

# The relationship between the consumption of fruits and vegetables and health status

**Report to Department of Health and Aged Care and the  
Strategic Intergovernmental Nutrition Alliance**

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## Executive summary

- This review was undertaken to assess the current knowledge about the links between fruit and vegetable consumption and chronic disease risk in relation to the Australian situation. A large number of original papers, meta-analyses and reviews were assessed and interpreted in relation to various diseases, to the various types of fruits and vegetables, to current population intakes and mechanisms of action. Estimates of attributable risk, potential savings in morbidity and mortality as well as health care costs are discussed in relation to those diseases for which suitable data exists. Reference is also made to the effect that recommendations to increase fruit and vegetable intakes might have on different sections of the community and potential adverse effects.
- Overall, the epidemiological data indicate a protective effect of fruits and vegetables against a number of chronic diseases. There are significantly more studies for cancer than any other disease condition and a moderate amount for cardiovascular disease. There are some indicative data for stroke, hypertension, cataracts, diabetes and other diseases such as arthritis, Alzheimer's, Parkinson's, inflammatory bowel disease, ulcers, gallstones, multiple sclerosis and osteoporosis but the data are too sparse to provide any meaningful assessment of the influence of fruits and vegetables.
- In recent years there have been three major reviews of the links between diet and cancer and the report discusses their findings alongside our own assessment. In our judgement, and that of the COMA expert panel from the UK, the evidence for an effect on cancer risk of increasing fruits and vegetables is moderately strong for some cancers but weak and inconsistent for others. The World Cancer Research Fund (WCRF) panel was more enthusiastic in their interpretation.
- Evidence for reduction in risk for cardiovascular diseases was also moderate and also relies more heavily on studies of related nutrients such as the antioxidant vitamins than on fruit and vegetable consumption per se. Data for other diseases were very limited but there are initial indications of potential benefit for increased consumption of fruits and vegetables
- There are insufficient data for any of the disease conditions to indicate promotion of any particular types of fruits and vegetables nor to identify any particular constituent. Neither is there compelling evidence from an examination of their nutrient and non-nutrient profile, to exclude canned, frozen or dried varieties or to exclude juice. Key reviews have highlighted the need to encourage variety of choice which could include use of fresh and processed fruits and vegetables. However, products which are based on fruit or vegetables but are heavily processed (eg certain pie fillings, biscuit fillings, health bars, jams etc) may have a quite different nutrient profiles and potential to influence health.
- Despite the more cautious judgement of the COMA panel, both they and we conclude that there is, however, still sufficient evidence to recommend an increase in the consumption of fruits and vegetables from the current levels. Intakes equivalent to 7 serves a day of fruits and vegetables (2 fruit; 5 vegetable) have been recommended by the NHMRC in their Core Food Groups. It should be noted, that these recommendations are not based on an analysis of the epidemiological data linking intake of fruits and vegetables to chronic disease outcome, but on estimates of amounts of various food groups required to achieve diets which conform to the Recommended Dietary Intakes, which are to a large extent based on avoiding deficiency disease. The data from epidemiological studies are not sufficiently robust to determine whether this level of consumption is optimal for chronic disease prevention but together with experimental and animal studies, they suggest that intakes substantially higher than currently consumed in Australia are likely to be beneficial
- Although some estimates have been made in Australia relating to the human and financial costs of a range of chronic diseases, no attempt has been made to look at individual dietary components. The only group, worldwide that has attempted such an analysis is the Wageningen group who assessed the potential effects for the Dutch situation with respect to cancer and cardiovascular disease. The work undertaken by the Wageningen group formed a key element in the quantified risk assessment made in the WCRF report but their methodology appears to have some

fundamental flaws, which would lead to overestimations of the protective potential. These are discussed in the body of the report. An analysis of the Wageningen data suggest that savings of some 6-7% could be made in cancer incidence and in cardiovascular mortality with diets higher in fruits and vegetables. The AIHW estimates cardiovascular disease costs Australia some \$ 4 000 million a year in direct health care costs and diet-related cancers some \$ 500 million in treatment costs.

- From a sociodemographic perspective, in Australia, adolescents and younger adults appear to be the subgroup in the Australian population whose intakes are of most concern compared to recommendations. There were no gender differences in absolute intake of fruit eaten per se or of vegetables other than potatoes. Potatoes were consumed more heavily in adult males than females. However, this means that as a proportion of total food or energy intake, males have a lower contribution to their diet from fruits and vegetables than females
- There were no overall differences in intake of total fruits and vegetables across people living in areas of varying social disadvantage but some indication of moderately lower fruit intake in those from areas of most social disadvantage. There were no significant differences in intake across metropolitan, rural centres and combined small rural/remote areas but the data could not be disaggregated to assess the intake in remote areas per se..
- In terms of ethnic groupings in Australia, the major difference seen was in lower total vegetable intake in those from an East Asian background but this mainly related to lower potato consumption as well as other root vegetables and tomato. Their intake of brassicae and green-leafy vegetables was significantly higher than other groups. There was significantly higher consumption of fruit from those from European background (non-UK/Ireland) compared to any other group
- Whilst there is some debate as to what foods should comprise the “fruits and vegetables” category, intakes in Australia for most age/gender groups, except the very young, are well below current the current NHMRC Core Food Group recommendations and those of the WCRF panel. It is worth noting that the NHMRC recommendations and those of WCRF for fruit and vegetable consumption are superficially very similar but the WCRF group recommendations excludes potatoes and legumes which makes a considerable difference in the Australian context.
- If recommendations are made to increase fruit and vegetable intake, the data would suggest that they should be targeted at the general population, possibly with an emphasis on adolescence and early adulthood, given the relatively low consumption at this age.
- Adhering to recommendations to increase consumption may bring difficulties to some groups in the community but more so, if campaigns centre on fresh food only. For fresh items there are considerations relating to storage, transport and need for more regular shopping that could prove a barrier to the elderly, those living in remote areas or those with limited time or facilities to store food. Many of these concerns can be overcome with inclusion of processed varieties. Whilst fresh varieties may have the optimal nutrient profile, this is not always the case and the nutrient profiles of many processed varieties can still be better sources of nutrients and bioactive components than the fresh version of other varieties.

## 1. Introduction

In the last two to three decades there has been a growing awareness of the role of diet in the etiology of the chronic diseases that are major contributors to morbidity and mortality in industrialised countries such as Australia, the United States and Europe. A multitude of bioactive substances in foods and drinks have already been identified and it is likely that many more exist. Beneficial effects of these nutrients or bioactive substances are often used to ascribe such effects to the foods containing them. However, each food is a complex mixture of biologically active substances and its overall effect on the health of the consumer will not only relate to the balance of these components within the food itself but how they interact with or complement components from other foods, how overall dietary intake interacts with other non-dietary risk factors for health and with the individual genetic and biological profile of the individual.

The complexity of foods is well illustrated with reference to fruits and vegetables. In recent years, a growing amount of attention has been given to fruits and vegetables and the role they might have in preventing a range of chronic disease conditions such as cancer, coronary heart disease, stroke, diabetes, cataracts, arthritis, Alzheimer's disease and inflammatory bowel disease (see refs 1-554 for original studies and reviews). There are many biologically active substances in fruits and vegetables including both nutrients and non-nutrients for which protective health effects have been postulated. These include vitamins C and E, folic acid, carotenoids, selenium, dietary fibre (including resistant starch), dithiolthiones, glucosinolates, and indoles, isothiocyanates and thiocyanates, coumarins, flavonoids, phenols, protease inhibitors, isoflavones, saponins, plant sterols, inositol hexaphosphate, allium compounds and limolene. They are also relatively low in fat and dietary energy.

Whilst fruits and vegetables are a source of a wide range of essential nutrients, as a food group they are relatively poor sources of many essential nutrients such as zinc, vitamin B12, iron and calcium. In addition, they may also contain substances with known adverse effects such as aflatoxin, biproducts from the pickling process, nitrates, phytates, goitrogens, and natural plant-produced or agricultural pesticides. Certain flavonoids, indoles, phenolic compounds and fibre have also been shown to have carcinogenic as well as anticarcinogenic properties. This is not surprising given the variety of structures or compounds within these categories and by the fact that the enzyme systems induced by some of them have both activating and detoxifying actions depending on the xenobiotic involved. Mutagenic activity has been identified in association with fruits and vegetables using the well known Ames test with the most potent being onions, grapes, raisins, peaches, strawberries and raspberries (555).

Nevertheless, on balance, it appears that fruits and vegetables contain more protective than harmful components and, as such, advice to increase consumption has been recommended by a number of international health authorities.

## 2. Current consumption and category definitions

Given the growing interest in the role of fruits and vegetables in health promotion, what then is the current consumption of fruits and vegetables in Australia. In describing current intakes it is necessary first to define what is meant by the term "fruit(s) and vegetables". In much of the epidemiological literature, lack of definition is a cause of much confusion and it is not clear what has and what has not been included.

### 2.1 Categorising fruits and vegetables

Where specific definitions have been given, as in some key major reviews (551, 552), the definition, particularly for vegetables, appears much narrower than that used by nutrition educators and health authorities involved in promotion of dietary guidelines. For example in two recent reviews of the effects of diet and cancer risk by the World Cancer Research Fund (WCRF 551) and the working group on diet and cancer of the Committee on Medical Aspects of the Food Supply (COMA 552) in the UK, bananas are excluded from the fruit category and potatoes, legumes and pulses from the vegetable category on the basis that they belong in a different food groups termed either "roots, tubers and plantains or "pulses /legumes" (WCRF) or "starchy foods" and "pulses/legumes" (COMA). The "roots, tubers and plantains" category of WCRF includes cassava or manioc, potatoes, sweet potatoes,

yams and taro as well as plantains (including banana) breadfruit and sago. In this definition, non-starchy root vegetables such as turnips, swedes, carrots and parsnips are included in the vegetable category

Given that “starchy” fruits and vegetables like potatoes, sweet potatoes and bananas contain some of the same protective components as other fruits and vegetables (such as vitamin C, carotenes, dietary fibre including the resistant starch component, potassium and many of the other non-nutrient bioactive compounds) it does not seem logical to exclude them from consideration simply on the basis that they contain starch. This is particularly relevant in the light of the emerging evidence of the potential of resistant starch to act in the same manner as some components of dietary fibre or non-starchy polysaccharides (556). Neither a “root, tuber, plantain” nor a “starchy food” category appear in the food guides or dietary guidelines in countries such as Australia, the United States, In the United Kingdom and some other European countries, potatoes are either included with cereal foods in a staple, starchy food category, in a root vegetable group (including carrots/turnips etc) or listed as a separate group in their own right. In the current Australian Food Guide (557) and in the NHMRC Core Food Group analysis, (558) potatoes were included in the vegetables group in developing consumption recommendations. As potatoes are the dominant component of the “vegetable” category, their exclusion would have major implications for promotional campaigns in the Australian context. Nevertheless many (but not all) of the epidemiological studies assessing links between “vegetable” consumption and health outcome have excluded potatoes and other starchy roots, often putting them in a category of their own, sometimes not assessing their effects. Other studies have been conducted in countries, such as China, where potatoes are not a key dietary ingredient.

In the light of these considerations, given the limited data relating to potatoes per se, the dominance of potatoes in the Australian diet compared to other vegetable items and the need to encourage variety of consumption, it might be wise to when developing educational campaigns to stress the need to increase consumption of other vegetable categories..

The “pulses /legumes” category contains beans, peas, lentils and groundnuts (peanuts) including items such as broad beans, chickpeas, kidney beans, soya beans and navy beans which are the more commonly consumed of the group in Australia. “Legumes” do appear in the Australian food guide as part of two categories. The first is “vegetables, legumes” and the second “meat, fish, poultry, eggs, nuts, legumes”. This reflects their high protein content and potential to substitute for animal-based protein foods. Because of their nutrient profile, legumes are a valuable addition to the diet. They are not currently consumed in very large amounts in the Australian diet, in a culinary or common-use sense they are regarded by most Australian as belonging to the “vegetable” category and it might be advisable therefore to include them as part of the “vegetable” category for educational purposes.

To encourage variety of consumption and through that the intake of a wide range of plant-based bioactive substances, education strategies may need to address subcategories of vegetables such as the starchy, red-yellow, green-leafy, cruciferous groupings with the degree of detail depending on the purpose of the promotion, the target population and the media used.

In this review, in assessing current intakes we use the term “fruits and vegetables” in its common use or culinary form to include potatoes, sweet potatoes, bananas and legumes and items such as sweet corn or corn-on-the-cob which are botanically members of the cereal group but which in common use or in a culinary sense are used as “vegetables” but have given data relating specifically to these items where available. To this end items such as tomatoes avocados, cucumbers, aubergines (egg plant), pumpkins (winter squash) and zucchini (courgettes) are also defined as “vegetables” even though botanically they are fruits. We also include all canned, frozen and dried fruits and vegetables as there is no compelling evidence that the overall nutrient profile of these foods falls outside the range for fresh fruits and vegetables even though their content may be reduced compared to their source item and as they have generally been included in epidemiological studies. Many of the non-nutritive components thought to influence chronic disease risk are also unaffected by treatments such as heating or freezing. For major items such as fruit juice and potatoes as well as legumes/pulses we have also given some analyses excluding these items.

As stated earlier, most major reviews especially those relating to cancer have excluded potatoes and pulses/legumes and as such their general conclusions and recommendations are based on a narrower definition For both the starchy roots and pulse/legume categories per se there is very little epidemiological evidence such that most reviewers have not been able to make a judgement about their

**Table 1. Definitions of fruits and vegetables (including legumes) commonly used in epidemiology and in the Australian National Nutrition Survey 1995/6 (559)**

Main category	Subcategories used in epidemiology	Equivalent NNS * category	Examples (includes fresh, frozen or canned)
Fruit	Citrus	Orange	Orange, mandarin, grapefruit, lime, lemon
		Other Citrus	
	Other	Pome	Apple, pear
		Berry	Raspberries, strawberries
		Stone	Peach, apricot, cherries
		Tropical	Pineapple, mango, banana
	Other	Grapes, kiwi, melons	
Dried	Dried, preserved	Figs, sultanas dates, others as above but dried/preserved	
Fruit juice	Fruit & vegetable juices and drinks (as part of non-alcoholic beverages)	Orange juice and other fruit juices	
Vegetables and legumes	Green-leafy	Leaf and stalk vegetables	Alfalfa bean sprout chives lettuce parsley spinach/silverbeet, celery, endive, brussel sprouts, cabbage, kohlrabi,
	Cruciferous/brassica	Cruciferous/brassica	Broccoli, cabbage, cauliflower, sauerkraut, brussel sprouts, kohlrabi
	Allium	Part of "Other vegetables"	Onions, garlic, chives, leeks
	Potatoes and other starchy roots	Potatoes only (not others eg sweet potato)	All forms of potato including boiled, mashed, baked, hot chips and salad potato
	Red-yellow; orange-yellow or red-yellow	Parts of "Carrot and similar roots", "other fruiting vegetables" and "Tomatoes"	Carrots, pumpkins, tomatoes
	Root vegetables	Carrots and similar root vegetables	Carrot, beetroot, parsnip, radish, sweet potato
	Legumes and pulses	Legumes and pulses	Kidney beans, chick peas, lentils, baked beans
		Peas and beans	Green beans, peas, snowpeas

health potential.. For this reason, in reviewing the epidemiological data the generic term 'fruits and vegetables' excludes consideration of the effects of potatoes and legumes. The classifications that have been used in epidemiological research and reviews as well as those used in the Australian National Nutrition Survey (559) included are shown in Table 1.

Difficulties arise in summarising studies on fruits and vegetables because of the wide variations in groupings used. Some studies report for broad categories only "all vegetables" or "all fruit"; others use terms such as "raw vegetables", "green vegetables" "citrus fruit" and some report individual fruits or vegetables. Sometimes a question is asked only about total fruit or vegetable consumption and the definition of what constitutes a fruit or vegetable is left up to the respondent, other times the researchers have given an exhaustive list of individual items for the subject to respond to and then totalled the items to give overall intake.

An analysis of the Australian National Nutrition Survey (559), shows that these various approaches can give vastly different results. For example the data from the 24hr recall for adults over 19 years of age indicated that subjects consumed just over 2.7 serves of vegetables a day (a serve being 75g). This was similar to the figure obtained in response to a single question about usual total vegetable intake which included sample serve sizes (mean just over 2.5 serves a day) but was very different from the figure of just under 7 "serves" a day derived from totalling responses to questions about usual intake of some 20 individual vegetables where no serve size was indicated. This relates to the wide range of serve sizes that vegetables can be consumed in (eg a slice of tomato in a sandwich versus a cup of peas). For fruit, the data was more consistent. Many epidemiology surveys, particularly the earlier ones, used a non-quantified frequency method for assessing individual vegetable intakes with a summary of this data for various sub-categories or for assessing total intake.

One other methodological issue that also needs to be borne in mind in assessing the epidemiological data relates to social desirability bias. Self-report figures for fruit and vegetable consumption in epidemiology studies often indicate intakes much higher than for the source population. It has been suggested that this may in part be due to self selection of higher social status groups into the studies but social desirability may also play a role (551). This latter effect will lead to more bias in the more numerous, case-control studies where cases are self-reporting diets after a period of illness, compared to the more rare, prospective cohort studies where tendency to conform is likely to be more evenly partitioned.

Generally speaking, in defining fruits and vegetables, two types of definition emerge - those based on a scientific or botanical description and those based on what is variously called culinary, dietetic or common-use criteria. In most epidemiological studies, the latter definition is used. In this sense it covers a wide variety of plants and plant parts. Botanically, they are not mutually exclusive. As Table 1 illustrates, for fruit the major sub-categories, if any, used in epidemiology are citrus as opposed to non-citrus fruit. Occasionally dried fruit is listed specifically but for no specifically identified reason. Citrus fruits are often listed separately because of their particularly high vitamin C profile as a group. However some other fruits have equally high levels as the citrus fruits. In addition, as vitamin C is not the only food component of interest in chronic risk reduction, most studies do not delineate between citrus and non-citrus sources. Perhaps the key area for discussion with respect to fruit is whether to include fruit juice and, if so, on what basis. This is of particular importance in the Australian context because of the popularity of the various types of fruit juices. Fruit juices and fruit juice drinks vary widely in terms of the amount of juice contained, the level of refinement and the techniques used to extract and reconstitute the juices. All these factors influence the final nutrient profile of the juice. However, it must also be stated that whole fruits vary widely in their content of key components such as vitamins C, beta carotene and fibre and the other bioactive compounds. Is it equitable then to exclude fruit juices if their known nutrient content falls within the range for whole fruits for many of these key nutrients?

