Nutrition. Mann J, Truswell AS (editors). New York: Oxford University Press. 2002.
2. National Health and Medical Research Council. Nutrient Reference Values for Australia and New Zealand including Recommended Dietary Intakes. Canberra, Australia, Commonwealth Department of Health and Ageing. 2006.
3. Food Standards Australia and New Zealand. NUTTAB 2006 (Australian Food Composition Tables). Barton, Food Standards Australia and New Zealand. 2006.
4. Ziegler RG. A review of epidemiologic evidence that carotenoids reduce the risk of cancer. Journal of Nutrition. 1989; 119(1): 116-122.
5. Omenn GS, Goodman GE, Thornquist MD, Balmes J, Cullen MR, Glass A et al. Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. N Engl J Med. 1996; 334(18): 1150-1155.
6. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. N Engl J Med. 1994; 330(15): 1029-1035.
7. World Cancer Research Fund and American Institute for Cancer Research. Food, nutrition, physical activity and the prevention of cancer: a global perspective. Washington DC: AICR. 2007.
8. World Health Organization. Diet, nutrition and the prevention of chronic diseases. Geneva, WHO. 2003.
9. International Agency for Research on Cancer. Carotenoids. Lyon: IARC. 1998.
10. Lin J, Cook NR, Albert C, Zaharris E, Gaziano JM, Van DM et al. Vitamins C and E and beta carotene supplementation and cancer risk: a randomized controlled trial. J Natl Cancer Inst. 2009; 101(1): 14-23.
11. Lee IM, Cook NR, Manson JE, Buring JE, Hennekens CH. Beta-carotene supplementation and incidence of cancer and cardiovascular disease: the Women's Health Study. Journal of the National Cancer Institute. 1999; 91(24): 2102-2106.
12. Cook NR, Le IM, Manson JE, Buring JE, Hennekens CH. Effects of beta-carotene supplementation on cancer incidence by baseline characteristics in the Physicians' Health Study (United States). Cancer Causes & Control. 2000; 11(7): 617-626.
13. de Klerk NH, Musk AW, Ambrosini GL, Eccles JL, Hansen J, Olsen N et al. Vitamin A and cancer prevention II: comparison of the effects of retinol and beta-carotene. Int J Cancer. 1998; 75(3): 362-367.
14. Albanes D, Heinonen OP, Taylor PR, Virtamo J, Edwards BK, Rautalahti M et al. Alpha-Tocopherol and beta-carotene supplements and lung cancer incidence in the alpha-tocopherol, beta-carotene cancer prevention study: effects of base-line characteristics and study compliance. Journal of the National Cancer Institute. 1996; 88(21): 1560-1570.
15. Dawson MI. The importance of vitamin A in nutrition. Current Pharmaceutical Design. 2000; 6(3): 311-325.
16. Mayne ST, Handelman GJ, Beecher G. Beta-Carotene and lung cancer promotion in heavy smokers--a plausible relationship? J Natl Cancer Inst. 1996; 88(21): 1513-1515.
17. Salganik RI. The benefits and hazards of antioxidants: controlling apoptosis and other protective mechanisms in cancer patients and the human population. J Am Coll Nutr. 2001; 20(5 Suppl): 464S-472S.
18. Bjelakovic G, Nikolova D, Simonetti RG, Gluud C. Antioxidant supplements for preventing gastrointestinal cancers. Cochrane Database of Systematic Reviews. 2008;(3): CD004183.
19. Wright ME, Virtamo J, Hartman AM, Pietinen P, Edwards BK, Taylor PR et al. Effects of alpha-tocopherol and beta-carotene supplementation on upper aerodigestive tract cancers in a large, randomized controlled trial. Cancer. 2007; 109(5): 891-898.
20. Malila N, Taylor PR, Virtanen MJ, Korhonen P, Huttunen JK, Albanes D et al. Effects of alpha-tocopherol and beta-carotene supplementation on gastric cancer incidence in male smokers (ATBC Study, Finland). Cancer Causes & Control. 2002; 13(7): 617-623.
21. Albanes D, Malila N, Taylor PR, Huttunen JK, Virtamo J, Edwards BK et al. Effects of supplemental alpha-tocopherol and beta-carotene on colorectal cancer: results from a controlled trial (Finland). Cancer Causes & Control. 2000; 11(3): 197-205.
22. Heinonen OP, Albanes D, Virtamo J, Taylor PR, Huttunen JK, Hartman AM et al. Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: incidence and mortality in a controlled trial. Journal of the National Cancer Institute. 1998; 90(6): 440-446.
23. Rautalahti MT, Virtamo JR, Taylor PR, Heinonen OP, Albanes D, Haukka JK et al. The effects of supplementation with alpha-tocopherol and beta-carotene on the incidence and mortality of carcinoma of the pancreas in a randomized, controlled trial. Cancer. 1999; 86(1): 37-42.
24. Virtamo J, Edwards BK, Virtanen M, Taylor PR, Malila N, Albanes D et al. Effects of supplemental alpha-tocopherol and beta-carotene on urinary tract cancer: incidence and mortality in a controlled trial (Finland). Cancer Causes & Control. 2000; 11(10): 933-939.

25. Frieling UM, Schaumberg DA, Kupper TS, Muntwyler J, Hennekens CH. A randomized, 12-year primary-prevention trial of beta carotene supplementation for nonmelanoma skin cancer in the physician's health study. Archives of Dermatology. 2000; 136(2): 179-184.
26. Cook T, Rutishauser IHE, Allsopp R. The Bridging Study - comparing results from the 1983, 1985 and 1995 Australian national nutrition surveys. Canberra, Commonwealth Department of Health and Aged Care. 2001.
27. Manzi F, Flood V, Webb K, Mitchell P. The intake of carotenoids in an older Australian population: The Blue Mountains Eye Study. Public Health Nutrition. 2001; 5(2): 347-352.
28. Blendon RJ, DesRoches CM, Benson JM, Brodie M, Altman DE. Americans' views on the use and regulation of dietary supplements. Arch Intern Med. 2001; 161(6): 805-810.
29. Brownie S. Predictors of dietary and health supplement use in older Australians. Australian Journal of Advanced Nursing. 2006; 23(3): 26-32.
30. O'dea JA. Consumption of nutritional supplements among adolescents: usage and perceived benefits. Health Educ Res. 2003; 18(1): 98-107.
31. O'dea JA. Consumption of nutritional supplements among adolescents: usage and perceived benefits. Health Educ Res. 2003; 18(1): 98-107.
32. Greenlee H, White E, Patterson RE, Kristal AR. Supplement use among cancer survivors in the Vitamins and Lifestyle (VITAL) study cohort. J Altern Complement Med. 2004; 10(4): 660-666.
33. McDavid K, Breslow RA, Radimer K. Vitamin/mineral supplementation among cancer survivors: 1987 and 1992 National Health Interview Surveys. Nutr Cancer. 2001; 41(1-2): 29-32.
34. Rock CL, Newman VA, Neuhouser ML, Major J, Barnett MJ. Antioxidant supplement use in cancer survivors and the general population. J Nutr. 2004; 134(11): 3194S-3195S.
35. National Health and Medical Research Council. Dietary Guidelines for Australian Adults. National Health and Medical Research Council. Canberra. 2003.
36. Children's Health Development Foundation & Deakin University. The Australian guide to healthy eating. Canberra, AGPS. 1998.