Chapter 1

Plant foods and health

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Introduction

The purpose of this introductory chapter is to pave the way for subsequent chapters by looking at the historical context of plant food consumption, reviewing the contribution plant foods make to intakes of essential nutrients (e.g. fibre, vitamins, minerals, protein and essential fatty acids), examining the evidence linking plant food intake to health, summarising current recommendations and policy regarding plant food intake, and comparing these recommendations with current intakes.

Historical changes in the plant content of the human diet

Throughout human history, communities and societies have developed a diversity of dietary patterns and habits that have taken advantage of the food plants and animals available to them as a result of personal skills, climate, geography, trade and economic status. It is a basic premise the diets that persisted were capable of providing sufficient energy and essential nutrients to support growth and reproduction. They may not, however, have been conducive to optimal health.

Archaeological investigations have been used to predict what the diet of early man was like. Nestle (1999) cites Eaton and Konner (1985) who proposed that by the time of the emergence of modern *Homo sapiens* 45 000 years ago (Table 1.1), meat intake was high, but lean, and plant foods provided levels of vitamin C that exceed current recommendations. The diets of those modern day communities who survive primarily through hunting and gathering have also been used as a source of information, although the extent to which the diets of such communities simulate those of early man can only be speculated. Estimates suggest that most of the modern day hunter-gatherer communities lived in areas where plant foods grew readily, one exception being the indigenous people living in the Arctic whose traditional diets were dominated by meat and who relied almost completely on hunting for much of the year (Eaton and Konner 1985). Also, anthropologists have examined the diets of closely related primates for clues about the possible diets of our distant

Table 1.1   Stages of evolution of human diets

	Time period elapsed (years)
Pleistocene: Stone Age	1.6 million
Homo sapiens: Archaic	400 000
Neanderthal	80 000
Modern	45 000
Holocene: Agriculture	10 000
Industrial revolution	200
Global food economy	50

Adapted from Eaton and Konner (1985).

ancestors. In general, primates seem to eat whatever is convenient, mainly plants but also insects, eggs, crustaceans and carrion (Nestle 1999). Recent documentary evidence has captured film of chimpanzees and other primates hunting and killing animals as prey, which has subsequently been shown on wildlife television programmes in the UK.

Archaeology has provided considerable evidence for meat consumption by early man, including characteristic marks on fossilised animal bones and stone artefacts consistent with meat eating. However, this information must be considered in context: bones are better preserved than vegetable matter and hence reliance on such evidence is likely to underestimate plant food consumption (Nestle 1999).

Plant foods can be categorised in many ways but the method used here can be seen in Table 1.2. It has been suggested that the plant foods gathered by our early ancestors were those that did not require digging with hands or sticks, such as fruits, leaves and stems, and seeds in pod-like structures (e.g. peas, beans) that would have provided protein. There is also early evidence of the cultivation and storage of legumes such as broad beans in the Middle East, where 'farming' is said to have begun, and among cave dwellers living as far apart as Mexico and Peru, and north-east Thailand (Toussaint-Samat 1992). Similar evidence exists for collection of wild chick peas, lentils and peas, followed by their cultivation.

In hot, humid areas where top soil is poor, root systems grow near to the surface and will have been easy to forage. In more temperate climates, such as the Middle East, a stick or similar pointed implement would probably have been required and its use was perhaps the first step towards farming. The digging stick is thought to have been the ancestor of the hoe and the plough (Toussaint-Samat 1992). Roots and tubers, gathered or cultivated, have been a dietary staple in tropical zones since early times, providing energy and being easy to acquire. A limited number are popular now but many other examples exist in nature. The sweet potato, for example, comes from the equatorial forests of South America but is thought to have reached Polynesia 2000 years ago, perhaps via early trade (Toussaint-Samat 1992). The potato and sweet potato reached the shores of Europe as part of a present to Queen Isabella of Spain from Christopher Columbus. The potato itself was not popular and had to wait until the eighteenth century before it came into its own, but the versatile sweet potato was a success in Elizabethan England, perhaps because of its sweet taste at a time when sugar was scarce and very expensive (Toussaint-Samat 1992). Following the example of the native Indians in North America, European colonists made sweet potato one of their national dishes. The Jerusalem artichoke, another tuber, is also well travelled.

Table 1.2 Categorisation of plant derived foods and drinks

Group	Examples
Fruits	
Tree Fruits	Apples, pears, plums, apricots, peaches, cherries, citrus fruit, dates, pineapple, mango, papaya, fig, olive
Soft fruits	Strawberries, raspberries, blackberries, cranberries, currants
Other	Melons, grapes, kiwi, bananas
Vegetables	
Root crops*	Potatoes, sweet potatoes, yam, cassava Carrots, turnips, swedes, parsnips
Cabbage family	Cabbage, broccoli, Brussels sprouts
Onion family	Onions, leeks, garlic
Salad vegetables	Lettuce, celery, cucumbers
Tomato family	Tomatoes, sweet peppers, chilli peppers, aubergine
Mushrooms and fungi	Mushroom varieties, Quorn™
Other	Squashes, sprouted seeds, sea vegetables
Cereals (grains)	Wheat, barley, maize (corn), millet, oats, rice, rye
Tree nuts and seeds	Walnuts, cashews, almonds, chestnuts, pecans, brazils, hazelnuts, pistachio, pine kernels, sesame seeds, pumpkin seeds
Pulses (legumes)	Soya beans and products e.g. tofu, red kidney beans, butter beans, chick peas, lentils, peanuts (groundnuts)
Beverages	Tea, coffee, cocoa, wine, spirits, beer
Oils	Seed oils e.g. sunflower oil, corn oil, rapeseed oil, linseed oil; olive oil, soya oil, peanut oil; evening primrose oil, borage oil
Other	Chocolate
Herbs, spices, condiments	Sage, rosemary, thyme, ginger, pepper, cumin, mustard, tomato-based sauces

*Potato, sweet potato and yam are classified as starchy foods, rather than vegetables, in many food guidance models.
From Buttriss 2003.

It was found growing wild in North America and transported across the Atlantic in the seventeenth century and is said to be the only food plant that has been introduced to Europe from North America (Toussaint-Samat 1992). The yam, of a different botanical family to the sweet potato, grows naturally in tropical forests all over the world and is relatively rich in protein. Tapioca, a popular milk pudding ingredient in the recent past, is derived from cassava. The cassava shrub is protected from parasites by the cyanide compounds (prussic acid) it contains in the skin of its tubers, which need to be carefully prepared before consumption because even a tiny quantity of the bitter cassava juice causes instant death. The complex methods for its preparation must presumably have been identified by trial and error among people with very limited dietary options.

There is also early evidence of the consumption of onions, which have the advantage that they can be eaten raw. They grow wild in a large part of the Middle East and the Indian subcontinent, and it is suggested they were used to relieve the monotony of frugal diets. Labourers working on the Great Pyramid were paid in onions, garlic and parsley,

and onions accompanied Egyptian mummies into their tombs (Toussaint-Samat 1992). The onion has been widely used over the centuries and was taken on long sea voyages in the hope that it might prevent scurvy. Garlic, also a member of the allium family, is thought to have come from a desert area of Central Asia and is surrounded by a remarkably rich and ancient body of folklore.