Similar considerations need to be weighed when deciding on the inclusion or exclusion of canned, tinned or frozen fruits. For the nutrients and biologically active non-nutrients we are aware of, it would seem that the form in which the fruit comes does affect some of its components but that the range of values obtained still fall within the range for whole fruits (see Section 3.3). It would seem illogical, therefore, to exclude these items as they add variety and may be more acceptable and accessible to many groups in the population. It is notable, for example that in the Northern Territory where fresh fruit is more difficult to access, the intake of fruit juice is almost equal to that of whole fruit whereas in most other mainland states, whole fruit consumption is at least twice the juice consumption. Having said that, it would still be advantageous to stress the added value of fresh fruit as a generally more concentrated source of beneficial nutrients. It should also be noted that products which are based on fruit but are heavily processed (eg certain pie fillings, biscuit fillings, health bars, jams etc) may have quite different nutrient profiles and potential to influence health.

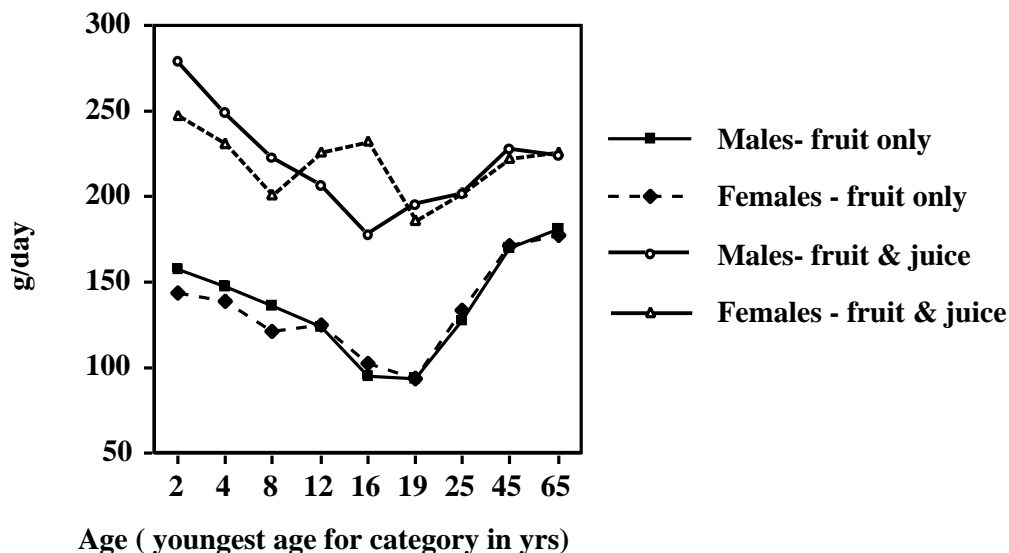
The same considerations apply to the vegetable category. Freezing and canning are used widely for the vegetable category and although use of vegetable juices is not as common in the Australian cuisine, inclusion or exclusion of soups casseroles needs to be considered given their popularity in the local cuisine. Within the vegetable category, the range of definitions are more diverse. Apart from the issue of exclusion or inclusion of potatoes, other starchy roots and legumes, there are a number of non-exclusive categories that have been used in the literature. In the crudest delineation, colour-related definitions (green or green-leafy; red-yellow or orange-yellow or red-orange) have been used based loosely in part on green-leafy vegetables being good sources of folic acid and red-yellow-orange vegetables, of beta carotene.

The colour-based approach also has appeal as an education approach for the general public. Other categories have emerged as our knowledge of food components has increased based on subcategories of carotenes (eg lycopenes in tomatoes) or to their content of non-nutrient bioactive compounds (eg the allium family or the crucifers). Some of the groupings overlap (eg green-leafy and leafy/stalk) and some individual foods can be included in more than one category (eg carrots in red-yellow and in root vegetables). It is likely that these categories will be further refined with increasing knowledge but what is essential is that future studies and recommendations clearly define the foods included in categories and the rationale for the categorisation.

## 2.2 Current intakes of fruits and vegetables in Australia

What then do we know of current Australian intakes of the various fruit and vegetables categories? The most recent Australian National Nutrition Survey was undertaken in 1995/6 (559). This survey was performed as an adjunct to the National Health Survey. Dietary data were collected on approximately 13,000 individuals between February 1995 and March 1996. Respondents were aged 2 years and over, and were drawn from both metropolitan and rural areas throughout Australia. In an interview, subjects were asked to recall all the foods and drinks consumed the previous day. For each food eaten, information was collected on portion size, time and place of consumption, and where the food was obtained. Respondents aged 12 years and over were also asked to complete an (unquantified) food frequency questionnaire containing 107 common food items. This supplied a measure of “usual intake” of core foods. There was an additional two questions asking for usual frequency of intake of “serves” of fruits or “serves” of vegetables with examples of a serve given in common household measures.

**Figure 1. Fruit intake by age\* and gender from National Nutrition Survey 1995/6**



\*Age categories used 2-3yrs, 4-7 yrs, 8-11 yrs, 12-15 yrs 16-18 yrs 19-24yrs 25-44 yrs, 45-64 yrs and 65 +

Excluding fruit juice, on the day of survey some 42% of adults did not eat any fruit with over 60% of young adult males being in this category. With fruit juice excluded, only 17% had the recommended 300g on the day of survey. With fruit juice included the figure still rose to only 28%. Some 16% had no vegetables at all with the figure rising to 29% if potato was excluded. With potatoes included, some 32% had over 300g of vegetables a day, the bottom end of the range recommended by the NHMRC Core Food Group guide (this guide included potatoes). The WCRF report on diet and cancer risk (551) recommended some 400-800g/day excluding potatoes and legumes - only 8% of adult subjects reached 400g/day on this basis.

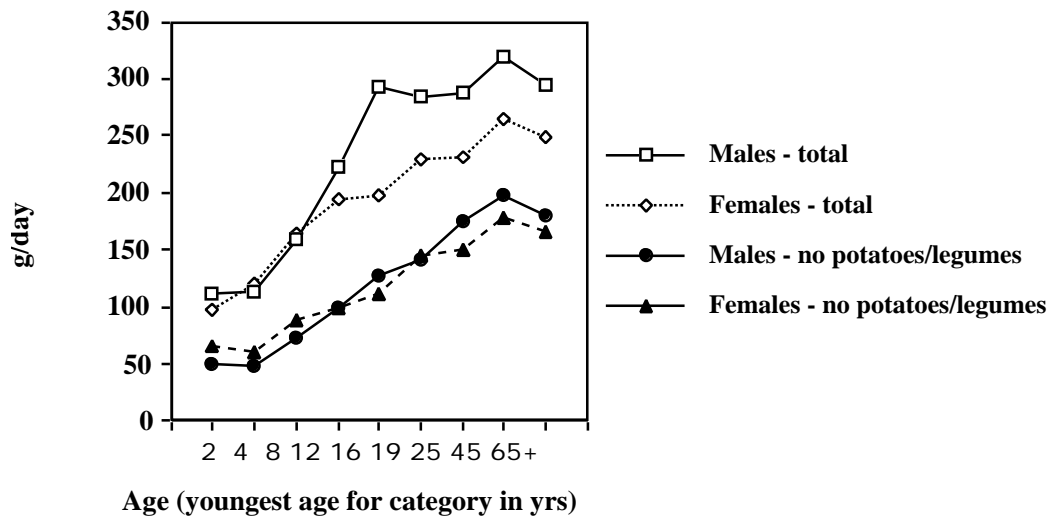
According to the 24hr recall data, mean intakes of whole fruit were approximately 150g/day in 2-3 year olds but fell sharply from that age to their lowest level of just under 100g/day by age 16-24 yrs after which they rose again to some 175g/day by age 45-64 yrs. (see Figure 1) Patterns for males and females were similar as were absolute amounts consumed except for slightly lower intakes (about 8-10%) in girls up to 12 years of age than in boys of equivalent age. When fruit juice was added to the total, a different pattern of total consumption emerged for the females but the pattern of consumption

was similar in males with adolescence, early adulthood continuing to be the period of lowest consumption. For females there was a relatively high intake of fruit juice in the 12-15 and 16-18 year age groups such that total intake in these ages was amongst the highest. The 19-24 year olds intake of juice was however, not sufficient to overcome their low whole fruit intake and they remained the lowest consuming group ( see Figure 1).

In contrast, vegetable consumption (including potato, other starchy vegetables and legumes) showed a steady increase over age with similar intakes in males and females up to early adolescence after which male intakes were considerably higher. Given the exclusion of potatoes and legumes in some reviews, Figure 2 also shows intakes without the inclusion of potatoes and other starchy roots and legumes. If potatoes and legumes are removed from the total, the difference between males and females in total intake is relatively small. The major difference between the genders was in potato consumption.

**Figure 2. Vegetable intake by age\* and gender from National Nutrition Survey 95/96**

\*Age categories used 2-3yrs, 4-7 yrs, 8-11 yrs, 12-15 yrs 16-18 yrs 19-24yrs 25-44 yrs, 45-64 yrs and



65 +

Table 2 shows a comparison of intakes measured in the 1995/6 survey with those recommended in the NHMRC Core Foods Document (558). It should be noted that specific mention of fruit juices is not made in the document, they are neither specifically included or excluded. Potatoes and legumes were included as vegetables in the calculations. The Core Food Groups were designed to produce diets which conformed both to recommended dietary intake recommendations for nutrients such as energy, protein, carbohydrate and vitamins and minerals together with recommendations for macronutrients such as fat and dietary fibre. The resulting recommendations were closely aligned with those produced earlier by CSIRO in the 12345+ Food & Nutrition Plan (560) and in a number of other Australian and overseas food guides. It should be noted that these recommendations and food guides are not based on an analysis of the epidemiological data linking intake of fruits and vegetables to chronic disease outcome, but on estimates of amounts required to achieve diets which conform to recommended dietary intakes, which are predominantly designed to prevent deficiency. On the basis of 150g of fruit and 75g of vegetables equating to one “serve” of the respective food groups, one serve of fruit a day was recommended for children up to 11 years, two to three serves for adolescents and two serves for all other ages. For vegetables, two serves a day were recommended for children up to 7 years, three for 8-11 yr olds, four for adolescents and four to five for those aged 19 years and over.

For fruit, even with fruit juice included, only the young children under 7 years have intakes in line with recommendations from the NHMRC Core Food group analysis. All other groups range from 49-76% of

recommended intake when juice is included or from 26-60% of the recommended value with juice excluded. The group that appears to be furthest from recommendations with juice included is 16-18 year old males and with juice excluded, males from 16-25 years and females from 19-24 years. The groups who most closely conform to recommendations are children under 7 years and older adults.

For vegetables, with potatoes and legumes included and using mid-points of recommended ranges where appropriate, intakes in males ranged from 71-98% recommended with those over 16 years having intakes closest to recommendations. Intakes in females were not generally as high compared to recommendations ranging from 64-80% but the advantage for males was removed when potatoes and legumes were taken out of consideration. When this was done, for both males and females, intakes ranged from only 32-60% of recommended. With 8-16 year olds being furthest from recommendations.

An analysis by social status (based on area of residence) for those over 19 years showed little difference across social groups for total vegetable consumption whether potatoes were included or excluded. This held true for both men and women. Intakes of fruit showed an upward trend with increasing social status. In women, those in the lowest social quintile had intakes some 23% less than those in the top quintile. With juice removed, the disparity was ameliorated a little to 19%. For men, with juice included the lowest

**Table 3 Intakes of fruits and vegetables in Australia in relation to recommendations from the NHMRC Core Food Group analysis**

Ages	Fruit				Recommended	Vegetables				
	Intakes % recommended		Recommended	Intakes as % recommended		Recommended				
	Including juice	Excluding juice		Including potato / legumes			Without potato / legumes			
M	F	M	F	M	F	M	F			
4-7	165	154	98	92	150	76	80	45	40	150
8-11	62	57	37	33	300-450	71	73	32	32	225
12-15	57	63	34	36	300-450	74	64	33	33	300
16-18	49	65	26	29	300-450	98	66	42	29	300
19-24	65	62	31	31	300	86	68	46	42	300-375
25-44	67	67	42	44	300	87	69	52	45	300-375
45-64	76	74	53	57	300	95	79	60	52	300-375
65+	74	75	60	59	300	88	75	54	49	300-375

*\* serve of fruit equals 150 g; serve of vegetables equals 75g; where recommendations are a range, the mid point has been used for calculations*

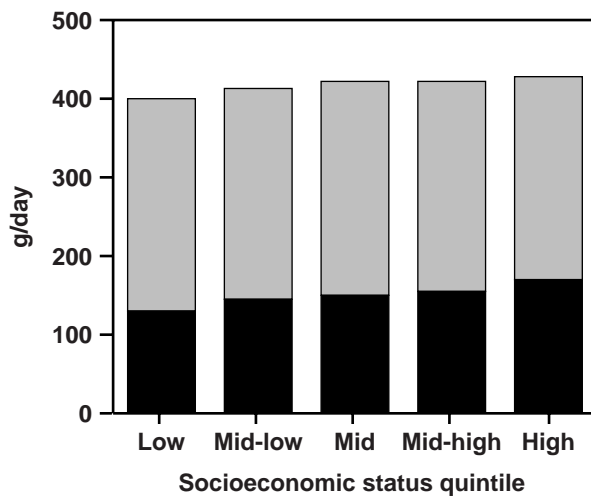
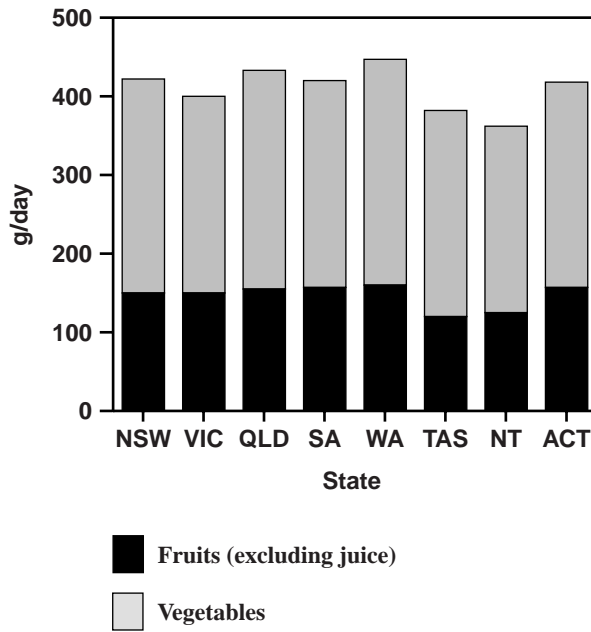
*\* note: WCRF recommends 400-800g/day excluding potatoes and legumes for adults*

quintile had 27% lower intakes and with juice excluded, some 24% less. Total consumption of fruits and vegetables with fruit juice, potatoes and legumes included ranged from 483g/day for the lowest social group to 531g/day for highest social group males and from 433g to 480g for females.

An analysis by state showed that the intakes for fruit per se were highest in WA and SA and lowest in Tasmania and Northern Territory. However, fruit juice consumption was particularly high in the Northern Territory and the ACT and particularly low in WA such that ACT, Northern Territory, South Australia and New South Wales had highest total fruit and juice intakes and WA and Tasmania the lowest. For vegetables, intakes were very similar across states (from 244–280g/day) but Tasmania had a somewhat larger proportion provided by potatoes (40% compared to most other states at 30-35%).

Average consumption of vegetables was somewhat higher in rural and remote areas (282g/day) compared to rural centres (255g) and metropolitan areas (249g) with much of the difference relating to potato consumption. There were no differences in total fruit consumption across these areas but fruit juice consumption was somewhat higher in metropolitan areas.

**Figure 3. Fruit intake (excluding juice) and vegetable intake (including potatoes/legumes) by state or social status**



People from European countries other than the UK and Ireland had higher fruit intakes than Australian born people or those from the UK/Ireland or East Asia. Fruit juice consumption was fairly similar across groups. In contrast, those from Asia had particularly low total vegetable consumption compared to other groups predominantly due to lower potato consumption (36g/day vs 65-105g in other groups). They also had fewer carrots, peas and beans and tomato but higher intakes of brassica and green-leafy vegetables compared to Australian born subjects.

To assess whether there have been significant changes in consumption over the past decade or so, a comparison was made with the 1983 National Dietary Survey of Adults (561). That survey was undertaken by a similar, but not identical, 24hr recall technique in capital cities only for people living within 16km or so of the centre of the city. In addition, no collection of data was undertaken in the months of December to April excluding peak consumption time for many seasonal fruits and vegetables. We could not access data for central metropolitan areas only so the 1995/6 data includes a wider sampling frame of people from capital cities and other metropolitan centres of greater than 100,000 population.

Given these limitations, mean intakes of vegetables as a whole do not appear to have changed since 1983 but fruit appears to have fallen some 15%. In the 1995/6 survey highest fruit consumption was recorded in the summer months when, for the 1995/6 survey, intakes were some 30% higher. This would have accounted for about one third of this difference between the two surveys but still indicate a fall in consumption in this food group. Overall vegetable intake did not vary across seasons in 1995/6.

#### **Summary of current consumption and category definition**

- Whilst there is some debate as to what foods should comprise the “fruits and vegetables” category, intakes in Australia for most age/gender groups, except the very young, are well below current the current NH&MRC Core Food Group recommendations and those of the WCRF panel. It is worth noting that the NH&MRC recommendations and those of WCRF for fruit and vegetable consumption are superficially very similar but the WCRF group recommendations excludes potatoes and legumes which makes a considerable difference in the Australian context.
- Adolescents and younger adults appear to be the subgroup in the Australian population whose intakes are of most concern compared to recommendations. There were no overall differences in intake of total fruits and vegetables across people living in areas of varying social disadvantage but some indication of moderately lower fruit intake in those from areas of most social disadvantage. There were no significant differences in intake across metropolitan, rural centres and combined small rural/remote areas but the data could not be disaggregated to assess the intake in remote areas per se.
- In term of ethnic groupings in Australia, the major difference seen was in lower total vegetable intake in those from an East Asian background but this mainly related to lower potato consumption as well as other root vegetables and tomato. Their intake of brassica and green-leafy vegetables was significantly higher than other groups. There was significantly higher consumption of fruit from those from European background (non-UK/Ireland) compared to any other group.
- The data would suggest that health promotion programs designed to increase fruit and vegetable intake should be targeted at the general population, possibly with an emphasis on adolescence and early adulthood, given the relatively low consumption at this age.
- Adhering to recommendations to increase consumption may bring difficulties to some groups in the community but more so, if campaigns centre on fresh food only. For fresh items there are considerations relating to storage, transport and need for more regular shopping that could prove a barrier to the elderly, those living in remote areas or those with limited time or facilities to store food.