The discovery and study of Palaeolithic refuse tips has been facilitated because grains found there were preserved from the ravages of time by carbonisation (parching) during their processing to remove the inedible husk. This primitive form of 'cooking' in stone age culture remained in use in the Middle Ages (Toussaint-Samat 1992). Perhaps the development of such techniques and the identification of areas where wild cereals grew in abundance or could be cultivated were triggers for people to become 'settled' in one place rather than living a more nomadic life, thus experiencing a less tenuous lifestyle and greater life expectancy. Early evidence shows that initially the cereals cultivated were identical to the wild types, but even as early as 10 000 BC there is evidence from Jericho of selection of the forms of barley and wheat that less readily shed their seed on ripening, allowing it to be harvested more effectively. Indeed there is evidence from all around the world of early cereal cultivation thousands of years ago, for example in the Dordogne in France in 8000 BC, Japan in 7500 BC, Mexico in 6000 BC, Denmark, China and Siberia in 4000 BC, and India in 3000 BC. By AD 100, rye and oat cultivation was widespread across Europe, joining wheat which had been in cultivation in many parts of Europe for some time (Toussaint-Samat 1992). The spread of cereal growing provides information about the migration of the people who consumed it, as they took their customs with them.

The most commonly consumed cereal grains in the human diet are wheat, rice and maize, although barley, oats, rye, millet and sorghum are more common in some countries than others, consumption patterns being largely determined by climate and cultural differences (Southgate 2000).

Current dietary patterns in developed countries have been largely shaped by the changes in food production that began with the industrial revolution during the 1800s. These dietary patterns have been fuelled by a global food economy in which food is now transported long distances, enabling a diverse range of plant foods to be available in shops all year round and removing the dependency on local, seasonal produce.

In developing countries in the twenty-first century, plant-based diets are associated with extreme poverty and poor health and, when economic conditions improve, low-income populations tend to increase their consumption of meat, and display fewer signs of nutritional deficiency (Nestle 1999). However, as such countries become still more prosperous and 'westernised' they begin to share the disease patterns prominent in Europe, North America and Australasia, characterised by obesity, type 2 diabetes, cardiovascular disease and particular forms of cancer such as colon cancer. In such populations, nutrition policy focuses on restoring the balance between foods derived directly from plants, such as fruits, vegetables, wholegrain cereal products and pulses, and, on the other hand, foods derived from animals, which can be relatively high in saturated fatty acids though good sources of essential vitamins and minerals, and processed foods rich in fat, sugar or salt.

It has also recently become apparent that the diversity of plant foods collected in the wild and consumed in developing countries is greater than previously thought. For example, East African food systems are based on a rich diversity of traditional cereals, legumes, leafy

vegetables, indigenous fruits (and animal source foods) that are cultivated or gathered from the wild (Johns and Eyzaguirre 2006). Retention of traditional food habits based on local knowledge and biodiversity is important for food security.

Changing composition of dietary constituents in the past 50 years

Improvements in agricultural practices and the development of new products have led to a change in both the composition of individual foods and the patterns of food consumption all over the world. Plants and animals used as food exhibit marked variations in composition, against which the effects of changes in production and processing need to be judged. Changes that have occurred in connection with new developments in farming and food processing often fall well within this natural variation (Paul 1977).

There are many factors that influence the composition of plants, the most important being genetic inheritance, growing conditions (light intensity, heat, moisture and fertilisers) and maturity when harvested. After harvesting, changes may also take place during storage and distribution. Furthermore, particularly with vegetables, nutrient content can be affected by cooking processes. Therefore, changes in the nature of the crops grown and growing conditions will have had an impact on their composition. For example, the vitamin C content of tomatoes is enhanced by direct sun, being outdoors, fast ripening, and use of potassium and manganese fertiliser, and is higher in the outer part of the fruit. It is decreased by shade, being under glass, slow ripening and use of nitrogen fertiliser (Paul 1977).

The major drivers for changes in food choice have been innovations in food processing. Although processes such as canning, freezing and drying are not new, continuous improvements have been made to these processes over recent decades and these techniques have been joined in recent years by other packaging and processing innovations. In particular, over the past 50 years almost ubiquitous home ownership of fridges and freezers has had a major impact on the types of foods that can be consumed all year round. Processing improvements have also enabled storage losses to be minimised, especially of labile nutrients such as vitamin C.

By the late 1970s, consumption of processed potato products had also increased, from contributing up to 2% of total potato consumption in 1955 to 30% (Paul 1977). This was of interest with regards to the vitamin C content of potatoes, which falls progressively during storage and varied between products available at that time.

In addition to changes in the type of a particular product bought, new products were coming onto the market, for example soya-based meat substitutes. These were designed to replace meat in the diet but had a different amino acid profile, notably lower methionine.

Thirty years on, these changes have been overtaken by a huge range of new processes, formulations and products, making it even more challenging to maintain good quality food composition data. Food composition databases are essential to the work of a variety of different users, including those involved in nutritional research, health care professionals, the food industry, regulatory bodies and caterers.

Since 2005, the British Nutrition Foundation has been a partner in a project known as EuroFIR (European Food Information Resource Network of Excellence), which has created

a pan-European databank of food composition information (Williamson and Buttriss 2007). The EuroFIR network has comprised around 50 organisations across Europe and beyond. Its work continues through EuroFIR Nexus (a further 2 year grant from the European Commission, 2011–12) and a not-for-profit organisation established in Brussels. A feature of the work of EuroFIR has been to develop a comprehensive database of published information about bioactive substances in plant foods. More information and progress to date with this database and the projects as a whole can be found at http://www.eurofir.eu.

Plants – nutrients and other constituents

Before discussing the evidence linking plant food intake with health, it is helpful to consider the range of different nutrients available to us from the plant kingdom and the plethora of other components, sometimes referred to as bioactive substances or phytochemicals, that may confer health benefits. A summary of these and examples of their plant food sources can be found in Table 1.3.

A summary of the evidence linking plant food intake and health

A substantial number of epidemiological studies have shown that people who consume a diet rich in fruits, vegetables and other plant foods (e.g. nuts and pulses) are at reduced risk of developing cardiovascular disease (CVD), i.e. coronary heart disease and stroke, and to a lesser extent cancer (Margetts and Buttriss 2003; Stanner et al. 2004; Hung et al. 2004; He et al. 2007; Crowe et al. 2011). As a result of their analysis of two large US cohorts, Hung and colleagues (2004) propose that the benefits, especially in relation to cancer, may have been overstated. This has been confirmed by the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) report published in 2007, which reported that the overall evidence for fruits and vegetables had reduced in strength as new research had been published since their report of 1997. However, with regard to dietary fibre and colon cancer, the evidence of a protective effect has strengthened and is now regarded as convincing (WCRF/AICR 2010).

The beneficial effects of diets rich in plant foods have also been reported for other chronic conditions, namely age-related macular degeneration (AMD) (Goldberg et al. 1998), cataract (Brown et al. 1999a), chronic obstructive pulmonary disease (e.g. asthma and bronchitis) (Miedema et al. 1993) and dementia (Morris et al. 2006). However, the associations are typically less strong and, as discussed later in more detail, little is known for certain about the mechanisms by which plant foods exert their apparent effects.

These associations have led to efforts to identify the mechanisms underpinning these health effects and the active components within plant foods, as mentioned earlier. There are several plausible reasons why there may be an association between fruit and vegetable consumption and a reduced risk of chronic disease, apart from possible confounders associated with other factors such as non-smoking and physical activity (Lampe 1999). These include changes to detoxification enzymes; stimulation of the immune system; reduction

Table 1.3   Nutrients and other constituents of plant-derived foods and drinks

Plant constituent	Main plant derived sources in the UK
Minerals	
Calcium	Bread (flour is fortified in the UK), pulses, green vegetables, (and if eaten regularly, dried fruit, nuts and seeds)
Chromium	Whole grains, and to a lesser extent legumes and nuts
Copper	Bread and cereal products, vegetables
Iodine	Sea vegetables, e.g. kelp, beer
Iron	Vegetables, pulses; to a lesser extent potatoes and dried fruit Fortified breakfast cereals and foods made from fortified flour are also important sources
Magnesium	Cereals and products (especially wholegrain), green vegetables, nuts and seeds
Manganese	Tea is a major source Other sources include wholegrain cereals, vegetables, nuts and seeds
Molybdenum	Vegetables, bread and other cereal products Also present in pulses
Potassium	Particularly abundant in vegetables, potatoes, fruit (especially bananas), and juices It is also found in bread, nuts and seeds
Selenium	Cereals, concentration being dependent on soil type
Zinc	Cereal products such as bread, especially wholemeal Other plant sources include bead and lentils, nuts, sweetcorn and rice Absorption is relatively poor from phytate-rich cereals
Vitamins	
Folate	Green leafy vegetables (raw or lightly boiled), especially sprouts and spinach; green beans and peas, potatoes; fruit, especially oranges
Niacin	Potatoes Also present in fortified cereals and bread
Riboflavin	Fortified breakfast cereals
Thiamin	All cereals, potatoes Also present in vegetables
Vitamin B6	Potatoes and breakfast cereals
Vitamin C	Richest sources are citrus fruit, citrus fruit juices, kiwi fruit, soft fruits Other sources include green vegetables, other fruit, peppers, potatoes (especially new potatoes)
Vitamin E	Vegetable oils, wholegrain cereals, vegetables (especially dark green leafy types), fruit, vegetable oils, cereals
Vitamin K	Green leafy vegetables are the richest source Also in other vegetables, fruit, vegetable oils and cereals
Other nutrients	
Dietary fibre	All cereals (especially wholegrain), vegetables, fruit, pulses, nuts
Fatty acids MUFA	Rich sources are olive oil and rapeseed oil Also present in other seed and nut oils
PUFA (n-6) PUFA (n-3)	Rich sources are sunflower, safflower and corn oils Also present in other seed and nut oils

(*Continued*)

Table 1.3   (Cont'd)

Plant constituent	Main plant derived sources in the UK
	There are no plant sources of the long chain n-3 fatty acids (EPA and DHA) associated with hear health, but the essential fatty acid α-linolenic acid is present in large amounts in linseed (flax) oil, grapeseed and rapeseed oils, walnut oil and walnuts It is also present in green leafy vegetables, soybeans (and soya oil) and hazelnuts
Other plant substances	
Carotenoids	Carrots, butternut squash, oranges, tangerines; other sources
α-carotene	include passion fruit andkumquats
β-carotene	Orange vegetables (eg carrots), green leafy vegetables (e.g. spinach), tomato products; other sources include apricots, guava, mangoes, orange melons, passion fruit
Lycopene	Tomato and tomato products
Flavonoids, eg flavanols, flavan-3-ols, flavones, flavanones, anthocyanidins	Tea, red wine, onions, apples are major sources of this large family of compounds Cocoa and hence dark chocolate also provide members of this family, primarily flavan-3-ols But sources of specific types of compounds also include grapes, berries and cherries (flavonols, anthocyanidins); parsley, thyme and celery (flavones); citrus fruit (flavanones)
Glucosinolates	Brassica vegetables eg sprouts, cabbage, broccoli
Phytoestrogens (isoflavones, lignans)	Soya, seeds, e.g. linseed, other pulses, grains, nuts
Sterols and stanols	Naturally present in vegetable oils eg soya oil Also present in cereals, nuts and vegetables
Sulphur-containing compounds	Onions, leeks, garlic, chives (also see glucosinolates)
Terpenoids other than carotenoids	Herbs and spices, e.g. mint, sage, coriander, rosemary, ginger

Adapted from Buttriss (2003).

of platelet aggregation; an effect on cholesterol synthesis, blood pressure or hormone metabolism; and antioxidant effects.

A popular explanation within the scientific community, and more recently among the general public, is that dietary antioxidants, including vitamins C and E, the carotenoids (e.g. beta-carotene, lycopene and lutein), selenium, and flavonoids may prevent carcinogenesis and the atherosclerosis associated with heart disease and stroke by blocking oxidative damage to DNA, lipids and proteins, as discussed in more detail later. Normal oxidative metabolism produces large quantities of potentially damaging oxidants (free radicals) that can damage cells and tissues in a number of ways, including disruption of normal repair mechanisms. The delicate balance between pro- and antioxidants determines the degree of oxidative stress, and this has been implicated in the pathophysiology of many chronic diseases, including heart disease, diabetes, cancer and the ageing process (Jackson 2003).

In relation to a potential protective role for antioxidant nutrients, a substantial amount of work has been done in the areas of CVD and cancer, and some of this is summarised here. To date, much of the research has concerned fruits and vegetables, although many of the compounds of interest are to be found in other plant-derived foods, such as tea, cocoa, cereals, wine and herbs.

Associated with this research effort, there has been interest in the use of health claims on foods. A European Commission (EC) regulation on nutrition and health claims was agreed in December 2006. It applies to all nutrition and health claims made in commercial communications, i.e. labelling, presentation or advertising of foods, and aims to provide a high level of consumer protection whilst allowing the European Union market to function effectively. The regulation came into force on 1 July 2007. It describes how nutrition and health claims should be used, and the procedures that need to be followed to obtain authorisation of a claim by the EC (http://ec.europa.eu/food/food/labellingnutrition/ claims/community_register/index_en.htm).

This regulation will provide a list of permitted nutrition and health claims that can be used by food operators across the EU and the process for assessing claims is ongoing. Ultimately, only health claims that are on this list will be permitted for use in the EU, although there are interim measures in place to give manufacturers and retailers time to adapt to the new rules.

Overall any claim made should be truthful and not attempt to mislead consumers. Nor should it call into question the safety or nutritional content of other foods or the adequacy of a balanced diet. The claim itself must apply to the food as eaten, prepared according to the manufacturer's instructions, and the effects described in the claim must be understandable to the average consumer.

The science underpinning each potential health claim is being assessed by the European Food Safety Authority (EFSA). A large number of potential claims have been submitted for consideration and many of these have received negative opinions. The EC makes the final decision on whether or not to approve the claim, as they must take consumer understanding as well as the science into account, but it is very unlikely that approval will be given to any of those claims for which EFSA has specified that a cause and effect relationship has not been established or that the constituent in question has not been sufficiently characterised.

Coronary heart disease and stroke

Fruits and vegetables

Armstrong and Doll were among the first to note associations between population food patterns, based on UK National Food Survey data, and data concerning mortality from coronary heart disease (CHD) (Armstrong and Doll 1975). CHD rates were higher in areas where fruit and vegetable consumption was lowest. Across Europe, countries whose populations consumed the most fruits and vegetables have been shown to have lower rates of CHD, and analyses of trends over time suggest an inverse relationship between declines in fruit and vegetable consumption and increasing rates of CHD.