### 3. Mechanisms by which components of fruit and vegetables may influence the risk of disease

Epidemiologic data relating health outcomes to dietary habits may be interpreted in various ways, and many texts have warned of the dangers of attributing causal relationships to associations which have been detected using observational, as opposed to experimental, data. A basic prerequisite for arguing that an association is causal is an appropriate underlying mechanism. (For example, the credibility of the hypothesis relating brain cancer to exposure to the electromagnetic radiation around mobile phones is a contemporary example in which proponents of the hypothesis are having difficulty convincing the sceptics that the energy of the radiation is sufficient to cause the damage deemed necessary to initiate carcinogenesis).

A wealth of plausible mechanisms relating dietary factors to modified risks of disease has been established in the past thirty years. However it must be acknowledged that the existence and details of these mechanisms have been established, of necessity, from studies using laboratory animals and chemically induced cancers and animal models of cardiovascular disease.. This immediately raises questions such as :

- Do these mechanisms operate in humans?
- Are chemically induced cancers or cardiovascular lesions true models of the cancers or vascular conditions experienced by humans?
- Are the tissue concentrations of phytochemicals required to have effects in laboratory animals the same as in humans?
- Are the tissue concentrations of phytochemicals required to have effects in humans achievable by dietary means?

The most convincing answers to these questions are usually provided by randomised clinical trials, but there are many situations when an randomised clinical trial is neither feasible or ethically sustainable.

Proposed mechanisms of action in relation to cancer and cardiovascular disease are outlined below. Specific mechanisms relating to other conditions are discussed together with the epidemiological evidence.

#### 3.1 Cancer

Some of the major groupings of dietary factors associated with reduced risks of cancer are discussed below:-

##### 3.1.1 Plant phenolics

The term plant phenols encompasses a wide variety of naturally occurring compounds which are structurally related to the extent that they all contain one or more benzene rings, each with one or more hydroxyl group substitutions. Under this general rubric are included (1)the *simple phenols* eg gallic acid (tea), p-cresol (raspberry and blackberry, vanillin (vanilla); (2) the *hydroxycinnamic acid derivatives*, eg chlorogenic acid, a major component of coffee; and (3) the *flavonoids* including catechins from tea, anthocyanins which determine the colours of many flowers and fruits, and the ubiquitous flavones and flavonols.

In broad terms these substances are important for:-

- Their antioxidant properties, ie their ability to scavenge naturally occurring free radicals before they can damage macromolecules directly or indirectly involved in either cell proliferation (relevant to carcinogenesis) or lipid metabolism (relevant to cardiovascular disease).
- Blocking the formation of carcinogenic nitrosamines arising from the reaction of dietary nitrates/nitrites with secondary amines and amides in the stomach.

- Their capacity to act as electrophile traps. In much the same manner in which they can scavenge nucleophilic free radicals, many plant phenols can also absorb highly reactive electrophiles thereby preventing damage to cellular components
- Inhibiting the generation of prostaglandins from arachidonic acid, and thereby retarding a 'promotional' phase of carcinogenesis.

### 3.1.2 Isothiocyanates

Cabbages, watercress and other cruciferous vegetables owe their sharp taste in part to isothiocyanates arising from the action of the enzyme myrosinase on glucosinolate conjugates. These isothiocyanates have been observed to inhibit chemically induced cancers in a variety of animal models. The mechanism involves the inhibition of the so-called Phase I enzymes whose normal function is to prepare foreign molecules for detoxification and excretion– but which sometimes generate highly reactive intermediates capable of far more damage than the original substrates.

### 3.1.3 Phytoestrogens

There is still no agreement on how to define a phytoestrogen. In the context of this report any phytochemical which can substitute for, or block the action of, natural, endogenously produced steroid sex hormones may be regarded as a phytoestrogen.

A recent definition of phytoestrogens as “plant derived compounds that can regulate gene expression that is mediated by an Estrogen Response Element, in a manner either comparable or apparently antagonistic to 17 $\beta$ -oestradiol, as a result of binding to the oestrogen receptor” (562), is too restrictive, and precludes a number of effects which are being increasingly linked in the literature with phytoestrogens.

A confusing aspect of the usage of the term 'phytoestrogenic' is the fact that compounds to which this adjective is commonly applied may either *mimic* the effects of natural endogenous oestrogen, or they may *block* them - and the same compound may be an agonist in one situation and an antagonist in others. A substance which is sufficiently similar to endogenous oestrogens to occupy an oestrogen binding site, but not sufficiently similar to reliably induce the event which normally ensues when natural oestrogen binds, would clearly be acting as an antagonist. However, when natural oestrogen is either absent, or present only in very low concentrations (postmenopausally, for example), the limited ability of a phytoestrogen to induce the secondary event may still be significant, and warrant its reclassification as an agonist.

Given the epidemiologic evidence of an increasing risk of breast cancer with increasing cumulative oestrogen exposure it is perhaps not surprising that historically, our interest in the relevance of phytoestrogens to breast cancer stemmed from their ability to act as antagonists of oestradiol. Oestrogens should not just be linked with unfavourable long-term health outcomes, however. Premenopausally women have much more favourable risk factor profiles for cardiovascular disease than men – and this may be due to direct and indirect effects of oestradiol. There is also considerable contemporary interest in the potential for phytoestrogens, acting as oestrogen agonists, to alleviate the morbidity (eg hot flushes) associated with the cessation of oestradiol production at the menopause, and to slow or halt the bone-loss which can eventually lead to osteoporosis.

Major classes of phytoestrogenic substances in the diet include flavonoid compounds (flavones, isoflavones, flavanones), lignans, and coumestrol from legume sprouts. While flavonoid compounds are widespread in foods of plant origin, the most significant compounds with oestrogenic activity in this class are genistein and daidzein, found in largest amounts in the soybean (563), and formononetin from clovers. Lignans, which are characterised chemically by a 2,3-dibenzylbutane structure are also widespread in plant foods, although the flaxseed contains concentrations which are two orders of magnitude higher than any other known source (564). Oestrogenic activity is critically dependent on the metabolism of these compounds by the microflora in the large bowel where daidzein may be either generated from formononetin or metabolised to equol (565,566), and the “mammalian lignans” enterolactone and enterodiol are generated from less oestrogenic precursors such as matairesinol and secoisolariciresinol (567).

Descriptive studies examining urinary excretion or plasma levels of phytoestrogens in groups with different experiences of hormone dependent cancers have been summarised by Adlercreutz and Mazur (568). While phytoestrogen intakes are highest in the populations with the lowest cancer risk, this evidence remains circumstantial - and experience with the correlational studies of per capita fat consumption and breast cancer should have taught us to regard this kind of evidence as encouraging, but open to many alternative interpretations.

An especially exciting finding, from a case-control study conducted in Western Australia by Ingram et al, of substantially reduced risks of breast cancer associated with high urinary excretion of phytoestrogens is currently in press (569).

Angiogenesis, the process by which new capillaries develop from pre-existing vessels, and on which 'solid' cancers are critically dependent for growth, has been shown to be sensitive to phytoestrogens - especially genistein (570).

Sex hormone binding globulins (SHBG) are circulating proteins which are synthesised in the liver, and which exhibit a high affinity for both oestradiol and testosterone. Since the biological activity of steroid hormones bound to SHBG is very low, their bioavailability is determined to a significant extent by the circulating levels of SHBG (571). Indeed SHBG concentrations increase in response to rising levels of either sex hormone and hence appear to be acting as regulators. The notion that phytoestrogens might stimulate synthesis of SHBG and thereby significantly reduce the bioactivity of endogenous oestrogens has been championed by Adlercreutz and coworkers (572) - but their human work was based on very heterogeneous groups of participants, and other studies, including unpublished work of our own, have failed to observe any dietary dependence of SHBG (573).

The observation that some phytoestrogens can inhibit growth in tumours with and without oestrogen receptors underscores the potential importance of mechanisms unrelated to phytoestrogenic activity in the prevention of malignancy. Genistein, for example, appears to be able to inhibit the tyrosine-protein kinase intimately involved in determining the activity of proteins which regulate cell proliferation (574); to inhibit topoisomerase II (575); and to arrest the cell division cycle around the G2 to M phases (576).

Within the context of breast cancer, an important property of phytoestrogens may be their ability to inhibit the cytochrome P450 aromatase, which catalyses the final step in the synthesis of oestrogen and oestrone from testosterone and androstenedione respectively (577).

For prostate cancer, the ability of phytoestrogens to inhibit the reductase which converts testosterone to its bioactive form in the prostate, dihydrotestosterone may be an important chemopreventive mechanism (578). Certainly this reductase has been the target of chemotherapeutic drugs such as finasteride that are currently undergoing Phase III clinical trials in the US.

In many ways the phytoestrogen and cancer story is a case-study in the contemporary status of the nutritional epidemiology of cancer. Weak ecologic data shows that countries whose populations consume the largest amounts of phytoestrogen-rich foods also have the lowest incidence of hormone dependent cancers. Laboratory studies in animal models of breast and prostate cancer together with observations of the effects of phytoestrogens on cell lines either in vitro or implanted, have been encouraging, and have assisted in the identification of a considerable number of mechanisms, although the relative importance of these mechanisms individually is largely undetermined, - and the ability of many phytoestrogens to act as weak agonists of endogenous oestrogens is confusing. Some of these mechanisms directly involve oestrogen signal transduction pathways, but others clearly do not. The evidence from analytical human epidemiology is both sparse and of variable quality - but generally supportive of the hypothesis that phytoestrogens may be chemopreventive agents. The information is still not sufficiently convincing, either with respect to their anti-carcinogenic properties or the 'doses' needed to achieve them, in order to make dietary recommendations of a public health nature.

#### **3.1.4 Monoterpenes**

Monoterpenes such as limonene and perillyl alcohol (found in the essential oils of citrus fruits, cherry, spearmint, dill and caraway - and also used as flavouring agents) can inhibit the biochemical modifications required to incorporate proteins into cell membranes. Many proteins whose functionality

depends on their location within membranes play important regulatory roles – and it has been demonstrated that monoterpenes can prevent the incorporation into membranes of the growth signalling *ras* proteins which become damaged and lose control early in the carcinogenesis process.

### **3.1.5 Organosulphur compounds**

Garlic and other *Allium* species (onions, leeks) contain organosulphides such as diallyl sulphide which can inhibit chemically induced cancers in laboratory animals. A definitive mechanism has not been established yet – but there is growing evidence that these compounds have differential effects on the Phase I enzymes (cytochrome P450 isozymes) involved in the activation/detoxification/excretion of ‘foreign’ dietary substances (579,580).

### **3.1.6 Dietary fibre**

The term dietary fibre is a rubric for dietary components entering the large bowel having survived the digestive processes in the stomach and small intestine. Non-starch polysaccharides make up the major component of dietary fibre. People who consume diets rich in fibre typically exhibit high stool weights and low (rapid) transit times through the gut, which is the basis for hypotheses that fibre simply reduces the extent to which epithelia in the gut are exposed to carcinogens such as the secondary bile acids produced by the bacterial action on the primary bile acids required for the dispersal of dietary fats.

Possibly more important, however, is the capacity of the bacterial flora in the large bowel to ferment non-starch polysaccharides. The short-chain fatty acids (SCFA) generated by fermentation include butyric acid, which, in addition to being a preferred energy substrate for colonocytes, is also capable of inducing aberrant cells to ‘differentiate’ and resume a quiescent state most closely related, in functional terms, to the mature colonocyte.

Fermentation may also release sequestered minerals (like calcium) and reduce bowel pH; with both effects acting in concert to precipitate harmful bile acids.

In recent years it has been increasingly appreciated that significant amounts of dietary starch may also resist digestion in the upper alimentary tract, and contribute to the fermentable substrates in the large bowel. Unripe bananas and cold cooked potatoes are rich sources of ‘resistant’ starch. Importantly, the SCFA mixture arising from the fermentation of resistant starch appears to be particularly rich in butyric acid.

### **3.1.7 Phytates (inositol phosphates)**

The outer layer (bran) component of most mature nuts and seeds is rich in phytates, which are well known for their ability to sequester metals and/or minerals. It is not known whether this property is relevant to the mechanism by which phytates appear to be able to inhibit carcinogenesis initiated by the polyaromatic hydrocarbon dimethyl benzanthracene in laboratory animals (581).

### **3.1.8 Indoles**

Indole-3-carbinol (derived from the glucosinolate glucobrassicin in *Brassica* vegetables) has been intensely studied by Bradlow and associates for its apparent ability to divert oestrogen metabolism along a pathway which results in greater production of a less bioactive 2-hydroxy metabolite instead of the more problematic 16-alpha-hydroxy metabolite. This property might be protective against breast cancer.

### **3.1.9 Carotenoids**

Responsible for the colouring, carotenoids are found in a variety of orange/yellow fruits and vegetables as well as some dark green leafy vegetables (spinach, cabbage and brussels sprouts). The most well known example is beta-carotene. Like many carotenoids, beta-carotene is a powerful antioxidant (a striking example being the protection it offers the algae from which it is commercially harvested against harmful ultraviolet radiation from the sun). It is also a precursor of vitamin A (retinol) and retinoic acid which have been demonstrated to have the ability to induce differentiation of neoplastic

and preneoplastic cells. Intervention trials in populations at risk of skin, cervix, colon and lung cancer have failed to demonstrate any health benefits, however.

The alpha-carotenoid lycopene (to which tomatoes owe their red colour) is a very powerful antioxidant which has been associated with reduced risk of prostate cancer.

### **3.1.10 Folic acid**

The vitamin folic acid, from green leafy vegetables, oranges and orange juice, and the outer layers of many seeds and grains, plays an important metabolic role in the synthesis of DNA, and in situations requiring the transfer of a methyl group to a biological acceptor molecule. Methylation of DNA itself appears to be an important mechanism for controlling the expression of many genes, including those involved in cell proliferation – and abnormal methylation states of DNA (usually low methylation) have been associated with a number of neoplastic and preneoplastic conditions.

### **3.1.11 Vitamins C and E and selenium**

The water-soluble antioxidant vitamin C is present in many fruits and vegetables, especially citrus and peppers.. It can prevent the formation of carcinogenic nitrosamines from nitrite and secondary amines in the stomach. It reduces the mutagenicity of gastric juices, and plays a role in immune function. It also regenerates the intracellular fat soluble antioxidant vitamin E (a collective term for a number of tocopherols and tocotrienols). Vitamin e in turn may also keep selenium, another antioxidant. in a reduced state.

## **3.2 Cardiovascular disease**

### **3.2.1 Effect of antioxidants on oxidation of Low Density Lipoprotein (LDL)**

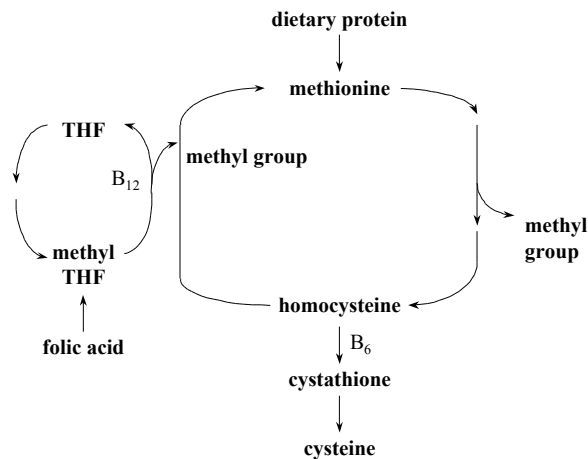
A key event in the development of atherosclerotic lesions is the oxidation of Low Density Lipoprotein (LDL). Any agent which can inhibit this oxidative step has the potential to influence adverse cardiovascular events due to accumulation of plaque. Historically, attention was focussed first on the antioxidants beta-carotene and vitamin C, but with an increasing understanding of the antioxidant properties of many other dietary phytochemicals, the more recent studies have also looked for protective effects of flavonoid compounds (present in a wide variety of vegetables, legumes, and in tea) and other carotenoids, including lycopene, of which tomatoes are the richest dietary source. The alpha-tocopherols (vitamin E) are also potent antioxidants, but they are largely found only in nuts and seeds, and may not fall within the scope of this review.

### **3.2.2 Effect of folate on homocysteine**

Homocysteine is a sulphur-containing amino acid derived from enzymic transformations of the essential dietary amino acid methionine. Interest in this substance stemmed initially from the observation that sufferers from a number of different rare genetic disorders which all manifested themselves in elevated levels of circulating homocysteine also had in common a greatly accelerated rate of atherosclerosis. This immediately begged the question of whether mild elevations of serum homocysteine were also associated with increased cardiovascular disease - and increasingly it seems that the final answer is likely to be 'yes'. Since 1976 more than 20 retrospective studies and three prospective studies have demonstrated a relation between moderate homocysteinuria and premature vascular disease in the coronary, cerebral and peripheral arteries. Infusion of homocysteine into experimental animals leads to damage of the endothelial lining of blood vessels with platelet activation.

Figure 4 shows methionine being released from dietary protein by hydrolysis. Homocysteine is then generated from methionine by three enzymically catalysed steps during which a methyl group is transferred to an appropriate acceptor. It is estimated that for the average Australian diet, around 50% of the homocysteine generated from dietary methionine is converted via a vitamin B6 dependent process to cystathione and then cysteine. The other 50% is recycled back to methionine by a complex of folic acid molecules (tetrahydrofolate or THF), in a process which requires not just folic acid, but vitamin B12 as well.

**Figure 4 Methionine-related metabolic pathways**



Supplementation using folic acid with and without vitamin B6 to reduce serum homocysteine levels has proved to be a successful strategy in some initial studies – and hence dietary folate from vegetables, whole grain foods and supplemented breakfast cereals may influence cardiovascular disease risk.

### **3.3 Effects of food preparation techniques on the availability of nutrients and non-nutrients in fruits and vegetables**

The epidemiologic data is far too variable and not sufficiently detailed to make any confident assessment question of whether fresh fruit and vegetables may confer more of a health benefit than cooked, frozen or canned produce. However, for a number of the nutrients, micronutrients and the so-called non-nutrients which have been identified in fruit and vegetables, data are available concerning the effects of food preparation techniques on their bioavailability, absorption, distribution and elimination.

Given the variety of phytochemicals which may have health benefits, it is hardly surprising that preparation methods have varying effects depending on the nature of the phytochemical. Some examples are cited below.