The Women's Health Study in the USA has shown that women who eat more fruit and vegetables had a lower cardiovascular risk, particularly in relation to myocardial infarction

(Liu et al. 2000a). Similar results have been reported in a cohort study of Swedish men (Strandhagen et al. 2000). A factor analysis using data from the Health Professionals' Follow-up Survey (Hu et al. 2000) showed that men following a 'prudent diet', characterised by higher intake of vegetables, fruit, legumes, wholegrains, fish and poultry, were less likely to develop coronary heart disease. Knekt et al. (1996) found that intake of apples and onions and intake of flavonoids were inversely linked to coronary mortality in a Finnish cohort. A more recent analysis (Knekt et al. 2000) has shown that apples remain protective against thrombotic or embolic stroke, after adjustment for intake of quercetin. This suggests that there may be other bioactive substances in apples that need further investigation.

In their meta-analysis of cohort studies investigating the relationship between ischaemic heart disease and markers of fruit and vegetable consumption (both the foods themselves and related nutrients), Law and Morris concluded that the risk of ischaemic heart disease is about 15% lower at the 90th than at the 10th centile of fruit and vegetable intake (Law and Morris, 1998).

After an average of 8.4 years of follow up of more than 313 000 men and women in the EPIC study, those consuming at least eight (80g) portions of fruit and vegetables a day had a 22% lower risk of fatal IHD than those consuming fewer than three portions a day (Crowe et al. 2011); a one portion (80g) increment was associated with a 4% lower risk.

Bobak et al. (1999) compared men in the Czech Republic, Bavaria and Israel and suggested that differences in fruit and vegetable intakes may explain differences in risk factors between eastern and western Europe. Ness and Powles reviewed the literature linking fruit and vegetable consumption with risk of CHD (Ness and Powles 1997) and compared this with the literature on stroke (Ness and Powles 1999). They found that in nine out of ten ecological studies, two of three case-control studies and six out of sixteen cohort studies there was a significant inverse association between coronary heart disease and intake of fruit and vegetables (or a nutrient used as a marker of intake) (Ness and Powles, 1997). For stroke, three out of five ecological studies, and six of eight cohort studies showed an association of this type (Ness and Powles, 1999). The authors concluded that although studies showing no effect may be under-reported, the results were consistent with a strong protective effect of fruit and vegetables for stroke and a weaker protective effect for coronary heart disease.

Using data from the Nurses' Health Study and the Health Professionals Follow-up study, an analysis by Hu (2003) identified relative risks of coronary artery disease associated with different categories of fruits and vegetables (Table 1.4). Again stronger support for an association with stroke was evident, especially for total fruit, citrus fruit and vitamin C rich fruits and vegetables (Hu 2003).

Joshipura et al. (1999) examined intakes of specific fruits and vegetables, as well as overall fruit and vegetable intake, in two large cohorts of US men and women, followed for 8 and 14 years respectively, and free of cardiovascular disease, cancer and diabetes at baseline. After controlling for standard cardiovascular risk factors, those in the highest quintile of fruit and vegetable intake (median 5.1 servings per day in men and 5.8 in women) had a relative risk for ischaemic stroke of 0.69 compared with those in the lowest quintile. An increment of one serving per day of fruit or vegetables was associated with a 6% lower risk of ischaemic stroke. Green leafy vegetables, cruciferous vegetables and

Table 1.4   Multivariate relative risks (RRs) of coronary artery disease based on a comparison of the highest and the lowest quintiles of fruit and vegetable intakes in the pooled analyses of the Nurses' Health Study and the Health Professionals' Follow-up Study

Food	RR (95% CIs)	
	Coronary artery disease	**Stroke**
All fruit	0.80 (0.69, 0.92)	0.69 (0.52, 0.91)
All vegetables	0.82 (0.71, 0.94)	0.90 (0.68, 1.18)
Total citrus fruit	0.88 (0.77, 1.00)	0.72 (0.47, 1.11)
Citrus fruit juice	1.06 (0.85, 1.32)	0.65 (0.51, 0.84)
Cruciferous vegetables	0.86 (0.75, 0.99)	0.71 (0.55, 0.93)
Green leafy vegetables	0.72 (0.63, 0.83)	0.76 (0.58, 0.99)
Vitamin C rich fruit and vegetables	0.91 (079, 1.04)	0.68 (0.52, 0.89)
Legumes	1.06 (0.91, 1.24)	1.03 (0.77, 1.39)
Potatoes (including French fries)	1.15 (0.78, 1.70)	1.18 (0.90, 1.54)

RRs adjusted for standard cardiovascular disease risk factors.
Source: Hu (2003).

citrus fruit including fruit juice contributed most to the apparent protective effect. A particular role for citrus fruit in reducing CHD risk has also been reported in the PRIME study of subjects in France and Northern Ireland (Dauchet et al. 2004).

Van't Veer and colleagues (2000) carried out a review of 250 observational studies (case-control and prospective) on cardiovascular disease and cancer, in which measurements were made of fruit and vegetable intake (excluding potatoes). The authors noted that, overall, testing the efficacy of fruits and vegetables in population trials is hampered by methodological factors such as 'blinding' (i.e. it is not possible to conceal the true exposure from either subjects or researchers), compliance and study duration. Relative risks (RR) or odds ratios (OR) (depending on the type of study) for high versus low intake of fruit and vegetables were calculated. The proportion of cases attributable to low consumption was estimated using three scenarios: best guess, optimistic (using stronger RRs) and conservative (using weaker RRs and eliminating the contribution of smoking and/or drinking). These RRs usually represented risk for subjects in the highest versus the lowest category of intake, typically a difference of about 150 g/day of fruit and vegetables. These estimates represent the overall effect of beneficial and adverse properties of fruits and vegetables. The researchers calculated the proportion of cases of CVD that could be prevented in the Dutch population if current average intakes of 250 g/day were increased to 400 g/day (the World Health Organisation recommendation). The 'best guess' estimate for cardiovascular disease was 16% (8000 cases annually), ranging from 6% (conservative) to 22% (optimistic).

A meta-analysis of nine independent cohorts (comprising 257 551 individuals and adjusted for major confounding factors), with an average follow-up of 13 years, reported a 11% reduction in risk of stroke in those consuming three to five servings of fruits and vegetables per day compared to less than three servings, and a reduction in risk of 26% in those consuming more than five servings (see Figure 1.1) (He et al. 2006). The authors
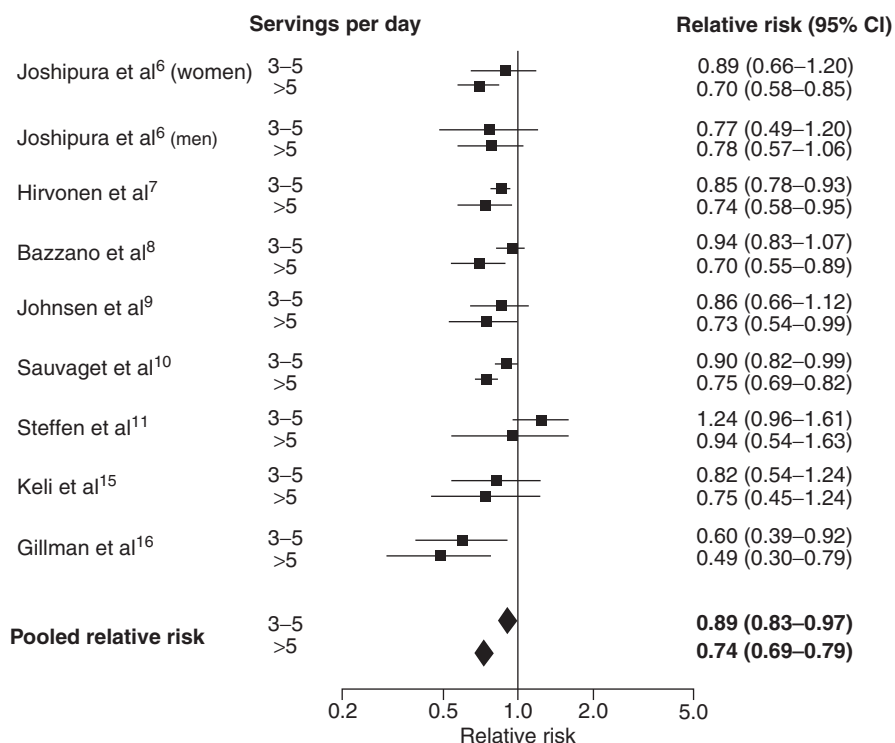
	Servings per day		Relative risk (95% CI)

	Servings per day	Relative risk (95% CI)
Joshipura et al[6] (women)	3–5	0.89 (0.66–1.20)
	>5	0.70 (0.58–0.85)
Joshipura et al[6] (men)	3–5	0.77 (0.49–1.20)
	>5	0.78 (0.57–1.06)
Hirvonen et al[7]	3–5	0.85 (0.78–0.93)
	>5	0.74 (0.58–0.95)
Bazzano et al[8]	3–5	0.94 (0.83–1.07)
	>5	0.70 (0.55–0.89)
Johnsen et al[9]	3–5	0.86 (0.66–1.12)
	>5	0.73 (0.54–0.99)
Sauvaget et al[10]	3–5	0.90 (0.82–0.99)
	>5	0.75 (0.69–0.82)
Steffen et al[11]	3–5	1.24 (0.96–1.61)
	>5	0.94 (0.54–1.63)
Keli et al[15]	3–5	0.82 (0.54–1.24)
	>5	0.75 (0.45–1.24)
Gillman et al[16]	3–5	0.60 (0.39–0.92)
	>5	0.49 (0.30–0.79)
Pooled relative risk	3–5	**0.89 (0.83–0.97)**
	>5	**0.74 (0.69–0.79)**

Relative risk scale: 0.2   0.5   1.0   2.0   5.0
Relative risk

Figure 1.1   Risk of stroke for 3–5 and 5+ servings of fruit and vegetables per day compared with less than 3 servings. Size of the squares is proportional to weight of the studies in the meta-analysis. Source: He *et al.* 2006.

speculate that the mechanism of effect may concern potassium, or possibly folate or dietary fibre, all of which are present in these foods.

A meta-analysis of 13 independent cohorts, followed prospectively, found that both fruits and vegetables had a significant protective effect on CHD risk and that increased consumption of fruits and vegetables from less than three to more than five servings a day was associated with a 17% reduction in CHD risk (He et al. 2007).

A number of studies have compared vegetarians with non-vegetarians. Key et al. (1996) studied a cohort of health-conscious men and women, 43% of whom said they were vegetarian. They found that daily consumption of fresh fruit was associated with significantly lower deaths from ischaemic heart disease after adjustment for smoking (rate ratio 0.76), deaths from cerebrovascular disease (rate ratio 0.68) and with significantly lower all-cause mortality (rate ratio 0.79). In a subsequent study, Key et al. (1998) conducted a pooled analysis of data from five major cohort studies in the USA, UK and Germany. Vegetarians (defined as not eating any fish or meat) had a 24% lower mortality rate from ischaemic heart disease than non-vegetarians (Key et al. 1998). This reduction in risk was greatest for the younger age groups; for example, the rate ratio for premature death from ischaemic heart disease (under the age of 65 years) was 0.55 and for those aged 65–79 it was 0.69 (Key et al. 1998). Although plant foods may contribute to this effect, the habits of vegetarians

tend to differ in a number of ways from the general population, for example they are typically more health conscious, less likely to smoke and more likely to be physically active.

Two of the most important risk factors for CVD are raised serum cholesterol and hypertension. Many experimental studies have explored the effects of changing diet on these two risk factors, although there are relatively fewer trials that have assessed the effects of changing food patterns. The most widely quoted study that has changed dietary patterns is the DASH trial (Appel et al. 1997). This study showed that a diet rich in fruits and vegetables, low in fat and incorporating low-fat dairy products, without changes in salt or weight loss, could lower blood pressure. Reducing salt had an additional benefit (Sacks et al. 2001). Other trials have broadly supported the results from DASH showing that moving dietary patterns towards a more plant-based food intake is associated with lower blood pressure.

Fruit and vegetable consumption has also been associated inversely with low-density lipoprotein (LDL)-cholesterol concentrations in men and women, for example in cross-sectional studies (Djousse et al. 2004). Subjects in the highest fruit and vegetable groups had LDL concentrations that were 6–7% lower than those in the lowest groups, an effect that the authors suggest may be attributable to dietary fibre (propionic acid derived from fermentation of fibre in the large bowel has been shown to reduce blood cholesterol). For a review on fibre and health, see Lunn and Buttriss (2007). However results of other studies have been inconsistent. For example, a similar response (a 7.3% reduction) was seen in the Indian Diet Heart Study, a 12-week intervention study (Singh et al. 1992), whilst no significant effect was reported in the 8-week DASH trial (Obarzanek et al. 2001).

Much less work has focused on bioactive substances in plants but a trial by Hodgson et al. (1999) showed that giving isoflavones (found in soya beans for example) did not reduce blood pressure compared with the response to a placebo, highlighting a need for caution in extrapolating from the effects of foods to specific compounds and vice versa.

The Lyon Diet Heart Study (de Lorgeril et al. 1999) showed that various modifications to a 'Mediterranean'-type diet, in patients who survived a first myocardial infarction, led to a statistically significant reduction in the occurrence of subsequent cardiac death and non-fatal myocardial infarction over a 4-year period. The dietary changes included fruit and vegetable intakes and the type of fat consumed. The percentage energy from fat in the diet of the control group was 33.6% compared with 30.4% in the experimental group; these fat intakes are well below current UK levels. No details on the exact dietary differences or the increase in plant-based food intake were given, but the authors noted that there seemed to be good compliance with dietary advice over the 4 years of follow-up.

Pulses and nuts

There have been relatively few studies that have looked specifically at the effects of pulses and nuts and risk of CHD and stroke. Participants in the National Health and Nutrition Examination Survey (NHANES) epidemiological follow-up study who ate more legumes (including dry beans, as well as peanuts and peanut butter) had a lower risk of CHD and CVD (Bazzano et al. 2001). No association was found between legume consumption and stroke in the two Boston cohort studies (Joshipura et al. 1999). Using a series of meta-analyses of prospective cohort studies, Hu (2003) compared the relative effects of fruit and vegetables, nuts and wholegrains on cardiovascular risk.