- Cutting, shredding, homogenising and juicing expose many phytochemicals to the oxygen in air – and this can have dramatic effects on the levels of the reducing agents/antioxidants such as vitamin C. Many juice manufacturers are aware of this problem, however, and fortify their product accordingly – so that it would be wrong to conclude that juices are not a good source of vitamin C. Heating and cooking further reduces vitamin C levels.
- Isothiocyanates occur as their glucosinolate conjugates in a wide variety of cruciferous vegetables. When vegetable cells are damaged by cutting and shredding, the enzyme myrosinase is released, and it is responsible for the hydrolysis of the glucosinolates and the subsequent generation of isothiocyanates. Similarly the action of the enzyme allinase generates a number of organosulphur compounds when garlic, onion, and other *Allium* vegetables are crushed in air.
- Flavonoid compounds including phytoestrogens appear to be reasonably heat-stable and are largely unaffected by cooking.
- Soy isoflavones are located largely in the outer layers, and hypocotyl of the bean which are removed in the preparation of some soy products, – so soy flours are generally better sources of phytoestrogens than soy milks, although it is likely that the latter will soon be available in fortified form.

- Beta-carotene, which is extremely sensitive to heat and light under isolated conditions is protected by its micro-environment within plant cells, and may even become more bioavailable as a result of cooking.
- Another fat-soluble carotenoid, lycopene, is derived largely from tomatoes. Studies have revealed that its bioavailability is increased significantly by cooking in the presence of a cooking fat or oil.
- A newly recognised type of dietary fibre, resistant starch, is generated by allowing cooked potatoes to cool before they are consumed.

In the face of this variation in optimal food preparation techniques, simple recommendations to eat foods raw rather than cooked, or fresh rather than canned are likely to be too simplistic. While recommendations can be formulated to optimise the bioavailable yield of specific phytochemicals, it would be dangerous to presuppose that all the beneficial phytochemicals in foods of plant origin have been identified and their biological actions and sensitivities to preparation techniques described.

### **3.4 Potential adverse effects of fruits and vegetables**

Whilst fruits and vegetables are a source of a wide range of essential nutrients, they are, as a group, relatively poor sources of many essential nutrients such as zinc, vitamin B12, iron and calcium. These nutrients are currently amongst those at greatest risk in the Australian diet., particularly amongst young women and others with limited food intakes. Thus when promoting a substantial increase in intakes of fruits and vegetables, it is essential that care is taken to also encourage consumption of foods rich in zinc, B12, iron and calcium. Promotion of meal solutions linking meats to vegetables or dairy foods to fruit might provide a framework for this whole of diet approach.

In addition, fruits and vegetables may also contain substances with known adverse effects such as aflatoxin, biproducts from the pickling process, nitrates, phytates, goitrogens, and natural plant-produced or agricultural pesticides. These latter remain a key consumer concern in relation to the food supply. Although levels of agricultural pesticides are monitored regularly by government authorities, and are below acceptable levels, residues remain a consumer issue and the perception needs to be addressed. Food safety issues are still high on the consumer agenda and have been revived through the recent debate on genetic engineering.

Certain flavonoids, indoles, phenolic compounds and fibre have also been shown to have carcinogenic as well as anticarcinogenic properties. This is not surprising given the variety of structures or compounds within these categories and by the fact that the enzyme systems induced by some of them have both activating and detoxifying actions depending on the xenobiotic involved.

Mutagenic activity has been identified in association with fruits and vegetables using the well known Ames test with the most potent being onions, grapes, raisins, peaches, strawberries and raspberries (555). However, in general, epidemiological data indicates that the protective effect of fruits and vegetables appears to outweigh the potential negative effects.

The potential for microbial contamination in relation to consumption of fresh fruits and vegetables and unpasteurised juices is another area that needs to be carefully monitored in the light of recent overseas and Australian experience.

### **Summary of mechanisms by which fruits and vegetables can influence health**

- There are a number of compounds in fruits and vegetables which have been found to have health promoting properties. These include plant phenolics, isothiocyanates, phytoestrogens, monoterpenes, organosulphur compounds, dietary fibre, indoles, carotenoids, folic acid, vitamins C, E and selenium.
- Some but not all of these can be adversely affected by food preparation techniques such as heat treatment. In some instances, such as the carotenoid lycopene, however, heat treatment increases activity. As such tinned, canned or frozen products can be included as part of fruit and vegetable intake but heavily processed products such as certain pie fillings and jams or heavily salted items, may have very different component profiles and health effects.
- Fruits and vegetables may contain compounds such as phytates and goitrogens which can have adverse effects and they are generally low in some vitamins and mineral such as iron, zinc, calcium and vitamin B12. There is also a potential problem related to consumer perception of pesticide residues. Whilst these issues need to be addressed, on balance, the evidence would suggest that these potential adverse effects are far outweighed by the benefits of increased fruit and vegetable consumption.

## **4. Methodological issues**

To assess the role that consumption of fruits and vegetables might play in the etiology of chronic diseases of importance in the Australian setting, an analysis was undertaken of over 500 original papers and a number of reviews including three major reviews of the link between diet and cancer, the disease which has received most attention in this context.

### **4.1 Methods for identifying suitable papers**

Four electronic databases were searched including Medline, the Science Citation Index (web-based version – Web of Science), Cambridge abstracts (CABI) and current contents. All indexes were searched for material indexed and published until April 1999. The following specific heading and text word term strategies were used: diet - fruit, vegetables, legumes and diet; and disease states - cancer, gallstone, cataract, arthritis, diabetes, osteoporosis, heart, cardiovascular and stroke. The two search strategies were then combined to locate matches between fruit and vegetables and each disease state. Major review articles were also examined and suitable references obtained together with any relevant citations from the studies themselves. Other chronic disease conditions including dementia and ulcers arose as the investigation progressed and these were added to the search list.

Data were extracted from the published studies on levels of fruit and vegetable intake (serves or quantity per unit time) together with various markers of fruit and vegetable consumption. Nutrients for which the proportion from fruit and vegetables was sufficiently high for them to be useful indicators of fruit and vegetable intake were beta-carotene and other carotenoids, some other phytochemicals including lycopene and lutein, vitamin C, folate and fruit and vegetable fibre. Total dietary fibre is generally not considered to be a good indicator of fruit and vegetable intake. When vitamin supplementation was accounted for in the results, the reported values were generally for the food component only unless stated otherwise. Most studies reported dietary intake of nutrients, however some used serum or plasma concentrations of marker nutrients and risk of disease and this was always stated in the tabulation of results.

Relative risk of each quantile of intake versus the referent quantile was the measure of association most often used when reporting effect of fruit and vegetables on disease conditions. However, many other measures of effect were used including correlations, regression coefficients and mean changes in intake between cases and controls. All measures were identified in the explanatory notes accompanying the tabulation of each study (see Appendix).

## 4.2 Epidemiologic tools used for assessing the possible effects of dietary components on disease risk.

The major tools used for associating food intake patterns and specific nutrients with disease risk are:

- *Ecologic studies* in which national per capita food intakes are correlated with national health statistics relating to the incidence, prevalence and mortality of diseases
- *Case-control studies* in which food intake patterns in individuals who have contracted a disease under study are gathered retrospectively, and compared with the food intakes of appropriately chosen individuals who do not have the disease
- *Cohort studies* in which food intake patterns in many study subjects are recorded while they are all free of the disease(s) of interest – and after an appropriate efflux of time (usually many years) the dietary patterns of those who develop disease(s) are compared with those who are still disease free.
- *Intervention studies*, in which subjects at (high) risk of the disease under study are randomly allocated to either a modified dietary regime or a control regime – and the two study groups are compared with respect to their subsequent disease incidence or progression.

Ecologic studies provide the weakest kind of evidence, since a diversity of other explanations may account for any observed association. The striking association between per capita consumption of fat and breast cancer mortality in women is a salutary example of a hypothesis generated by an ecologic study that could not be sustained in subsequent analytic studies. A case-control study is the most popular analytic tool for investigating chronic disease aetiology, but it is extremely vulnerable to biases arising from either inappropriate selection of control subjects, or from selective recall by cases of the foods they ate prior to the diagnosis of their condition.

While cohort studies are far less vulnerable to the problems of the case-control study, the huge numbers of study subjects required to ensure the future accrual of a sufficient number of ‘cases’ and the time required for the disease to develop has meant that very few cohort studies have ever been conducted. Finally in a few instances, there has been sufficient confidence in the disease preventive capacity of a specific food component or micronutrient to initiate an intervention trial. Modelled on the randomised clinical trial, an intervention study provides the most reliable information for confirming a direct causal relationship between a dietary components and a disease outcome.

It is salutary to note, however, that despite the enormous enthusiasm generated by the other epidemiologic tools, for the notion that the dietary carotenoid beta-carotene can prevent DNA-damaging steps in the genesis of cancer, intervention studies involving the use of beta-carotene in people at high risk of cancer of the lung, colon and cervix have either found no effect, or have been discontinued due to the apparent impetus to progression in the study subjects.

The epidemiologic data collated for this report, and on which other recent summary reports have been based consist very largely of case-control studies, and a very much smaller number of cohort studies. For reasons outlined briefly above, evidence obtained from cohort studies can usually be regarded as more reliable than evidence collected using case-control studies.

## 5. Disease specific assessments

### 5.1 Cancer

Cancer has received by far the most attention in the epidemiological literature in relation to the potential effect of fruits and vegetables. Three major reviews of the area have been undertaken in recent years and our summary of the literature has been undertaken with reference to the findings of these reviews. These reviews were the World Cancer Research Fund/American Institute of Cancer Research review of 1997 (551), the review undertaken by the working group on Diet and Cancer of the Committee on Medical Aspects of the Food Supply (COMA) in the UK completed in 1998 (552) and two reviews by researchers from Wageningen University in Holland (Jansen et al of 1995 (553) updated by Klerk et al in 1998 (554)). As these are major, original reviews, the methodologies and terminologies used by these reports are summarised below

### 5.1.1 Methodologies used in major reviews

#### 5.1.1.1 World Cancer Research Fund Review methodologies (WCRF)

Judgement was based first on consistency, strength and quality of epidemiological evidence then on experimental and other biological evidence including plausible mechanisms. There were four levels ascribed to evidence. The terms used were:

##### **Convincing:**

Evidence of causal relationships is conclusive and sufficient for making dietary recommendations:

- Epidemiological studies had to show consistent associations with little or no evidence to the contrary. There should be a substantial number of acceptable studies (more than 20) preferably including prospective designs, conducted in different population groups, controlled for possible confounding factors.
- Dietary intake data should refer to the period preceding occurrence of cancer
- Any dose-response relationships should be supportive of a causal relationship.
- Associations should be biologically plausible.
- Laboratory evidence is usually supportive or strongly supportive

##### **Probable:**

Evidence is strong enough to conclude that a causal relationship is likely – usually also enough for dietary recommendations to be made.

- Epidemiological studies showing associations are either not so consistent, with a number and/or proportion of studies not supporting the association or else the number and type of study is not so extensive enough to make definite judgement
- Mechanistic and laboratory evidence are usually supportive or strongly supportive

##### **Possible:**

Causal relationship may exist but evidence is not strong enough to generate recommendations

- Epidemiological studies are generally supportive but are limited in quantity, quality or consistency.
- There may or may not be supporting mechanistic and laboratory evidence.
- Alternatively, there are few or no epidemiological data, but strongly supportive from other disciplines

##### **Insufficient:**

Suggestive evidence but too scanty or unbalanced to make judgement.

- There are only a few studies., which are generally consistent but really do no more than hint at a possible relationship
- Often more well-designed research is needed

#### 5.1.1.2 COMA review methodologies

The procedure was based on criteria developed by International Agency for Research in Cancer (582). The factors guiding deliberations were:

- Type of epidemiological study
- Consistency of results between studies
- Quality of studies reviewed
- A general tendency for results to be in the same direction
- Size of relative risk
- A graded response
- Evidence of effect from randomised controlled trials
- Exposure preceding effect
- Evidence for plausible mechanism

A scoring system was developed to assess studies

- Separate scoring systems were used for case-control and cohort studies as it was felt that results from cohort studies are a priori less prone to bias than case-control studies
- Scoring focussed on study design, method of assessing dietary exposure, analysis and, for cohort studies, the definition of the cohort
- Scoring was intended to reflect amount and reliability of information on diet and cancer risk.

- The repeatability of the scoring system was found to be robust
- On the basis of the score, studies were classified as low, intermediate or high.

As part of the process, the evidence was broken down into broad viz

*Epidemiology data*

- None / few / some /many
- Insufficient
- Inconsistent
- Weakly consistent
- Moderately consistent
- Strongly consistent

*Extent of evidence for mechanism*

- No / little / some / substantial
- Evidence exists in animals / in vitro
- Evidence that operates in humans exists

*Strength of evidence for mechanism*

- The Working Group was convinced
- Evidence is equivocal
- Evidence is unconvincing
- Evidence is lacking/no evidence

*Overall evidence for link*

- Not enough evidence
- Evidence is weak
- Evidence is moderate
- Evidence is strong

*5.1.1.1.3 Wageningen review methodologies*

The Wageningen group did not undertake their review *ab initio* but relied heavily on other reviews, made some comment on additional studies and then presented, without detailed justification, summary estimates or ranges of estimates for the relative risks in “high” consumers versus “low” consumers. The definition of these later terms varied as discussed later in the text.

**5. 1. 2. Specific cancers**

Many of the epidemiology studies use relative risk estimates (or the closely related odds ratios) to describe associations between dietary variables and disease risk. A relative risk of “1” implies no difference in risk between various categories of dietary consumption. A risk above “1” implies increased risk and below 1, decreased risk, however it must be noted that many estimates of relative risk in the literature, while below or above unity, are nevertheless not significantly different from unity, ie there is a reasonable chance that many of these estimates of reduced or increased risk were obtained in the complete absence of a relationship between fruit and vegetable intake and cancer risk (this, of course, may apply to other disease entities). This immediately begs the question of whether the estimates from many different studies with individually non-significant results can somehow be ‘pooled’ to generate a ‘best’ risk estimate with narrower confidence limits. However, due to the heterogeneity of study conditions with respect to the choice of controls, food/nutrient items selected for study, the instruments used to measure dietary intake, and the choice of consumption categories (sometimes not reported!) most reviewers have chosen not to attempt this process. However, Block et al (393) and the Wageningen group (553,554) have attempted to provide numerical estimates which are discussed later.

*5.1.2.1 Colorectal cancer (1-74)*

57 case-control studies and 9 cohort studies were reviewed and are summarised in the Appendix. With very few exceptions the case-control studies report relative risk estimates below one in the highest consumption category of a wide variety of individual fruits, vegetables (or nutrient markers thereof), ie high consumption was associated with lower risk of colorectal cancer.

Of the 32 relative risk estimates obtained from the more methodologically reliable cohort studies very few were lower than 0.7 (indicating a reduction of risk of some 30% or more) . One US study reported

increased but non-significant risks for men consuming higher levels of fruits and vegetables compared to non-significant reductions in risk for women (57). In contrast, Hirayama in Japan (20) found a higher risk (non-significant) for women and lower significant risk for men with increased green and yellow vegetable consumption.

- The WCRF report concluded that “*Evidence that diets rich in vegetables protect against cancers of the colon and rectum is convincing. The data on fruit are more limited and inconsistent: no judgement is possible*”.
- While the COMA Report concluded that... “*There is moderately consistent evidence from case-control studies, especially the higher scoring studies, that higher consumption of vegetables is associated with a lower risk of colon cancer, but the evidence from cohort studies is only weakly consistent. The relative risks for highest consumption versus lowest consumption are generally between 0.5 and 0.9. There is only limited and inconsistent evidence of an effect of fruit consumption*” and finally that “*Overall there is a moderate risk to conclude that higher intakes of vegetables would reduce risk of colorectal cancer*”
- The Wageningen report of 1995 identified 27 case-control studies and 11 cohort studies of colorectal cancer. Only relative risks for the highest consumption category were reported and used for obtaining summary estimates. They considered, without giving detailed justification, that the data indicated high consumers exhibited a 30-50% reduction in risk relative to the low consumers – and chose a mid-range summary relative risk of 0.6 which they moderated to 0.63 in their 1998 report.

#### 5.1. 2.2 Stomach Cancer (4,5,28,33,45,63,75-123)

A total of 46 case-control studies and 9 cohort studies are summarised in the Appendix. Amongst the cohort studies the lowest estimate of relative risk in the high consumption category was from a sparsely documented Swedish study which used only a 23 item food frequency questionnaire to assess dietary intake and reported low consumers of fruit and vegetable having 5.53 times the risk of gastric cancer relative to high consumers, which translates to a relative risk of 0.18 of high relative to low consumers (117). In another study very low relative risks of 0.31 were obtained for high consumers of onions in a Dutch study (85). At the other extreme, one Japanese (108) and one Hawaiian study (113) reported increased risks of 1.77 and 1.2 for high consumption of pickled vegetables respectively All the remaining estimates for high consumption were in the range 0.5 – 1.2.

The case-control studies yielded a slightly wider range of estimates. There was one case-control study in Japan which gave very high relative risks for higher consumption of a range of fruits and vegetables (65) Other than that, where there were increased risks associated with higher consumption, these were generally related to specific types of vegetables such as pickled vegetables or chilli peppers. By far the majority of studies reported risks in the range 0.3 to 0.9 – presenting, among all the cancer sites, the most consistent picture of an apparent protective effect of fruit and vegetables.

- The WCRF Report concluded that “*The evidence that diets high in vegetables and fruits, collectively and separately, decrease the risk of stomach cancer is convincing. The evidence for raw vegetables, allium vegetables and citrus fruits is particularly abundant and consistent for a protective effect. Any evidence not consistent with a protective effect relates almost entirely to salted and pickled vegetables*”.
- While the COMA Report concluded “*There is moderately consistent evidence that higher intakes of fruit and vegetables are associated with lower risk of gastric cancer. Although it is possible that confounding by Helicobacter pylori infection may partly account for these findings, the strength, consistency and dose response relationship argue against this*” and finally that “*Overall there is moderate evidence to conclude that higher fruit and vegetable consumption would reduce the risk of gastric cancer*”
- In 1995, the Wageningen group chose a summary relative risk of 0.45 for high versus low fruit and vegetable consumers, but moved this estimate to a more conservative 0.49 when they revisited their estimates in 1998.

### 5.1.2.3 Lung cancer(28,124-153)

Despite the dominant role of a specific preventable behaviour, viz tobacco smoking, in the aetiology of lung cancer, there has been considerable interest in whether fruit and vegetables can at least partially mitigate against the dangers of smoking. Summary findings from 24 case-control studies and 7 cohort studies are reported in the Appendix.

Most of the seven cohort studies identified one or more fruit and/or vegetable items that were associated with decreased risks after adjustment for smoking status, with a number of risk estimates for the high consumption category in the range 0.3 to 0.6.

The findings from case-control studies report decreased risks for a variety of fruit and vegetables.

Intervention trials designed to test whether beta-carotene is the active component of vegetables responsible for a reduced risk of lung cancer have either found no effect (582) or increased risk (583,584).

- The WCRF Report concluded that *“Seven cohort and 17 case-control studies are almost entirely consistent with a protective effect of vegetables and fruit against lung cancer. The evidence is most abundant for green vegetables and carrots. The evidence that diets high in vegetables and fruits decrease the risk of lung cancer is convincing”*
- On the other hand the COMA Report felt that there was a stronger case for fruits rather than vegetables. *“There is moderately consistent evidence that higher consumption of fruit and weakly consistent evidence that higher consumption of vegetables are associated with a lower risk of lung cancer. It is likely that the effects of smoking have not been taken into account completely. The estimated relative risks for high consumption versus low consumption vary considerably between studies but are generally between 0.5 and 0.7.”*
- In 1995, the Wageningen group chose a summary estimate of 0.55 for the relative risk of high fruit and vegetable consumers versus low consumers, and 3 years later increased this estimate to 0.58, which is consistent with the COMA Report

### 5.1.2.4 Breast Cancer (28,45,154-197)

A total of 37 case-control studies and 5 reports from 4 cohort studies are summarised in the Appendix.

Among the prospective (cohort) studies of breast cancer which collected data on fruit and vegetable intake (or surrogate measures such as vitamin C and carotenoids), the Nurses Health Study (196) found no association between any of 10 intake measures and breast cancer risk in postmenopausal women, but some modest decreases in risk in the top 20% of total fruit and total vegetable premenopausal consumers. A Canadian prospective (187) study found negligible risk reduction with beta-carotene intake; the Iowa Women's Health Study (174) reported no decrease in risk with either vitamin C or carotenoids, and a small Finnish study (29) which looked at flavonoid intakes reported rather variable decreases in risk with increasing intake which had no consistent trend. Steinmetz and Potter (399) judged the evidence for a protective role of fruits and vegetables in hormone-related cancers as less consistent than for hormone-related cancers.

Studies of the dietary determinants of breast cancer risk have been very closely scrutinised in recent years and it is salutary to note that the results obtained from case-control studies are not consistent with those obtained from the prospective studies with as many case-control studies showing no or increased risk as showed protection. Thus a meta-analysis of data relating to fat intake and breast cancer risk by Boyd et al, in 1990 (586) found risks of breast cancer were elevated in high fat consumers according to case-control studies, but not prospective studies, and a subsequent meta-analysis of seven prospective studies by Hunter et al in 1996 (587) failed to find even a hint of a trend of increasing cancer risk with increasing dietary fat intake. If case-control methodology, on which so much nutritional epidemiology is based, is really as flawed as these meta-analyses of fat and breast cancer suggest, then the general case for the impact of fruit and vegetables on cancer risk may be overstated.

- The WCRF/AICR Report concluded: *“A large amount of evidence has accumulated regarding vegetable and fruit consumption and the risk of breast cancer. Almost all of the data from epidemiological studies show either decreased risk with higher intakes or no relationship; the evidence is more abundant and consistent for vegetables, particularly green vegetables, than for fruits. Diets high in vegetables and fruits probably decrease the risk of breast cancer”*.
- The British COMA Report concluded: *“The evidence from case-control studies is weakly consistent that higher intakes of fruits and moderately consistent that higher intakes of vegetables are associated with a lower risk of breast cancer. There are few cohort studies on the effect of consumption of fruits and vegetables on the risk of breast cancer. Such evidence as there is, is weakly consistent that higher intakes of fruits are associated with a lower risk of breast cancer and moderately consistent that higher intakes of total and green/yellow vegetables are associated with lower risk”*
- The Wageningen group in 1998 nevertheless concluded that *‘All case-control studies and cohort studies provided evidence for a risk reduction with higher intakes of both fruits and vegetables. The reduction in risk seems stronger in pre-menopausal women. Two studies showed a protective effect with raw vegetables, but another did not. Based on these recent studies, risk reduction [in high consumers] is estimated at 15-50% which was higher than their earlier estimates of 0-25%’*.

#### 5.1.2.5 Prostate cancer (28,45,198-217)

A total of 16 case-control studies and 5 cohort studies are summarised in the Appendix. It is immediately apparent that the results from case-control studies are remarkably discrepant. In addition to many risk estimates being near unity in high consumers, there are a number of estimates above unity (ie indicating increased risk) – with statistically significant estimates of 2.5 for the top quarter of papaya intakes in Hawaii (207) and 3.4 for high vitamin C intakes in New York (204). Statistically significant reductions in risk were associated with high fruit and green vegetable consumption in an Italian study (46), and with baked beans and peas in a multi-centre UK study (206).

Among the prospective studies, non-significant elevations in risk were associated with increasing flavonoid intakes in Finland (29), and with cruciferous vegetables in Minnesota (205); and statistically significant increases in risk were reported for both fruit and citrus consumption in Holland (213).

Two other cohort studies conducted in the US reported significantly decreased risks among high consumers of legumes, citrus, nuts and tomatoes (210), and in high consumers of tomato, tomato sauce and lycopene (202). An apparently consistent case for a protective role of lycopene cannot be sustained in the face of a case-control study in Quebec (209) which estimated the relative risk of prostate cancer in the top quarter of lycopene intakes to be 1.73. In 1991, Steinmetz and Potter concluded that no epidemiologic evidence exists to support a lower prostate cancer risk at high consumption of fruits and vegetables.

- The summary statement from the WCRF Report is also conservative: *The pattern of association that emerges is not clear. Nevertheless, most studies found no association or even increased risk with some fruit categories and a marginally greater suggestion, but still with a number of null studies, of decreased risk with vegetables. Diets high in vegetables possibly decrease the risk of prostate cancer. Evidence on diets high in fruits is markedly inconsistent; no judgement is possible”*.
- The COMA Report concluded that: *‘The limited evidence is moderately consistent that higher vegetable consumption, especially raw and salad vegetables, is associated with lower risk of prostate cancer. The evidence for an association between consumption of fruit and risk of prostate cancer is inconsistent. There are insufficient data on the intakes of soya products to reach a conclusion on the association of soya products with prostate cancer’*
- In 1995, and again in 1998 the Wageningen group adopted the Steinmetz and Potter position that there was no epidemiological evidence to support a link, although they used a 7-10% reduction in risk among high consumers to estimate the proportion of cancers preventable by eating more fruits and vegetables.

#### 5.1.2.6 Bladder cancer (28,45,218-228)

It is generally agreed that smoking and exposures to chemicals required in occupational settings are major risk factors for this disease.

Among the 10 case-control studies summarised in the Appendix, several reported decreased risks in 'high' consumers of fruit and vegetables, with fruits and vegetables assuming equal importance in some studies and inconsistently opposite importance in others.

The Seventh Day Adventist cohort (225) experienced reductions in risk with both fruit and vegetables; the Finnish Mobile Clinic Health Examination Survey (29) found an essentially null association with flavonoid intake and a Hawaiian study (219) reported decreased risk in high fruit eaters, but increased risk with fried vegetables, pickles and miso soup.

- The WCRF Report summarised as follows: *Almost all studies have reported either a decreased risk or no relationship with higher consumption for a variety of specific vegetable and/or fruit categories. Some studies have observed decreased risk after adjustment for cigarette smoking. The evidence has been most abundant and consistent for fruit, green vegetables, and carrots. Diets high in vegetables probably decrease the risk of bladder cancer*".
- The COMA Report concluded that *'The limited evidence is moderately consistent that consumption of vegetables and fruit is inversely associated with risk of bladder cancer'*.
- The Wageningen group first adopted a relative risk of 0.6 for high fruit and vegetable consumers and later moderated this to 0.65, which was slightly inconsistent with a statement in their text that the "average" risk reduction estimate is 15-30%.

#### 5.1.2.7 Oesophageal cancer (5,33,45,229-256)

Tobacco, alcohol, betel nut and maté (a beverage drunk extremely hot) are well established risk factors for oesophageal cancers. Since the use of betel quid and maté are restricted to certain communities, studies conducted in those areas are likely to be less relevant in developed countries where these practices are rare. A total of 26 case-control studies have examined the association of fruit and vegetable intakes with the risk of oesophageal cancer. It is apparent that a substantial proportion of these found decreased risks associated with increased intakes. The exceptions are reasonably consistently identified with preserved, salted and fermented vegetable foods, for which increased risks have been observed in East Asian countries.

The only prospective study, the Linxian cohort study in China (253), found a significantly reduced risk for the top 50% of fresh vegetable eaters, but found no association with other fruit or vegetable foods.

- The WCRF Report (which is written with a more global perspective) states simply: *"The evidence that diets high in vegetables and fruits decrease the risk of oesophageal cancer is convincing"*.
- The COMA Report concludes briefly: *"The evidence that higher consumption of fruits and vegetables reduces the risk of oesophageal cancer is strongly consistent, but the relevance to the UK where there are no prospective data is unclear"* and finally that *"Overall there is not enough evidence to conclude that consumption of fruits and vegetables influences risk of oesophageal cancer in the UK."*
- The Wageningen group estimated a 55% reduction in risk in high consumers of fruits and vegetables in their 1995 report moderated to 46% in their 1998 update.

#### 5.1.2.8 Oro-pharyngeal cancers (mouth and pharynx) (33,45,235,239,242,244,253,257-276)

Cancers of the mouth and pharynx are usually studied together as a group. However cancers of the larynx and/or oesophagus are sometimes included – as noted in the Appendix. which summarises results from 20 case-control studies and 2 cohort studies. As for cancers of the oesophagus, tobacco, alcohol, betel nut and maté are well established risk factors – and they are far more common in the developing world.

A high proportion of the case-control studies summarised in the Appendix reported a statistically significant protective association for at least one vegetable and/or fruit category. Although there was a preponderance of cases from developing countries, significantly lower risks among high fruit and vegetable consumers were also reported from studies conducted in Switzerland (265), Northern Italy (264) and the USA (266).

Two cohort studies included other sites and observed only 130 cases, which complicates interpretation of their results.

- The WCRF report concluded that *“Evidence that diets high in vegetables and fruits decrease the risk of cancers of the mouth and pharynx is convincing”*
- However, the COMA report was much more conservative concluding that *“The evidence from case-control studies is weakly consistent that high fruit consumption and inconsistent that high vegetable consumption are associated with reduced risk of oropharyngeal cancer but no cohort studies were identified”*
- The Wageningen Group gave a summary estimate of 55% for the reduction in risk in high fruit and vegetable consumers for both their 1995 and 1998 calculations of the proportion of preventable cancers.

#### 5.1.2.9 Pancreatic Cancer (see “other cancers” 277-390)

Twenty case-control studies and five cohort studies are summarised in the appendix. The two methodologies do not yield consistent findings. The Seventh Day Adventist Study (343) was the only cohort study to find significant reduction of risk associated with any food items (specifically dried fruit and beans).

Almost all the case-control studies identified some fruit or vegetable items with significantly reduced risks associated with high intakes.

- The WCRF report concluded that *“There is substantial evidence that diets high in vegetables and fruits probably decrease the risk of pancreatic cancer”*.
- The COMA report, which appears to interpret the findings of prospective studies in the elderly more strongly than we could (ie the relative risk whilst 0.8 was not significant) conclude: *“The limited data relating fruit and vegetables consumption and pancreatic cancer are strongly consistent that higher intakes of fruit and vegetables are associated with reduced risk of pancreatic cancer”*. Overall however, they felt that the data was too limited to make a final conclusion.
- The Wageningen group estimated that the risk reductions in high fruit and vegetable consumers was between 10 and 35% – but then chose summary relative risks of 0.6 (in 1995) and 0.62 (in 1998) , which corresponds to 38% and 40% respectively !

#### 5.1.2.10 Cervical, endometrial and ovarian cancers (see “other cancers” 277-390)

Summaries in the Appendix include 10 case-control studies of cervical cancer (and 2 for pre-malignant conditions), 13 for endometrial cancer, and 3 for ovarian cancer. A single prospective study of ovarian cancer in the US was also identified.

The majority of cervical case-control studies identified some fruit and vegetable items for which high consumption was apparently protective, but the pattern was inconsistent, with a New York study (336) reporting significantly increased risk with cruciferous vegetables.

- The WCRF concluded: *“Overall the evidence on vegetables and fruit and the risk of cervical cancer is generally consistent. Diets high in certain vegetables and fruit possibly decrease the risk of cervix cancer and its precursor lesions.”*
- The COMA Report considered that the data were reasonably consistent but opined that they were *“too limited to draw firm conclusions”*.
- The Wageningen group assumed a 15% reduction in risk in high consumers.

Most of the 13 endometrial cancer studies identified some fruit and vegetable items for which high consumers had reduced risks. Case-control studies in the US (350) and Shanghai (358) found no relationships and a large study in Milan (46) reported increased risk with fruit but decreased risk with vegetables.

- The WCRF concluded: “Diets high in vegetables and fruit possibly decrease the risk of endometrial cancer”.
- The COMA Report concluded there was “insufficient data”
- The Wageningen group encapsulated the inconsistency of results with an estimated range of 0-40% reduction in risk in high consumers

For ovarian cancer it is generally agreed that there are too few studies of fruit and vegetable consumption to draw any conclusions.

**Table 3 Comparison of WCRF/AICR and COMA conclusions on the the association between fruits & vegetables consumption and cancer risk**

Cancer site	WCRF	COMA
Breast	Diets high in vegetables and fruits PROBABLY decrease risk of breast cancer	Overall, the evidence to conclude that higher intakes of fruits and vegetables would reduce the risk is WEAK
Colorectal	Evidence that diets high in vegetables decreases the risk is CONVINCING Data on fruit are more limited and inconsistent; no judgement can be made	Overall MODERATE EVIDENCE to conclude that higher intakes of vegetables would reduce the risk
Lung	The evidence that diets high in vegetables and fruits protect against lung cancer is CONVINCING (overwhelming cause is use of tobacco)	Overall, NOT ENOUGH EVIDENCE to conclude that higher fruit and vegetables would mitigate the overwhelming effect of smoking in reducing the risk
Stomach	The evidence that diets high in vegetables and fruit protect against stomach cancer is CONVINCING	Overall MODERATE EVIDENCE that higher fruits and vegetables would reduce risk
Oesophagus	The evidence that diets high in vegetables and fruits decrease the risk is CONVINCING	Overall, NOT ENOUGH EVIDENCE to conclude that consumption of fruits & vegetables influences the UK risk
Mouth/Pharyngeal	The evidence that diets high in vegetables and fruits decrease the risk is CONVINCING	Evidence limited – no overall judgement made
Larynx or Pancreas	Diets high in vegetables and fruits PROBABLY decrease risk	Evidence limited – no overall judgement made
Ovary or endothelium	Diets high in vegetables and fruits POSSIBLY reduce risk	Evidence limited – no overall judgement made
Prostate	Diets high in vegetables are POSSIBLY protective	Evidence limited – no overall judgement made
Cervix	NO CONVINCING evidence that dietary factors modify risk	Evidence limited – no overall judgement made

### 5.1.3 Summary

The summary findings from the WCRF and report from the COMA group in the UK are shown in Table 3. Overall the COMA panel was much more cautious in their conclusions with their overall judgements either being that the evidence was moderate, weak or insufficient. Our interpretation of the literature would more closely align with the COMA report. It is worth noting that the WCRF report had a global perspective whereas the COMA report was assessing evidence in the light of the UK situation. Nevertheless the COMA group still felt that fruit and vegetable consumption in the UK should be increased.

The WCRF and Wageningen reports were more closely aligned but it should be noted that the earlier work of the Wageningen group was used as the key evidence for estimates of the quantification of preventive potential of fruits and vegetables in the WCRF report.

The Wageningen group themselves, in their 1998 report, highlight the fact that with increasing numbers of studies being published, their estimates of the preventive capacity of fruits and vegetables in relation to most cancers have become more conservative. They felt this could be due to increasing quality of studies in some areas and perhaps also to earlier publication bias (ie a tendency for papers reporting accepted wisdom to be more readily accepted for publication).

#### **5.1.4 The effects of different fruits and vegetables on cancer risk**

On the whole, evidence for a protective effect of vegetables is rather stronger than that for fruits perhaps reflecting the fact that vegetables are generally consumed in greater quantities than fruits and thus in more variable quantities within populations..

The WCRF review concluded that in the present state of science, it is probably best to consider vegetables and fruits collectively. However, different types of vegetables and fruits such as dark green leafy vegetables, cruciferous vegetables, allium vegetables and citrus fruits have been investigated separately as have some individual fruits and vegetables (see Table 4 below)

The WCRF concluded that the evidence that diets high in green vegetables protect against lung cancer and stomach cancer is convincing and that they probably protect against mouth and pharyngeal cancer. Diets high in cruciferous vegetables they concluded were probably protective against colo-rectal cancer and thyroid cancer. They also felt that the evidence that diets high in allium vegetables and in tomatoes and in citrus fruits protect against stomach cancer was convincing and that diets high in carrots were probably protective against lung, stomach and bladder cancers. For legumes, the WCRF panel felt that whilst there are theoretical reasons to believe that diets high in pulses or roots tubers and/or plantains might protect against some cancers, evidence was currently very limited. They also felt that data relating to starchy roots and other starchy foods was too limited for comment.