Table 1.5 Impact of wholegrain consumption on cardiovascular disease risk

Risk Factor or end point	Study and no. of subjects	Outcome	Reference
Death rates from CVD	Iowa Women's Health Study (baseline data from 1984, follow-up to 1995) 34 333 women	HR of all CVD across quintiles of whole-grain intake was 0.82 (95% CI 0.66. 1.01; $P = 0.02$) HR for deaths from CHD across quintiles of whole-grain intake was 0.82 (95% CI 0.63, 1.06; $P = 0.03$) HR for deaths from stroke and other CVD were not significantly different across quintiles of whole-grain intake.	Jacobs et al. (1999)
Incidence and deaths from IHD	California Seventh-day Adventists (baseline data from 1976, 6-year follow-up) 13 857 men, 20 341 women	RR of fatal IHD was lower (0.89; $P<0.005$) and non-fatal IHD was lower (0.56; $P<0.01$) in those who preferred wholegrain bread compared with those who preferred white bread	Fraser (1999)
Incidence and deaths from CHD	Nurses' Health study (baseline data from 1984, average 10-year follow-up) 75 521 women	RR for cases of CHD across quintiles of whole-grain intake was 0.47 (95% CI 0.27, 0.79; $P = 0.006$) for never smokers, and was 0.79 (95% CI 0.62, 1.01 $P = 0.07$) for the full cohort	Liu et al. (2000b)
Incidence of Ischaemic stroke	Nurses' Health study (baseline data from 1984, average 12-year follow-up) 75 521 women	RR of incident IHD across quintiles of whole-grain intake was 0.69 (95% CI 0.50, 0.98; $P = 0.03$)	
Death rates from CHD and CVD	Bread eaters in Norwegian County Study (data from 1977 to 1994) 16 933 men, 16 915 women	HR of death from CHD across quintiles of wholegrain bread consumption was 0.75 (95% CI 0.65, 0.88, $P = 0.006$) HR of CVD across quintiles of wholegrain bread consumption was 0.77 (95% CI 0.60 0.98 $P = 0.016$)	Jacobs et al. (2001)
Incidence of coronary artery and ischaemic stroke	Atherosclerosis Risk in Communities cohort (baseline data in 1987–9, 11-year follow-up) 11 940 subjects	HR of incident coronary artery disease across quintiles of whole-grain intake was 0.72 (95% CI 0.53, 0.97; $P = 0.05$) HR of incident ischaemic stroke across quintiles of whole-grain intake was 0.75 (95% CI 0.46, 1.22; $P = 0.15$)	Steffen et al. (2003)
Non-Fatal myocardial infarction and fatal CHD	Health Professionals Follow-up study (data from 1986 to 2000) 42 850 men	HR of CHD between highest and lowest quintile of whole-grain intake was 0.82 (95% CI 0.70, 0.96; $P = 0.01$)	Jensen et al. (2004)

Source: Seal (2006).

Legumes, including soya and its products, have been associated in clinical studies with decreased serum cholesterol. Anderson et al. (1995) reported that their meta-analysis of 38 studies, which provided an average of 47 g/day of soya protein, showed an average reduction in total and LDL cholesterol of 0.6 and 0.56 mmol/L, respectively. It should be noted that despite a wide range of soya protein intakes (17–124 g/day) in these studies, no dose–response effect was evident. Also, only seven of the studies used intakes of soya protein of 25 g or less. Achievement of an intake of 25 g within the context of the UK diet would require replacement of dietary items at each meal with soya-derived foods, e.g. soya drink or tofu (BNF 2002).

A review of five large cohort studies (the Adventist Health Study, the Iowa Women's Health Study, the Nurses' Health Study, the Cholesterol and Recurrent Events (CARE) Study and the Physicians' Health Study) showed that eating nuts more than once a week was associated with a decreased risk of CHD in both men and women (RRs varied from 0.45 to 0.75) (Kris-Etherton et al. 2001). They also reviewed 11 clinical trials of the effects of diets containing nuts on lipid and lipoprotein endpoints: they concluded that it was not possible to attribute the lipid-lowering effect to nuts alone because of the complex nature of most of the dietary interventions. Four clinical trials compared the lipid lowering effects of diets with or without nuts, and suggested that the diets with nuts had a greater effect. As well as being low in saturates, nuts contain fibre, various micronutrients and other bioactive substances such as phytosterols, recognised for their lipid lowering properties (see later). There has been particular interest in almonds (Berryman et al. 2011) and also walnuts (EFSA 2011a). Potential mechanisms, including a vasodilatory effect via the arginine-nitric oxide pathway have been summarised (Hu 2003; Berryman et al. 2011).

Cereals

Cereal grains and their products are an important part of most diets around the world (Truswell 2002). Several prospective cohort studies have specifically explored the association between wholegrain cereals and risk of CVD (Pietinen et al. 1996; Jacobs et al. 1999; Liu et al. 1999; Steffen et al. 2003; Jensen et al. 2004) and these studies have been reviewed (Seal 2006; see Table 1.5). The consensus from these studies is that people who eat a healthy diet, of which wholegrain cereals form a part, have a lower risk of CVD and that the effect is independent of an effect of dietary fibre (see Seal 2006; Seal et al. 2006). In another meta-analysis of seven studies, a pooled average of 2.5 servings per day versus 0.2 servings per day was associated with a 21% lower risk of CVD events. Nevertheless, the exact mechanism remains unclear and analysis is complicated because wholegrain consumption is often a marker of a healthy diet in other respects (Mellen et al. 2008).

To date there have been few large intervention studies to support the epidemiological findings. The Wholeheart Study, a 16-week intervention in 100 subjects, found no effect on LDL cholesterol of enhanced wholegrain consumption (3×20 g servings per day or 3 rising to 6 servings per day compared to control), and no effect on blood pressure or other markers of CVD risk (Brownlee et al. 2010). In another (12-week) intervention that assessed the effects of three daily portions of wholegrain foods (provided as only wheat

or a mixture of wheat and oats) on cardiovascular risk factors in over 200 relatively high-risk subjects, systolic blood pressure and pulse pressure were significantly reduced by 6 and 3 mmHg respectively (Tighe et al. 2010). Other CVD markers were largely unchanged. The reduction in systolic blood pressure was judged to be sufficient to reduce the incidence of coronary artery disease and stroke by ≥15% and 25%, respectively.

Recently, evidence from meta-analysis has emerged that consumption of wholegrains may be associated with weight control and reduced obesity, especially central adiposity (Harland and Garton 2008).

In contrast to the relatively small number of studies on wholegrains, there have been many studies, including large prospective cohort studies and smaller intervention studies, that have considered interactions between dietary fibre intake and risk of cardiovascular disease. Individuals consuming high-fibre diets (13–14.7 g/1000 kcal) have a substantially (15–59%) reduced their risk of developing coronary heart disease compared with those consuming the lowest amounts of fibre (3–6 g/1000 kcal). Several large-scale cohorts have estimated the effect on coronary heart disease risk of increasing fibre intake (see Lunn and Buttriss 2007 for a review). An increase in intake of 6 g/day of dietary fibre has been shown to be associated with a 33% reduction in risk of coronary heart disease in women and a 24% reduction in men (Khaw and Barrett-Connor 1987). A similar study reported a 19% decrease when fibre intake was increased by 10 g/d (Rimm et al. 1996). A pooled analysis of 10 prospective cohort studies reported a 14% decrease in the risk of CHD for each 10 g/day increase in dietary fibre intake (Pereira et al. 2004). Intervention trials have also demonstrated the effectiveness of dietary fibre in modifying blood lipid concentrations.