The COMA report, in contrast felt that there was insufficient evidence to recommend particular types of fruits or vegetables, nor to make recommendations about legumes or starchy roots like potatoes. They felt that dietary advice to eat more fruits and vegetables should emphasise the advantages of variety rather than focussing on particular types. They felt that although the lack of demonstrable effects of vitamins C and beta-carotene might be due to methodological problems with the intervention trials used to assess their effects, the evidence that they are responsible for the protective effect of fruits and vegetables is at best equivocal and that it was likely that a range of compounds including fibre and the essential nutrients is involved. There are many potentially protective chemical constituents in foods and a variety of mechanisms through which they act and the COMA reviewers felt that current knowledge does not suggest that any one should be singled out as of paramount importance

The COMA panel also felt that although the evidence for a protective effect of components of fruits and vegetables such as fibre, folates, antioxidants and other metabolically active compounds was not conclusive and was insufficient to recommend an increase in their intake specifically, an increase in fruit and vegetables consumption would *inter alia* lead to an increase in the intake of these substances

**Table 4 Cancer risk and specific types of fruits and vegetables**

Category	Relationship to cancer risk					
	Number of studies			% total studies		
	Inverse	Null	Positive	Inverse	Null	Positive
Vegetables	59	6	9	80%	8%	12%
Fruit	36	156	5	64%	27%	9%
Raw vegetables	40	4	2	87%	9%	4%
Cruciferous vegetables	38	9	8	69%	16%	15%
Allium vegetables	27	4	4	77%	11%	11%
Green vegetables	68	6	14	77%	7%	16%
Carrots	59	7	7	81%	10%	10%
Tomatoes	36	5	10	71%	10%	20%
Citrus fruit	27	8	6	66%	20%	15%

*Summary of 217 studies tallying results including both statistically significant and insignificant associations*

The COMA panel also felt that there was insufficient evidence to quantify the optimum level of fruit and vegetables consumption associated with lowest cancer risk. There is some suggestion from observational studies that there might be a level of consumption above which no further benefit is seen but this is well above current intakes in countries like Australia. They did however, conclude that any increase in fruit and vegetable intake would be expected to confer benefit.

The more cautious approach of the COMA panel to apportioning protective roles for individual fruit and vegetable types is more in line with our assessment of the data than are the judgements of the WCRF panel.

Neither the WCRF nor the COMA report, nor indeed many of the epidemiological studies have addressed the specific issue of the role of fresh produce as opposed to frozen or canned varieties. The data is insufficient to make informed comment, other than to refer back to the discussion of the effects of processing on key nutrient and non-nutrient components thought to affect cancer or cardiovascular risk ( section 3.3).

### 5.1.5 Effects of cancer-related nutrients

Much of the original interest in fruits and vegetables and their potential role in cancer arose from experimental observations in animal models of the effects of a number of nutrients or non-nutritive substances on cancer risk. To this end both the WCRF and COMA reviews assessed the evidence in human epidemiological studies for Vitamins A, C and E, beta-carotene and fibre. Data for other components is sparse.

The WCRF report felt that vitamin C was probably protective for stomach cancer and possibly for mouth and pharynx, oesophagus, lung, pancreas and cervix. For carotenoids they felt the evidence showed that they were probably protective for lung and possibly protective for oesophagus, stomach, colorectal, breast and cervix. For fibre/non-starch polysaccharides they felt that there was evidence of a possible preventive role in pancreatic cancer, breast and colorectal.

The COMA report concluded that overall there was not enough evidence that AC and E or beta-carotene protected against the development of various cancers. They stated that higher intakes of these components had been variously associated with lower risk of breast, colorectal, lung, gastric and cervical cancer in case-control and cohort studies but that most intervention trials with supplements of these vitamins had failed to confirm a protective effect. Whilst this may be due to methodological problems with timing of supplementation they also felt that the observational findings might relate too intake of other substances for which these antioxidant vitamins were markers.

For dietary fibre/non-starch polysaccharides, the panel felt that overall there was not enough evidence to draw conclusions about their relationship to breast cancer, but moderate evidence for reducing risk of colorectal cancer. They concluded there was insufficient evidence to draw conclusions for other except pancreatic where there was moderately consistent evidence that higher intakes would lower risks cancers. On the basis of this the COMA report recommended an intake of non-starch polysaccharides for adults of some 18g/day, a target already achieved in Australia.

## 5.2 Cardiovascular disease risk

The potential for antioxidants, specifically beta-carotene, vitamin C ( and to a lesser extent vitamin E), to prevent atherosclerotic lesions and hence ischaemic heart disease has so dominated the epidemiologic research, that the health benefits of high intakes of fruit and vegetables are often inferred from studies which only measured the serum concentrations of these micronutrients. Since vitamins C, E and beta-carotene are found in negligible quantities in foods of animal origin, the use of serum levels as a marker for fruit and vegetable intake would appear to be entirely reasonable – but there are difficulties. Firstly serum levels are not always linearly related to dietary intakes, and secondly smokers generally exhibit lower levels of these micronutrients, and it is not clearly understood whether this is a direct effect of smoking, or arises because smokers are less concerned about their personal nutrition. Recognition of the antioxidant properties of other dietary components, especially flavonoids occurred sufficiently recently that flavonoid intake has not been specifically addressed in most studies available to this time. There have been two recent major reviews of fruit and vegetables in relation to cardiovascular disease - Ness and Powles reporting in 1997 (451) and the Wageningen group (553,554) whose findings are summarised below in relation to our findings.

### 5.2.1 Coronary heart disease (CHD) and acute myocardial infarction (AMI) (94, 402-470)

In the Appendix, 12 case-control studies and 27 cohort study reports are summarised. Only 3 of the case-control studies reported results in terms of individual foods. A Dutch study (408) observed a significant decrease in risk of AMI in high onion consumers but little effect with other fruits and vegetables; an Italian study (423) recorded significantly reduced risks with green vegetables, fruit and carrots, but an Indian study (462) saw no differences for total fruit and vegetable intake (g/day) or fibre from fruit and vegetables.

The studies which measured beta-carotene intake or tissue levels reported relative risks in as low as 0.4 to 0.5 for 'high' vs 'low' consumers, in several instances, although there was minimal associations in two Scottish studies looking at CHD and angina respectively (406, 456).

High vitamin C was associated with lower risk of coronary artery disease (CAD) in India (463) but not in a case-control study in Greece (470). The Scottish Heart Health Study reported a non-significant increase in risk in men and a no effect in women (406). In the other Scottish studies (456) there was a slight non-significant decrease in risk of angina.

Inconsistent findings were reported from the impressive number of cohort studies which have examined the association between dietary factors and CHD or IHD (ischaemic heart disease). No associations with bioflavonoid intakes were found in the Health Professionals Follow-up Study in the US (459), but significant risk reductions were found in the Zutphen study in Holland (427).

No reduction in risk was associated with high vitamin C intakes in the Iowa Women's Health Study (441), or in a UK study (417) but significant reductions were reported in the US Nurses Health Study (448), India (464), NHANES I (414) and in Finland (454), and non-significant decreases were observed in Chicago (453), the Caerphilly Study in South Wales,(415), and Switzerland (422).

For carotenoids no associations were found in Finnish men (435) or Iowa women (441); non-significant reductions were observed in Chicago (453) and Finnish women (435); but significant reductions were reported from Massachusetts, US ( 418), the Lipid Research Clinics Coronary Primary prevention Trial (450), the Health Professional Follow-up Study (460), Switzerland (422) and the Netherlands (434) and Madison US ( 467).

A secondary prevention trial in Lyon (412) reported significantly reduced mortality from AMI following an intervention to increase *inter alia* fruit and vegetable consumption to mimic a more Mediterranean diet, although the numbers of deaths observed were rather small.

- Ness and Powles made no attempt to arrive at summary measures of the associations between fruit and vegetable consumption and cardiovascular risk as the studies varied so much in type, quality and exposure measures assessed. Nevertheless, they concluded that fruits and vegetables were weakly protective.

- The Wageningen group (Klerk et al 1998) concluded that the risk of coronary heart disease would be reduced by 20-40% with high intake of fruits and vegetables.

### 5.2.2 Stroke (94,417,422,426,431,437,442,443,461,463,471-485)

Only a limited number of studies has been conducted on dietary associations with the risk of cerebrovascular disease. With the exception of a cohort study in Shanghai (483) which found no association with serum levels of vitamin C or beta-carotene, there is reasonable consistency across the 14 studies summarised in the Appendix in terms of a reduced risk of stroke for various measures, direct or indirect (ie serum micronutrient levels) of high fruit and vegetable intake. There are insufficient data to make recommendations with respect to fruits versus vegetables.

- Ness and Powles concluded that fruit and vegetables were strongly protective, but gave no quantitative estimate.
- The Wageningen group (Klerk et al 1998) estimated (by a process that seemed to be dependent on a visual inspection of reported risk estimates) that the reduction might be of the order of 0 – 25%.

### 5.2.3 Hypertension (437,442,443,463,486-495)

There appears to be only one epidemiological study of fruit and vegetable consumption per se, and high blood pressure. This ecological study showed no link with hypertension (442). Several studies have examined the association between surrogate markers of fruit and vegetable consumption, (viz, plasma and serum levels of vitamin C and beta-carotene and hypertension) - and most have found an inverse relationship (see Appendix). Some studies of vegetarian communities have shown reduced risk of hypertension (588) but the mechanism of reduced risk is unclear. A recent experimental intervention trial did find reductions in blood pressure in a high fruit and vegetable diet compared to an “average” US diet (589).

- Neither the Ness and Powles review nor the Wageningen group assessed hypertension in relation to fruit and vegetable consumption

## 5.3 Cataracts (496-516)

An accumulation of photo-oxidised proteins in the lens of the eye is a major cause of blindness throughout the world and a number of studies have been undertaken to assess whether dietary antioxidants are capable of delaying the development of this condition. While other foods (including meat) contain antioxidants, these studies have focussed mainly on fruits and vegetables, or nutrients such as vitamin C and beta-carotene which are, in effect, surrogate markers of plant foods.

Results from 9 case-control studies and 7 cohort studies are summarised in the Appendix. Apart from an Indian study, which showed an increased risk with high vitamin C intake (507), and a sparsely documented Italian study (515), which showed no associations, the other 7 reported risk estimates, which, if not always statistically significant, were indicative of lower risks among high consumers of fruits and vegetables. Results from the prospective (cohort) studies were qualitatively similar, although the Baltimore Longitudinal Study of Aging (516) found little suggestion of a ‘protective’ effect.

It is perhaps worth noting that even in the presence of apparent benefits from other carotenoids, both types of study consistently reported little or no reduction in risk associated with the carotenoid lycopene (derived mainly from tomatoes and tomato products).

The Linxian trial of antioxidant supplementation in China (512) found a 43% reduction in risk among study subjects in the age range 65-74yrs but not in younger age groups.

- Klerk et al (1998) from Wageningen considered the evidence ‘too limited’ to estimate a preventable proportion of cataracts.

## 5.4 Other chronic diseases

There were few papers for other diseases. Those that have been published are summarised below.

Condition	Evidence	Refs
Arthritis	One case-control study and one small cohort study are both indicative of lower serum levels of vitamin C and beta-carotene, and hence possibly lower fruit and vegetable intake, in people with arthritis – although the only study which appears to have reported actual intakes is an Italian survey, which found significantly fewer arthritis cases in the top third of vegetable intakes (in serves/week)	442,463,537,
Alzheimers disease and cognitive impairment	One case-control study of Alzheimer's disease yielded inconsistent differences in fruit and vegetable intakes when comparing controls with moderate, severe and hospitalised cases. Of two prospective studies of cognitive impairment one recorded a decrease risk in the highest third of vitamin C intakes and plasma levels; the other reporting a decreased risk (0.87) associated with a Healthy Diet Indicator based on WHO guidelines.	519, 524,544
Parkinson' Disease	The Honolulu Heart Study reported a risk of only 0.27 in men who consumed legumes (mainly dried beans and peanut butter). A case-control study in India found lower vitamin C and beta-carotene levels in sufferer's from Parkinson's Disease.	463,536
Inflammatory Bowel Disease	Two European case-control studies were identified. A Swedish study reported lower risk estimates for high intakes of vegetables and fibre for Crohn's Disease but not ulcerative colitis. A Dutch study reported a 50% reduction in risk for both conditions in the top third of citrus consumers (>5 serves/week).	541, 545
Ulcers	The Honolulu Heart Study reported lower risk of gastric and duodenal ulcers in high pickle consumers, but not fruit and vegetables. The Italian Household Multipurpose Survey found a 25% reduction in risk in the top two thirds vegetable consumers.	526,442
Diabetes (Type I?)	Ecological studies: Italian Household Multipurpose Survey found no relation between vegetable intakes and diabetes prevalence; while a British study reported an inverse correlation (-0.19) between vitamin C intakes and diabetes mortality Analytic studies: A case-control study in India reported significantly lower intakes of vitamin C and beta-carotene in cases. A case-control study in New Guinea saw no difference in fibre intakes	442,463,523, 437
Gallstones	The Zutphen cohort study reported no relationship between fruit, vegetable, legume and potato intakes and the Italian Household Multipurpose Survey found little decrease in prevalence among the top third of vegetable consumers. Three of five case-control studies focussed on fibre intakes and reported no consistent differences. A case-control study in Holland found a significantly lower risk in the middle and top third of legume consumption which was consistent with a similar, but non-significant finding in a Spanish case-control study. The latter study saw no association with total vegetable intake in either men or women but did see an association with low fruit intakes in female but not male cases. Mechanisms for a fruit vegetable/fibre effect are speculative	442,533,534, 535,538,546, 548,
Multiple sclerosis	A single case-control study conducted in Montreal, Canada measured intakes of several categories of vegetables, fruits, and juice. Only high juice (and vitamin C) intakes were associated with lower risk.	521
Osteoporosis	An Italian cohort study found little 'effect' of green vegetable or pulse intake on bone mineral density. A case-control study nested in a Swedish cohort study found no relation between risk of hip fracture and the frequency of consumption of fruits and vegetables.	518,529

### Summary of disease specific assessments

- Overall, the epidemiological data indicate a protective effect of fruits and vegetables against a number of chronic diseases. There are significantly more studies for cancer than any other disease condition and a moderate amount for cardiovascular disease. There is some indicative data for stroke, hypertension, cataracts, diabetes and other diseases such as arthritis, Alzheimer's, Parkinson's, inflammatory bowel disease, ulcers, gallstones, multiple sclerosis and osteoporosis but the data is too sparse to provide any meaningful assessment of the influence of fruits and vegetables.
- In recent years there have been three major reviews of the links between diet and cancer and the report discusses their findings alongside our own assessment. In our judgement, and that of the COMA expert panel from the UK, the evidence for an effect on cancer risk of increasing fruits and vegetables is moderately strong for some cancers but weak and inconsistent for others. The World Cancer Research Fund (WCRF) panel was more enthusiastic in their interpretation.
- Evidence for reduction in risk for cardiovascular diseases was also moderate and also relies more heavily on studies of related nutrients such as the antioxidant vitamins than on fruit and vegetable consumption per se. Data for other diseases was very limited but there are initial indications of potential benefit for increased consumption of fruits and vegetables
- There is insufficient data for any of the disease conditions to indicate promotion of any particular types of fruits and vegetables nor to identify any particular constituent. Neither is there compelling evidence from an examination of their nutrient and non-nutrient profile, to exclude canned, frozen or dried varieties or to exclude juice. Key reviews have highlighted the need to encourage variety of choice which could include use of fresh and processed fruits and vegetables. However, products which are based on fruit or vegetables but are heavily processed (eg certain pie fillings, biscuit fillings, health bars, jams etc) may have a quite different nutrient profiles and potential to influence health.
- Despite the more cautious judgement of the COMA panel, both they and we conclude that there is, however, still sufficient evidence to recommend an increase in the consumption of fruits and vegetables from the current levels. Intakes equivalent to 7 serves a day of fruits and vegetables (2 fruit; 5 vegetable) have been recommended by the NHMRC in their Core Food Groups. It should be noted, that these recommendations are not based on an analysis of the epidemiological data linking intake of fruits and vegetables to chronic disease outcome, but on estimates of amounts of various food groups required to achieve diets which conform to the Recommended Dietary Intakes, which are to a large extent based on avoiding deficiency disease. The data from epidemiological studies are not sufficiently robust to determine whether this level of consumption is optimal for chronic disease prevention but together with experimental and animal studies, they suggest that intakes substantially higher than currently consumed in Australia are likely to be beneficial

## 6. Attributing disease risk to food intakes

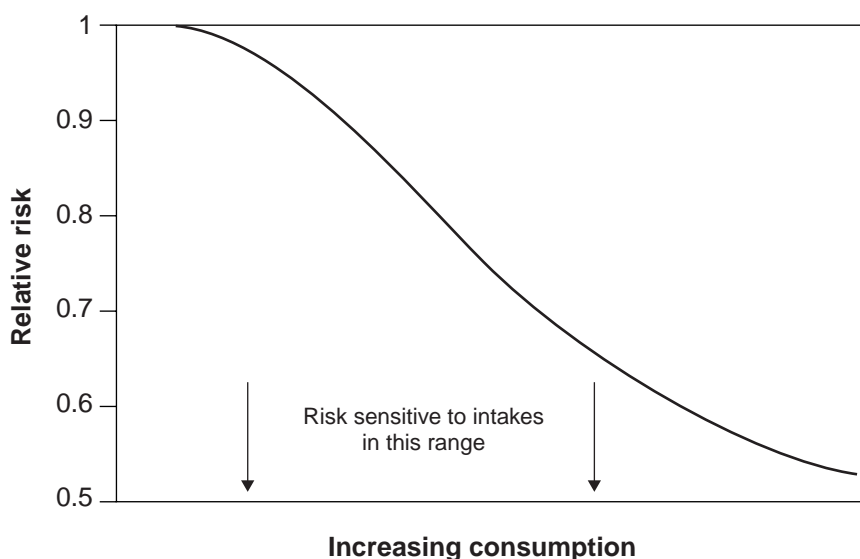
### 6.1 Dietary complexity

A major problem of nutritional epidemiology which makes it stand apart from other attempts to contrast the health/disease outcomes of 'exposed' and 'unexposed' populations is that there is invariably no absolute 'unexposed' category with which to compare the 'exposed' population. All people must eat to stay alive – and the vast majority of foods (with exceptions like water and table sugar) contain a wide variety of individual nutrients. So while it will always be possible to identify individuals who eschew an individual food, a comparison of their health status with people who do not shun that food will, in general, be pointless, since the nutrient components avoided by abstaining from one particular food will usually be obtained in another.

A few exceptions may be identified, where for example a compound like lycopene is found almost exclusively (but not entirely) in tomatoes, so people who never eat tomatoes or tomato products will have extremely low intakes of lycopene. Strict vegetarians are by definition a group whose diet is devoid of meat and meat products, but they still consume fat, protein and most of the other substances found in meat, in a variety of alternative foods. For this reason nutritional epidemiologists are usually forced to work with individuals who all consume varying amounts of the dietary component under scrutiny, and very few whose 'exposure' to that dietary component is zero. This obliges the nutritional epidemiologist to make comparisons between people whose consumption of a dietary element is 'low' with people whose consumption is 'high'. The difficulty here, is that 'low' and 'high' are context dependent. 'Low' vegetable consumption in China may be quite high in comparison to 'high' vegetable consumption in Scotland.

The problem might be partially overcome by expressing observed differences in disease risk in terms of a change in risk per unit (100g, say) of daily vegetable intake, but this assumes that risk changes linearly with intake – and the study results reported in the Appendix do not always support this assumption. This could be because studies conducted in different countries may be located in different regions of the generalised hypothetical response curve depicted in Figure 5, but in many instances the variability in the estimates of risk associated with each category is simply so high that little dose-response information can be inferred. Most 'trend' statistics can confirm that data contain a linear component of trend – but they are generally insensitive to the curvature associated with higher order trend.

**Figure 5. The relationship between relative risk and consumption**



In the meta-analytic studies which have been conducted to date, most reviewers, when confronted with numerous studies in which different measures and categorisations were used to summarise food and/or nutrient intake, have adopted one of the following crude strategies:-

- *Scoring each study according to whether it finds an increased consumption of fruit and vegetables is associated with increased risk of disease, decreased risk of disease, or no association at all.* This strategy ignores all other information on how risk varies with 'dose' or relative consumption, and a higher proportion of studies finding a decreased risk as opposed to an increased risk (or no association) is taken as support for a 'protective effect'. At first glance it appears to be a reasonably robust strategy, but there are still difficult decisions to be made. Does the association have to be statistically significant or not in order to be counted? It cannot be inferred that because an association is not statistically significant there is no association whatsoever. The study may simply have lacked statistical power – and an appropriate pooling of information from several such studies may provide stronger evidence for a real association. But if we classify non-significant results according to whether they indicate increased or decreased risk, how is a 'no association' defined?
- *Comparing risk estimates in 'high' consumers with risk estimate in 'low' consumers.* While this introduces a quantitative element into the analysis, the assumptions necessary to take this extra step are breathtakingly bold. As mentioned previously, the range of intakes may vary considerably from one country to another, so there is no guarantee that 'low' consumption in one study is comparable with the 'low' category in another. Secondly, the number of categories varies from study to study. Some researchers split intakes into (approximately) equal halves or thirds, some use quarters, and in studies with sufficient numbers of study subjects, fifths are used. The common terms 'high' and 'low' are then applied to the groupings at either end of the consumption range regardless of whether 'high' stands for the top 50% or the top 20% of consumers – with similar arguments applying to the meaning of 'low' consumption. Unfortunately the actual quantile values used to make these splits (or the mean/median consumption levels within each category) are not always reported, and they are generally only discussed by reviewers when the findings appear to be considerably at variance with those of other studies.

Because of the difficulties outlined above, and other differences in study methodology, such as the handling of statistical confounders, the selection of controls, and the choice of instrument for assessing dietary intakes, some reviewers have stopped short of making summary numeric estimates of the proportion of disease that can be attributed to 'inadequate' intakes of fruit and vegetables. A few (Block et al, 1992) and (Klerk et al, 1998) have not been so reticent.

Using both the strategies described above, Block et al classified 156 studies of diet and cancer according to whether they found a significant ( $p < 0.05$ ) decrease in risk between 'high' and 'low' consumers and they also summarised estimates of relative risk in terms of a median estimate and range (see Table 6). From their description

*“In some studies, results were reported separately for 20 or more foods. In such instances, we focused on foods widely accepted as potentially important, such as leafy green vegetables, carrots and citrus fruits”*

it will be apparent that such a process creates problems in terms of preconceptions relating to particular foods, and the weightings that should be applied to a study which, examined say, 20 foods and found 2 significant associations, as opposed to a study which reported a non-significant result for a single summary fruit and vegetable intake.

If the process by which such approximate estimates can be accepted, then a rough estimate of the proportion of disease preventable by increasing fruit and vegetable intake might be obtainable by making further assumptions concerning the risk of disease in groups with intermediate levels of consumption, and calculating the overall reduction in risk if each of those groups could be persuaded to adopt the 'high' level of consumption. Unfortunately the variability of the epidemiological data obtained using current methods is such that accurate dose-response curves are not available. And yet the shape of the dose-response curve is an extremely important determinant of attributable risk, as the following hypothetical example of a study in which consumption is reported by quarters, will show.

If we suppose that the risk of disease in 'high' consumers is 0.5 relative to low consumers (a figure chosen because it is close to many of the summary estimates reported by other reviewers), then the risks associated with intermediate intake may lie on one of several different stylised dose-response curves depicted diagrammatically in Figure 6. In more practical terms, however, intervention programs designed to increase fruit and vegetable intake are likely to have more modest impacts – and Table 7 shows that a program which increases everyone's consumption by one quarter will have an impact of just 12.5% for all the hypothetical dose-response curves, and between 12.5% and 25% if everyone's consumption is increased by two quarters.

Klerk et al (554) simply applied their risk estimates of 'high' versus 'low' consumers to the most current cancer incidence data in the Netherlands, thereby making the tacit assumption that all incident cancer cases had 'low' fruit and vegetable intakes. On the basis of the hypothetical example above, their estimates of the proportion of cancers preventable by increasing fruit and vegetable intake might be overestimated by 200% if the dose-response is linear, 33% if it follows the J2 shape and 400% if it follows the J1 shape.

The early version of the estimates (553) appears to have been embraced by the Panel responsible for developing the WCRF review of diet and cancer (551).

**Table 6: Summary of case-control and cohort studies of fruit and vegetables intake and cancer prevention**

Sites	No. of studies	Protective (p<0.05)	Harmful (p<0.0-5)	Relative Risk*
All	170	132	6	
Lung	25	24	0	0.45 (0.14-0.83)
Larynx	4	4	0	0.43 (0.36-0.48)
Oral Cavity, Pharynx	9	9	0	0.50 (0.4-0.59)
Oesophagus	16	15	0	0.50 (0.21-1.43)
Stomach	19	17	1	0.40 (0.17-2.0)
Colorectal	27	20	3	0.52 (0.3-3.3)
Bladder	5	3	0	0.48 (0.48 <sup>a</sup> -0.63)
Pancreas	11	9	0	0.36 (0.16-0.71)
Cervix	8	7	0	0.50 (0.21-0.83)
Ovary	4	3	0	0.56 (0.43-0.91)
Breast	14	8	0	0.77 (0.36-0.91)
Prostate	14	4	2	0.77 (0.29-1.67)

\* Median RRs and ranges of RRs for high consumption versus low consumption

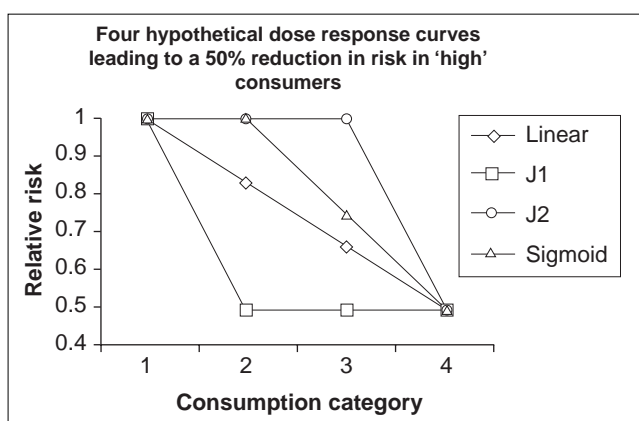
Source: Block G, Patterson B, Subar A. Fruit, vegetables and cancer prevention: A review of the epidemiologic evidence. *Nutr Cancer* 1992; 18:1-29.

Since Block et al used 'high' consumption as the reference category for relative risk estimates, we have calculated the reciprocal of all values reported in their original table.

<sup>a</sup> We believe this value may be in error in the original publication, since the median and the lower end of the range cannot be identical.

If everyone in the community could achieve levels of fruit and vegetable intake previously achieved only by the top quarter, then the fraction of disease preventable would be 25% for the linear response curve, 12.5% for the J1 curve, 37.5% for the J2 curve and 31.3% for the sigmoid curve.

**Figure 6. The effects of different dose response curves**



**Table 7. Expected percentage reduction in disease for various dose-response curve shapes with a common maximum risk reduction of 50% in the top quarter of fruit and vegetable consumers**

Increase (in quarters) in fruit and vegetable consumption	Curve shape( <i>see figure</i> )			
	Linear	J1	J2	Sigmoid
1	12.5	12.5	12.5	12.5
2	20.8	12.5	25.0	25.0
3	25.0	12.5	37.5	31.3

## 6.2 Confounding by smoking and alcohol

For the major diseases considered in this review, viz, cancers and cardiovascular disease, many other risk factors other than poor diet have been identified. For cardiovascular disease, smoking, obesity and lack of exercise are important risk factors. From the summary in Table 8, it will be apparent that with the exception of colorectal cancer and stomach cancer, smoking and/or alcohol are by far the most important risk factors for all the other 'diet-sensitive' cancers. This raises the question of whether an appropriate proportion of all disease cases due to smoking should be eliminated from any calculation of the apparent impact of high fruit and vegetable consumption on those diseases. The WCRF panel argues that despite the overwhelming evidence for smoking effects on several cancers, there is sufficient evidence to conclude that high fruit and vegetable consumption may still confer some degree of protection on smokers, and hence a proportion due to smoking should not be eliminated. On the other hand, the COMA panel expresses the reservation that many of the apparent effects of high fruit and vegetable consumption may arise through inadequate adjustment for exposure to tobacco and tobacco products.

## 6.3 Attributable risk estimations

### 6.3.1 Cancer

Given the issues raised in the discussions above, most researchers, with the exception of the Wageningen group have not been willing to estimate attributable risk estimates for the effect of dietary variables on chronic disease risk. Table 8 shows their estimates of the proportion of incident cancers that might be prevented by high consumption of fruit and vegetables in the Netherlands.

**Table 8. Known and suspected risk factors for cancers, and the proportion due to unknown factors in developed countries**

Cancer sites	% of total cancers				
	A	B	C		
	Known, preventable risk factors	Preventable proportion	Suspected risk factors	Further preventable proportion	Proportion probably due to unknown, unsuspected risk factors
Oral cavity and pharynx	Alcohol & tobacco	60-80%	Low consumption of fruit and vegetables	10%	10-30%
Oesophagus	Alcohol & tobacco	75%	Diet poor in fruit, vegetables and fresh meat products	10-20%	10%
Stomach		-	Low consumption of fruit and vegetables, high consumption of salt and salted foods; Helicobacter pylori infection	50-60%	40-50%
Colon-rectum		-	Low consumption of fruit and vegetables, high intake of animal fats and/or meat	30-40%	60-70%
Liver	Alcohol Hepatitis B	10-15% Very small			85-90%
Pancreas	Tobacco smoking	30%	Low consumption of fruit and vegetables	10-20%	40-50%
Larynx	Tobacco & alcohol – Occupational exposures	85% 10%	Low consumption of fruit and vegetables	10% (?)	5-10%
Lung	Tobacco smoking  Occupational exposures, including radiation Air pollution Environmental tobacco smoke	60-90%  10% Uncertain Uncertain	Low consumption of fruit and vegetables	5-10% (?)	2-5%
Skin (melanoma)	Sun bathing	>40%			Uncertain
Breast	Overweight after menopause	10%	High intake of fat and foods of animal origin	10-20%	70-80%
Cervix	Tobacco smoking Sexually transmitted infections	Uncertain 50%			50%
Endometrium	Overweight Post-meno-pausal unopposed oestrogens	25% 40%	Diet, excess energy intake, fats	Uncertain	40%
Ovary		-	Dairy products (lactose?)		Very high
Prostate		-	'Western life style'	Uncertain	Very high
Bladder	Tobacco smoking Certain occupational exposures	30-70% 10-20%	Some dietary factors High-fat diet, low consumption of fruit and vegetables		20%
Kidney	Tobacco smoking	30-40%	Ochratoxins	Uncertain	60%
Leukemia	Radiation Benzene	Uncertain Uncertain	Tobacco	Uncertain	Very high

b Very approximate estimate

c 60-80% in women, 80-90% in men

d Exposure to tobacco smoke can cause lung cancer in non-smokers but estimates of RR and AR are uncertain

e Certain characteristics of sexual maturation and reproduction are associated with increased risk (age at menarche, age at menopause, age at first pregnancy, number of pregnancies) but are not amenable to practical preventive measures

f Significant protection conferred by the use of oral contraceptives

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**Table 9. Proportion of incident cancer cases that might be prevented in The Netherlands**

Site	Relative risk estimate for 'high' versus 'low' consumption			% contributed by alcohol & tobacco	% of all cancers	Percent of all cancers preventable		
	Scenario I	Scenario II	Scenario III			Scenario I	Scenario II	Scenario III
Lung					15	-	-	1.4
Males	0.55	0.45	na	90	(24)	5.4	6.6	
Females	0.55	0.45	na	60	(5)	1.1	1.4	
Oesophagus	0.45	0.40	0.50	75	1.4	0.8	0.8	0.2
Pharynx	0.45	0.40	0.50	70	2.3	1.3	1.4	0.3
Larynx	0.45	0.40	0.50	85	1.2	0.7	0.7	0.1
Stomach	0.45	0.40	0.50	0	4.3	2.4	2.6	0.2
Colon/rectum	0.60	0.50	0.70	0	13	5.2	6.5	3.9
Pancreas	0.60	0.35	0.70	30	2.3	0.9	1.5	0.5
Bladder	0.60	0.50	0.70	50	3.4	1.4	1.7	0.5
Breast	0.85	0.75	1.00	0	15	2.3	3.8	0.0
Ovary	0.85	0.50	1.00	0	2.1	0.3	1.0	0.0
Cervix	0.85	0.55	1.00	0	1.3	0.2	0.7	0.0
Prostate	0.90	0.75	1.00	0	7	0.7	1.8	0.0
Other	1.00	1.00	1.00		32	-	-	-
Total					100	22.7	30.5	7.0

Scenario I: 'Best guess' estimates, ie mid-points of ranges proposed for each cancer site by Jansen et al, 1995  
Scenario II: 'Optimistic' estimates, ie estimates of Block et al, 1992  
Scenario III: 'Conservative' estimates, first eliminating all cancers attributable to smoking, and then applying the lower end of the range estimate proposed by Jansen et al, 1995

In Table 9, the Wageningen group present proportions of incident cases of cancer that might be preventable through increased consumption of fruit and vegetables according to three different scenarios. Scenario I is based on their 'best guess' estimates as reported throughout the discussions of individual diseases above. Scenario II, referred to as 'Optimistic' is based on estimates of Block (393).

The importance of smoking and alcohol was recognised by excluding a proportion of incident cases from the Dutch data according to the attributable proportions in Table 8. At the same time they used relative risk estimates from the conservative end (as opposed to the midpoint) of their estimated ranges, and thereby devised their conservative 'Scenario III'. In Table 9 it is immediately apparent that the proportions of cancers (7%) preventable by improving consumption of fruit and vegetables under this conservative scenario are very much lower than those obtained with the 'best guess' relative risk estimates of Scenario I (23%) or with the 'optimistic' calculation (31%) based on estimates of Block et (393) in Scenario II.

Several important comments need to be made:

1. As noted earlier in this document the attributable risk calculation of the Wageningen group appears to be flawed. The intrinsic assumption that all cancer cases were in the 'low' consumption category is untenable. Their method would have yielded over-estimates of the proportion preventable.
2. The WCRF Report accepted (and reproduced) the Dutch estimations, but argued that the conservative estimate of 7% underestimated the worth of high fruit and vegetable intakes, because a number of studies had indicated that high fruit and vegetable consumption was associated with lower cancer risks (even lung cancer) in smokers as well as non-smokers – and hence the exclusion of tobacco-associated cases was unwarranted.
3. By the same token there is also evidence that tobacco smoke causes a proportion of cancers in non-smokers, although numerical estimates of the attributable risk are not available.

Taking points (1 –3) above into account the Wageningen group’s conservative Scenario III (7% of cancers attributable to low fruit and vegetable consumption) may be far more realistic than has hitherto been recognised.

### 6.3.2 Cardiovascular risk

In relation to cardiovascular disease the Wageningen group concluded:

- *The risk of CHD is reduced by 20-40%, based on studies using extreme dietary plus supplemental levels of relevant components. For beta-carotene, this reduced risk is already seen in the normal range of dietary intake*
- *The risk of CHD is reduced by 30-50% for high versus low blood or biopsy levels of beta-carotene, based on recent studies (Basle Prospective Study and EURAMIC)*
- *The above associations of CHD with carotenoid intake and plasma levels may be limited to smoking subjects. Among the smokers, the inverse associations appear to be stronger.*
- *The above associations of CHD with carotenoid intake and plasma levels are likely to be due to dietary intake of vegetables and fruits. The exact quantitative relationship between fruit and vegetable intake and biomarkers of carotenoids has not been established, however.*

As with the cancer estimates the Wageningen group devised 3 different scenarios, viz, ‘Best guess’, ‘Optimistic’, and ‘Conservative’ for calculating proportion of CVD deaths that is preventable (Table 10).

- ‘Best guess’. Owing to doubts associated with extrapolating from tissue antioxidant levels to fruit and vegetable intakes they used only half the lower risk reductions based on intake.
- ‘Optimistic’ – used the midpoint of the range of risk reduction
- ‘Conservative’ – eliminated the proportion of deaths attributable to smoking assuming a relative risk of 2.0 for smoking and 1990 data for the prevalence of smoking

Their projected mortality savings associated with achieving ‘high’ fruit and vegetable intake for the entire population were 4%, 13%, and 3% for ‘best guess’, ‘optimistic’ and ‘conservative’ respectively.

As noted previously, owing to the flawed calculation of attributable risk, these estimates, like those for cancer incidence, are likely to be over-estimates.

**Table 10 Relative risk estimates and proportions of cardiovascular disease prevented**

	<i>Relative Risk Estimates</i>				<i>Proportion prevented</i>			
	Scenario I	Scenario II	Scenario III	Proportion contributed by tobacco	Proportion of total CVDs	Scenario I	Scenario II	Scenario III
Site								
Men								
Coronary	0.90	0.70	0.90	28	50	5.0	15.0	3.6
Cerebrovascular								
Other								
Total					100			
Women								
Coronary	0.90	0.70	0.90	24	37	3.7	11.1	2.8
Cerebrovascular					29			
Other					34			
Total					100			
Men plus women					100	4.4	13.1	3.2

### 6.3.3 Other chronic diseases

No attempt has been made by any research group to estimate the proportion of cases of other chronic diseases attributable to low fruit and vegetable consumption.

## 7. Health cost considerations

Two types of cost are readily identifiable for all diseases, viz, the human cost in terms of lives lost or years lived with a disability, and direct financial costs to the health system. Indirect financial costs due to factors such as lost productivity are not considered here. Sufficient data relating to the role of fruits and vegetables in chronic disease etiology exists only for cancer and cardiovascular disease. Thus this section deals only with these conditions.