Some of the strongest associations have been in studies focusing on particular fibre components, e.g. oat bran or oatmeal. It has been estimated that consumption of at least 3 g/day of soluble fibre from oats lowers blood cholesterol levels by 0.13 mmol/L in people whose blood cholesterol levels were less than 5.9 mmol/L i.e. only moderately elevated. EFSA has published a positive opinion regarding the association between beta glucan consumption and maintenance of healthy cholesterol levels (EFSA 2011b). Similar cholesterol lowering effects have been reported when other viscous fibres – such as guar gums, pectin and psyllium – are fed (Brown et al. 1999b; Lunn and Buttriss 2007).

There is now emerging evidence that the type or source of dietary fibre is especially relevant in terms of CHD prevention. A review by Flight and Clifton (2006) has demonstrated the importance of cereal grains in reducing CHD risk and a recent analysis (He et al. 2010) reported an association between the bran component of wholegrain foods and reduced CVD specific mortality (and all cause mortality) in women with type 2 diabetes. Viscous, soluble fibres such as gums, psyllium and beta-glucan are believed to reduce cholesterol concentrations by altering cholesterol and bile acid absorption, and by effects on hepatic lipoprotein production and cholesterol synthesis. But when the whole grain is considered, mechanisms involving the other components of whole grains, e.g. magnesium, folate or vitamin E, cannot be discounted; indeed there may be a complex interplay between other components present in plant foods.

Cereal grains (and soya beans, flaxseed, fruits and vegetables) also contribute lignans, rye being a particularly rich source. These are converted to enterolactones by gut bacteria and have been suggested to have beneficial health effects (see Seal 2006).

Antioxidant nutrients

Dietary antioxidants have been the focus of much research interest with respect to CVD (Buttriss et al. 2002; Stanner et al. 2004; Bruckdorfer 2005).

Although there are some exceptions, cross-sectional studies comparing different populations within one country or between different countries have found that the incidence of CVD, particularly in Europe, is inversely associated with plasma levels of beta-carotene, vitamin E and, to a lesser extent, vitamin C (see Stanner et al. 2004). For example, plasma vitamin C concentration was inversely related to mortality from all causes and from CVD and ischaemic heart disease in men and women in the Norfolk cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC) (Khaw et al. 2001). Risk of death during the 4-year study period in the top vitamin C quintile was about half the risk in the lowest quintile, the association being continuous through the whole distribution of concentrations. A 20 μmol/L difference in vitamin C, approximately equivalent to a 50 g/day difference in fruit and vegetable intake, was associated with a 25% fall in the risk of all-cause mortality, which was independent of other risk factors. The authors concluded that a small increase in fruit and vegetables, amounting to an extra daily serving, has encouraging prospects in helping to prevent disease.

Some case-control studies have also reported similar relationships between cardiovascular risk and nutrient status. For example, subjects with CVD have been shown to have lower levels of plasma vitamin E and selenium than subjects without CVD (Beaglehole et al. 1990), and lower leucocyte concentrations of vitamin C have been reported in subjects with angiographic coronary artery disease compared with controls (Riemersma et al. 1990). However, case-control studies cannot exclude the possibility of changes in nutritional status as a consequence of the disease. A more convincing source of evidence is prospective studies in which nutrient status is measured years before the onset of the disease. Several large studies of this type have considered the relationship between dietary antioxidant nutrients or vitamin supplements and the incidence of CVD. They have generally identified a trend towards decreasing risk of CVD incidence or mortality with higher dietary intake of vitamin E, beta-carotene and vitamin C, and with higher plasma levels of these vitamins, each of which is largely derived from plant foods (see Stanner et al. 2004 for a review). It is of note that the studies that investigated dietary supply of vitamins were generally more convincing than those that investigated the impact of supplements.

In their review of relative risks for CHD, Tavani and La Vecchia (1999) found that whilst case-control studies and six cohort studies suggested inverse associations between beta-carotene and relative risk of CHD, four more recent cohort studies showed no association. Four randomised controlled trials of beta-carotene supplementation were found to give relative risks close to unity for the association. The authors concluded that the apparent benefit in observational studies may be linked to consumption of foods rich in beta-carotene rather than beta-carotene itself (Tavani and La Vecchia, 1999).

In their meta-analysis of cohort studies, in which a 15% reduction in risk of ischaemic heart disease between the top and bottom deciles of fruit and vegetable consumption was estimated, Law and Morris (1998) concluded that intakes of beta-carotene or vitamin E are unlikely to be important but that the combined effect of potassium, folate and possibly fibre in fruit and vegetables could account for the difference in risk.

The findings of prospective studies investigating the link between low selenium intake/status and heart disease have been more mixed, and an association has only been found in countries where selenium status has been low until recently, such as Finland (Salonen et al. 1982; BNF 2001).

Although not perfect, intervention trials are usually considered to be a superior type of study design because this approach is able to measure causal relationships between diet and a health outcome. A number of large studies have been conducted and some of the most positive evidence comes from the Cambridge Heart Antioxidant Study (CHAOS), which showed that vitamin E treatment significantly reduced the rate of non-fatal heart attacks although it had relatively little effect on CVD deaths (Stephens et al. 1996). Other smaller trials have also demonstrated the benefit of antioxidant supplementation in groups of high risk patients but the majority of primary and secondary prevention trials have failed to detect any benefit of supplementation with vitamin E or other dietary antioxidants (see Stanner et al. 2004). Examples include the Heart Protection Study of a cocktail of vitamins in 20 000 UK adults with CHD (Heart Protection Study Collaborative Group 2002), the HOPE trial of almost 10 000 subjects aged 55 years and over that showed no effect of dietary supplementation on the risk of stroke (Health Outcomes Prevention Evaluation (HOPE) Study Investigators 2000) and the Alpha Tocopherol Beta Carotene Prevention Study (ATBC), in which supplemental beta-carotene actually increased the incidence of cerebral haemorrhage in a high risk group (Leppala et al. 2000) and led to an increase in fatal heart attacks (see Stanner et al. 2004).

In summary, systematic reviews and meta-analyses of trials (e.g. Marchioli et al. 1999; Asplund 2002; Morris and Carson 2003; Vivekananthan et al. 2003) have concluded that despite evidence from observational studies suggesting an association between occurrence of CVD and low intakes or plasma levels of antioxidant nutrients, supplementation with single antioxidants or cocktails has not been found to be of benefit in either primary or secondary prevention trials. So, despite considerable effort in the antioxidant nutrients field, it remains unclear as to which components of fruits and vegetables are responsible for their apparent protective effect in CVD risk reduction.

Other bioactive substances

This failure to demonstrate an effect for antioxidant nutrients in CVD risk reduction has led researchers to look at other plant components with antioxidant properties, such as flavonoids, in the search for a protective mechanism in CVD. But, to date, the findings have not been particularly consistent and the stronger findings have often been associated with case-control studies, which are generally regarded to be less convincing than prospective studies. However, more progress has been made in other fields, such as cognitive function, as described later.