### 7.1 Calculation of Potential years of life lost (PYLL) and Disability Adjusted Life Years (DALYS) lost due to chronic disease

One of the simplest measures of the burden of diseases with fatal outcomes is Potential years of life lost (PYLL). A potential limit to life  $L$ , is chosen arbitrarily (commonly 75 years) and the duration of life lost due to a single death at age  $x$  is simply the potential limit to life minus the age at death,  $L-x$ . For the population as a whole the PYLL is simply the sum over all deaths, viz,

$$PYLL = \sum d_x(L-x)$$

where  $d_x$  is the number of deaths at age  $x$ . A number of variations on this definition has been summarised by Murray in 1996 (590):-

- Expected Years of Life Lost, (or EYLL), where  $EYLL = \sum d_x e_x$ , and  $e_x$  is the local period life expectancy at each age of death
- Period expected years of life lost (PEYLL) defined similarly to EYLL, but with  $e_x$  taken to be the local PERIOD life expectancy at age  $x$  (this sometimes yields perverse results because  $e_x$  varies with time and across communities).
- Cohort expected years of life lost (CEYLL), where life expectancies at age  $x$  are COHORT as opposed to PERIOD expectations of life
- Standard expected years of life lost (SEYLL), where life expectancies at age  $x$  are based on some ideal standard.

Most chronic disease health statistics reported in Australia use the basic PYLL, with an arbitrary cut-off of 75 years of life. It is simple to calculate, but it should be kept in mind that deaths at age 75 and above contribute nothing to this estimate of the burden of disease.

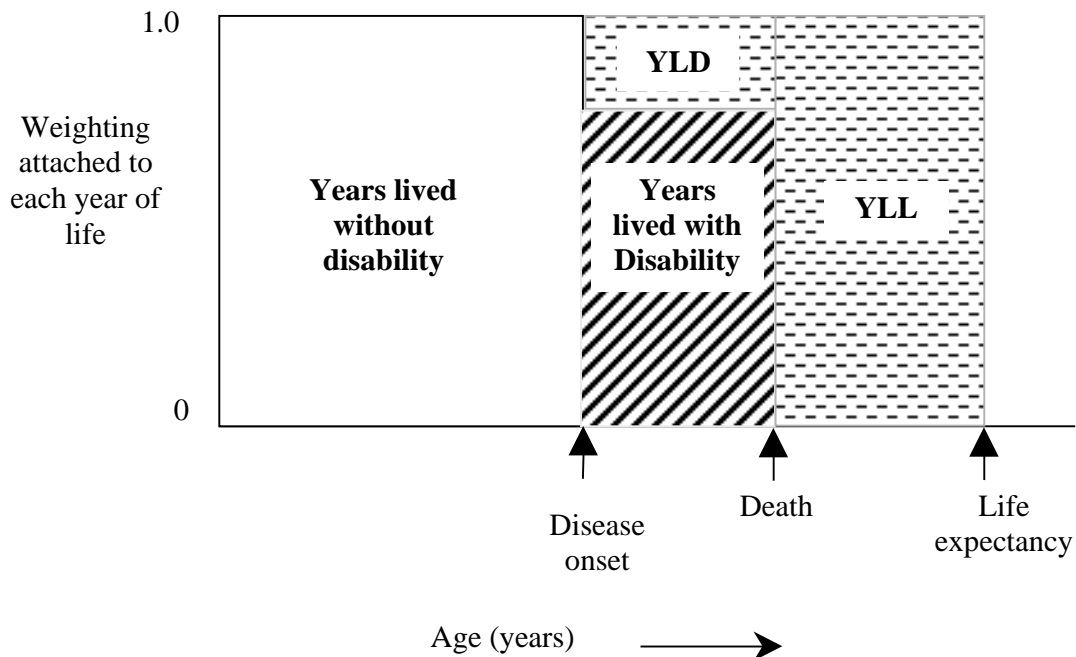
For most diseases there is, of course, a period following diagnosis during which the individual must live with a level of disability depending on the nature of the disease. Years Lived with Disability (YLD) is simply time lived in a health state which is less than perfect, weighted by a preference weight depending on the health state (approaching one for very disabling conditions, and zero for mildly disabling conditions) and whether the condition is being treated or not. The choice of disability weights is very context dependent – and there are none for Australia, although some are currently being developed (Colin Mathers, Australian Institute of Health & Welfare, personal communication).

The Disability Adjusted Life Years lost due to a condition is defined simply as the sum of years of life lost and the (weighted) years lived with disability:-

$$DALY = PYLL + YLD$$

Since no reliable weightings are available yet for calculating YLDs, this review will report only potential years of life lost to age 75, or PYLL 75. From the discussion above, and Figure 7, it will be readily apparent that the PYLL 75 underestimates the true burden of disease.

### Figure 7 Calculation of disability-adjusted life years (DALYS)



## 7.2 Cancer costs

The human cancer burden, expressed as years of life lost to age 75 for cancers at the major sites is summarised in Table 11. Lung cancer, colorectal cancer and breast cancer are among the most burdensome according to this measure, which understates the situation with respect to prostate cancer because such a high proportion of all prostate cancer deaths occur beyond the age of 75yrs.

Estimates of the direct financial cost to the health system in Australia were first published in 1998 and are based on data relating to treatment costs in the years 1993 and 1994 – and may therefore need to be inflated by a factor appropriate for the rising costs of treatment and medical technology over the past 5-6years. In terms of *treatment costs per case*, leukemia, for which there is no good evidence of dietary links, is the most expensive. In terms of *total national treatment costs*, however, colorectal cancer, costing \$147 million in 1993-4 is amongst the most expensive, coming second only to non-melanoma skin cancers estimated to cost \$183 million.

Given that there is epidemiologic evidence (albeit by no means unanimous) for a role of dietary factors in colorectal cancer, and this evidence is probably not confounded by effects due to cigarette smoking, it is likely that this component of cancer care costs, both human and financial, would be the most sensitive to increased consumption of fruits and vegetables (although both COMA and WCRF prefer evidence for the latter). However, our conclusion is that current data are insufficient to determine what proportion of these human and financial costs could be saved by increases in fruits and vegetables which might be achievable in the Australian situation.

Thus although some estimates have been attempted in relation to cost savings due to the potential effect of fruits and vegetables by the Wageningen group (5513, 554), as discussed above, our conclusion would be that there is insufficient data to make reliable estimates.

**Table 11 . Potential years of life lost to age 75 due to cancer deaths  
– Australia 1995**

Site	Males	Females	Persons
mouth & pharynx			
nasopharynx			
larynx			
oesophagus			
lung	31648	14108	45755
stomach	5378	2543	7920
pancreas	5928	3793	9720
liver			
colon,rectum	17570	12943	30513
breast	213	29378	29590
ovary			
endometrium			
cervix			
prostate	6660		6660
thyroid			
kidney	3736	1912.5	5650
bladder	2028	760	2788
All	143408	118508	261915

Source: Cancer in Australia 1995. Cancer Series No 10. AIHW, Canberra. 1999

**Table 12 Treatment costs by cancer site in Australia**

<i>Cancer site</i>	<i>Treatment costs per case (\$)</i>	<i>New cases</i>	<i>Treatment costs (\$million)</i>
1. Leukemia	57,777	1,662	96.0
2. Other sites	237,690	7,2548	270.3
3. Brain and CNS	25,333	1,118	29.9
4. Oesophagus	21,624	885	19.1
5. Bladder	19,447	2,388	46.4
6. Lymphoma	18,519	3,698	68.5
7. Liver	18,266	469	8.6
8. Stomach	16,305	1,788	29.2
9. Kidney	15,891	1,646	26.2
10. Pancreas	15,820	1,432	22.7
11. Colorectal	15,374	9,538	146.6
12. Lung	14,298	6,911	98.8
13. Head and neck	12,825	2,400	30.8
14. Ovary	12,786	1,059	13.5
15. Uterus	11,020	1,227	13.5
16. Breast	10,680	8,448	90.2
17. Cervix	9,802	1,002	9.8
18. Prostate	9,110	10,013	91.2
19. Melanoma	2,402	6,954	16.7
20. Non-melanoma skin	750	243,691	182.7
<b>All cancer excluding non-melanoma skin</b>	<b>17,671</b>	<b>69,960</b>	<b>1,128.1</b>

Source: Mathers C, Penm R, Sanson-Fisher R, Carter R, Campbell E. Health System costs of cancer in Australia 1993-94. Health and Welfare Expenditure Series No 4., Aust Inst Health Welfare, Canberra, 1998.

### 7.3 Cardiovascular disease costs

Table 13 summarises the human costs in terms of total deaths, and potential years of life lost to age 75 for ischaemic heart disease and cerebrovascular disease (stroke) as calculated by the Australian Institute of Health & Welfare. High blood pressure, or hypertension, while considered to be responsible for only a small percentage of CVD deaths costs the nation almost as much as ischaemic heart disease in terms of total treatment costs. As for cancer, the epidemiology data is not sufficient to estimate the contribution of fruits and vegetables.

**Table 13. Summary of direct costs to the health system, and the human burden (deaths and potential years of life lost to age 75) of cardiovascular diseases whose etiology may depend on fruit and vegetable consumption.**

	Total costs (\$ million)	% of total costs	per case cost (\$)	estimated % prevalence (treated) - all ages	Deaths (1994)	PYLL 75
Ischaemic heart disease	894	22.8	na		30,575	112,339
Hypertension	831	21.2	572	8		
Cerebrovascular disease	630	16.1	25,780		12,838	30,571
Cardiac dysrhythmias	224	5.7	na			
High blood cholesterol	199	5.1	214	5.1		
Other	1141	29.1	na			
<b>Total</b>	<b>3919</b>	<b>100</b>			<b>53,770</b>	<b>181,437</b>

Source: AIHW. Health system costs of cardiovascular disease and diabetes in Australia 1993-4. Health and Welfare Expenditure Series No. 5 AIHW, Canberra 1999

### 7.4 Other chronic disease

Although there are estimates being undertaken of both PYLLs and DALYS for other chronic diseases, the epidemiological evidence for these conditions is such that no attempt has been made here to assess the potential effects of fruits and vegetables in the Australian context.

### 7.5 Potential economic costs and savings

As can be seen from the discussion above, it is not possible, with any certainty, to estimate the potential economic savings of increasing fruit and vegetable consumption. The AIHW data above indicate that the cost of cardiovascular disease and diet-related cancers in Australia may be in the vicinity of \$ 3 000 million per year. Our assessment of the Wageningen data discussed above, indicates that the reduction in chronic disease burden brought about by increased fruit and vegetable consumption might, be in the order of 6-7% for cancer incidence and cardiovascular mortality (no estimate is available related to cardiovascular incidence). If we apply a simplistic 6-7% saving on costs for cancer incidence and cardiovascular mortality reduction, this would give us an apparent economic saving of some \$ 200 million per year. However, this is a very simplistic extrapolation from economic and epidemiologic data which in themselves are not very reliable.

### **Summary of health cost considerations**

- Although some estimates have been made in Australia relating to the human and financial costs of a range of chronic diseases, no attempt has been made to look at individual dietary components.
- The only group, worldwide that has attempted such an analysis is the Wageningen group who assessed the potential effects for the Dutch situation with respect to cancer and cardiovascular disease.
- The work undertaken by the Wageningen group formed a key element in the quantified risk assessment made in the WCRF report but their methodology appears to have some fundamental flaws, which would lead to overestimations of the protective potential. These are discussed in the body of the report.
- An analysis of the Wageningen data suggest that savings of some 6-7% could be made in cancer incidence and in cardiovascular mortality with diets higher in fruits and vegetables. The AIHW estimates cardiovascular disease costs Australia some \$ 4 000 million a year in direct health care costs and diet-related cancers some \$ 500 million in treatment costs.

## **8. General conclusions**

Overall, the epidemiological data indicate a protective effect of fruits and vegetables against a number of chronic diseases. There are significantly more studies for cancer than any other disease condition and a moderate amount for cardiovascular disease. There are some indicative data for stroke, hypertension, cataracts, diabetes and other diseases such as arthritis, Alzheimer's, Parkinson's, inflammatory bowel disease, ulcers, gallstones, multiple sclerosis and osteoporosis but the data are too sparse to provide any meaningful assessment of the influence of fruits and vegetables.

In our judgement, and that of the COMA panel in the UK, the evidence linking fruits and vegetables to risk of cancer is moderate for some cancers and weak and inconsistent for others, but the WCRF panel was more enthusiastic in their interpretation. Estimates of attributable risk undertaken by the Wageningen group formed a key element in the quantified risk assessment made in the WCRF report but their methodology appears to have some fundamental flaws which would lead to overestimations of the protective potential. Nevertheless, both the COMA group and we, as well as WCRF, believe there is sufficient evidence of potential public health benefit to encourage consumption of greater amounts of fruits and vegetables in relation to cancer risk reduction. Evidence for cardiovascular disease is less abundant and more reliant on surrogate measures of antioxidant vitamins and other exposure measures. Nevertheless, the results do suggest a protective effect. The data for other diseases is very limited but there are indications of wider benefits..

There are insufficient data to indicate promotion of any particular types of fruits and vegetables nor to identify any particular constituent. Neither is there compelling evidence to exclude canned, frozen or dried varieties or to exclude juice. However products which are based on fruit or vegetables but are heavily processed (eg certain pie fillings, biscuit fillings, health bars, jams etc) may have a quite different nutrient profile and potential to influence health. Research into the protective effects of components parts of fruits and vegetables, particularly in relation to cancer, highlights the need to take a food-based approach encompassing a variety of sources rather than an approach concentrating on "good" sources of known components such as antioxidant vitamins or fibre. Key reviews have thus highlighted the need to encourage a wide variety of choice which could include use of fresh and processed fruits and vegetables.

Despite the more cautious judgement of the COMA panel, both they, and we, conclude that there is still sufficient evidence to recommend an increase in the consumption of fruits and vegetables. Whilst fruits and vegetables do contain some components which may have adverse effects on health and some epidemiological studies have shown apparently adverse effects under some circumstances, the evidence for potential advantage appear to outweigh that for disadvantage. Intakes equivalent to 7 serves a day of fruits and vegetables (2 fruit; 5 vegetable) have been recommended by the NH&&MRC in their Core Food Groups. It should be noted, that these recommendations are not based on an analysis of the epidemiological data linking intake of fruits and vegetables to chronic disease outcome, but on estimates of amounts of various food groups required to achieve diets which conform to the Recommended Dietary Intakes, which are to a large extent based on avoiding deficiency disease. The data from epidemiological studies are not sufficiently robust to determine whether this level of consumption is optimal for chronic disease prevention but together with experimental and animal studies, they suggest that intakes substantially higher than currently consumed in Australia are likely to be beneficial

Whilst there is some debate as to what foods should comprise the “fruits and vegetables” category, intakes in Australia are well below the current NH&MRC Core Food Group recommendations and those of the WCRF panel.

If recommendations are made to increase fruit and vegetable intake, the data would suggest that they should be targeted at the general population, possibly with an emphasis on adolescence and early adulthood, given the relatively low consumption at this age. Adhering to recommendations to increase consumption may bring difficulties to some groups in the community but more so, if campaigns centre on fresh food only. For fresh items, there are considerations relating to storage, transport and the need for more regular shopping that could prove a barrier to the elderly, those living in remote areas or those with limited time or facilities to store food. Many of these concerns can be overcome with inclusion of processed varieties. Whilst fresh varieties may have the optimal nutrient profile, this is not always the case and the nutrient profiles of many processed varieties can still be better sources of nutrients and bioactive components than the fresh version of other varieties. Within categories, there were obviously preferred sources according to gender, age and ethnic background which could be used as a basis for promotion but, again, variety needs to be promoted to maximise effectiveness.

## 9. Glossary

Aetiology	The cause or causes of disease
AICR	American Institute of Cancer Research
Allium	A plant genus which includes onion, garlic and leeks
Antioxidant	A substance that inhibits oxidation
Bias	A characteristic of a study which tends systematically to produce results that depart from the true values (to be distinguished from random error)
Brassica	A plant genus which includes broccoli, cabbage, cauliflower, Brussels sprouts, kale and mustard
Cancer	Any malignancy either solid tumour or more diffuse myelo or lympho proliferative disorders. The term cancer encompasses all neoplastic diseases in which normal cells are transformed into malignant ones
Cardiovascular disease	Disease of the heart and blood vessels
Carotenoids	A group of about 100 red and yellow pigments derived from and found principally in plants, comprising carotenes, many of which eg beta-carotene are precursors for retinol, and xanthines eg lycopene, which are not. They may act as antioxidants
Case-control studies	A study that starts with the identification of persons with a condition of interest and a control group of persons without the disease. The extent of past exposure to known or suspect risk factors is measured in each group and the risk associated with each factor is estimated
Cohort or prospective study	A study of a population whose exposure to factors hypothesised to influence the probability of occurrence of a given disease is measured at recruitment. The participants are followed over time and development of disease ascertained. Such a sample identified at one period of time, is called a cohort
Confounding variable	A factor that distorts the observed relationship between two other variables
Cruciferous	A family of plants which includes the genus <i>Brassica</i>
Ecological studies	Epidemiological investigations in which various measures of the characteristics of a whole population are associated with measures of disease occurrence
Free radical	Atoms or molecules that contain an unpaired electron and that seek out another electron to attain a more stable state – and that by so doing can damage molecules such as DNA, lipids or proteins
ICD Codes	International Classification of Disease Codes
Incidence	The number of new cases of a disease occurring in a given size of population during a specific time, usually a year
Intervention studies	Investigations in which some aspect of the status of an individual is changed intentionally
Lycopene	The red carotenoid pigment of tomatoes, some berries and fruits
Mutation	A permanent change in the amount or structure of the genetic material in an organism
Mutagenic	The property of an agent to produce mutation
Phytoestrogens	Compounds found in plants which may mimic or block the action and metabolism of naturally occurring steroid sex hormones
Prevalence	The number of cases observed in a given size of population at a designated time
Prospective studies	See Cohort studies
Randomised Controlled Trials (RCT)	Intervention studies in which groups are randomly allocated to receive specific interventions
Relative Risk	The ratio of the risk of an event among those ‘exposed’ to a factor to that of those ‘unexposed’
Risk	The probability of an adverse health effect such as cancer developing in a human population within a defined set of circumstances
Wageningen group	Authors of two reports both entitled <i>Fruits and vegetables in chronic disease prevention</i> the first of which was first published in 1995 by authors Jansen MCJF, van’t Veer P, and Kok FJ, and which was then substantially updated in 1998 with authorship Klerk M, Jansen MCJF, van’t Veer P and Kok FJ
WCRF	World Cancer Research Fund

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