A number of studies have investigated associations between flavonoids and CHD. An ecological study of middle-aged men from 16 different cohorts showed an inverse association between flavonoid intake and coronary mortality (Hertog et al. 1995). Also, in some, but not all, prospective studies, a diet rich in the flavonoids (found mainly in apples, onions, tea and wine) has been associated with a reduced risk of subsequent heart disease (Hollman and Katan 1999). The Iowa postmenopausal women's study reported flavonoid

intake to be associated with a decreased risk of death from CHD after adjustment for age and energy intake. Of the foods contributing to flavonoid intake, only broccoli was strongly associated with a decreased risk (Yochum et al. 1999); there was no association between flavonoid intake and stroke. In a review of prospective epidemiological studies, Hollman and Katan (1999) found that intake of flavonols and flavones was inversely associated with subsequent CHD in most but not all studies.

The findings of subsequent studies have continued to be inconsistent. A meta-analysis of seven prospective cohort studies (including 105 000 people aged 30–84 years), designed to overcome the fact that many studies have been small, suggested a 20% reduction of risk of CHD deaths when the top and bottom tertiles of intake were compared (RR 0.80, 95% CI 0.69–0.93) (Huxley and Neil 2003). Mean duration of follow-up of subjects was 6–26 years. In four of the seven studies, intake was assessed at baseline using a food frequency questionnaire validated against 7-day weighed intakes and in the remaining studies the information was obtained from an interview with a trained dietitian. A cross-sectional analysis with the SU.VI.MAX cohort in France suggested, perhaps confusingly, that women with a high intake of flavonoids were at lower risk and men at higher risk of CVD (Mennen et al. 2004).

Other studies have focused on flavonoid-rich foods or on specific classes of flavonoids. Sesso et al. (2003) reported non-significant inverse associations for CVD risk and tea consumption (four or more cups per day), broccoli and apples, although their interpretation has been criticised (Donovan 2004). Conversely, others have reported a stronger association (Arts et al. 2001a).

There has also been interest in flavonols present in cocoa, red wine and tea in the context of a possible beneficial effect on endothelial function and hence cardiovascular health. To date there have been some clinical trials (in healthy volunteers and in subjects with cardiovascular risk markers) that have been suggestive of a beneficial effect on endothelial function but they have typically been short term (see Kay et al. 2006; Heiss et al. 2006, Hodgson 2006 for reviews). Whilst these findings are promising, longer term studies and mechanistic investigations are needed to establish whether these short-term effects on endothelial function translate into long-term cardiovascular health benefits.

As reported earlier, case-control studies frequently provide more optimistic findings than studies with more robust designs such as prospective cohort studies, although these too can be sources of measurement error. A case control study in Italy looked at the impact of intake of specific flavonoids on risk of myocardial infarction and reported a reduced risk with high intakes of anthocyanins, which are abundant in berries (Tavani et al. 2006) and another in Greece reported an inverse association between CHD risk and flavan-3-ols, which are largely found in tea and wine; they reported that an increase in intake of about 24 mg/day corresponded to a 24% reduction in risk (Lagiou et al. 2004).

A major difficulty with such studies is delivering an accurate assessment of flavonoid intakes given the limitations of current food composition databases in this respect, the diversity of flavonoid compounds and the general problems associated with assessing dietary intakes. Accessibility to high quality data on plant bioactives is being addressed by the EU-funded project *EuroFIR* (www.eurofir.eu).

Antioxidant hypothesis

In conclusion, the results of the various trials concerning the link between antioxidants and CVD are generally not supportive of the oxidation hypothesis. Bruckdorfer (2005) has suggested various possible explanations of this:

- The habitual diets of many of the subjects studied are unlikely to have been low in the antioxidant vitamins studied, and supplementation may saturate body tissues. For example, intakes as low as 100 mg/day will saturate body tissues in most individuals.
- The limited range of antioxidants selected for the studies may not have been the most appropriate because antioxidants are not necessarily interchangeable in terms of their effect in quenching free radical reactions.
- The oxidation process is initiated at an early stage in the atherosclerosis process; supplementation later on in the process may not be able to reverse the process.
- Antioxidants may be unable to enter the necrotic core of unstable atherosclerotic plaques, which pose the highest risk for CVD, making late antioxidant therapy ineffective. Evidence that antioxidants do have beneficial effects on vasomotor tone suggests that the intimal regions may be more accessible.
- Under conditions where free transitional metal ions or delocalised iron-containing proteins are available, antioxidants can exert pro-oxidant properties and may promote further damage.
- The role of oxidation processes in the development of atherosclerosis may be a contributing one rather than a central one.

It is quite plausible that mechanisms other than those involving antioxidants potentially may be responsible for some of these observations, for example displacement or binding of potentially toxic compounds, enzyme inhibition or activation, selective interaction within cell signalling cascades or a direct effect on gene expression within tissues. There is ongoing work focusing on other potential mechanisms by which flavonoids might exert a beneficial effect on cardiovascular health, including platelet reactivity and increased fibrinolysis (Holt et al. 2006) and potentially anti-inflammatory effects (Selmi et al. 2006). In addition, non-antioxidant nutrients found in plants may be involved. For example, it is also now recognised that dietary folate/folic acid intake is inversely associated with blood levels of homocysteine, a recognised risk factor for CHD, but despite a number of large trials totalling about 14 000 participants, there is no clear evidence of the benefit of B vitamin supplementation on the risk of vascular disease (Clarke, 2009).

Phytosterols and –stanols

In contrast there is now a large body of evidence to support a link between consumption of plant stanols and plant sterols and cholesterol lowering (Caswell et al. 2008), and associated health claims have been approved (http://ec.europa.eu/food/food/labellingnutrition/claims/community_register/index_en.htm).

Conclusions for coronary heart disease and stroke

Plant-based diets are associated with a lower risk of CVD (e.g. CHD and stroke). Fruit and vegetable consumption is generally associated with other health-promoting activities, e.g. being physically active and not smoking, as well as a higher consumption of wholegrain cereals. Adjustment for such factors does not explain the association between high fruit and vegetable intake and lowered risk, although adjustment often attenuates the strength of the association. There is evidence of a dose–response relationship that is consistent with current recommendations to increase intakes of these foods. It is difficult to separate out the role of diet in general and of specific nutrients in particular, and so the causal mechanism(s) associated with this dietary pattern remain to be established. Most epidemiological research has focused on a number of individual antioxidants studied in relative isolation (see previous sections) and it is likely that at the very least there is a complex interaction between the many components found in plant foods, and the rest of the diet, that may have an integrated effect on CHD risk.

Cancer

The COMA Working Group on The Nutritional Aspects of Cancer (Department of Health, 1998) systematically reviewed the data on associating diet with various forms of cancer. This subject was also reviewed by the World Cancer Research Fund (WRCF) and the American Institute of Cancer Research (AICR) in 1997 and again in 2007 (WCRF 1997; WRCF and AIRC 2007).

Fruit and vegetables

These major reviews used different methodologies and the WCRF/AICR reviews looked at the available data from a global perspective. Although the conclusions of the UK report were more guarded, the two reports reached similar conclusions in the majority of cases, as shown in Table 1.6.

In summary, the UK COMA Working Group concluded that, overall, there is moderate evidence that higher vegetable consumption will reduce the risk of colorectal cancer, and that higher fruit and vegetable consumption will reduce the risk of gastric cancer. There is weak evidence, based on fewer data, that higher fruit and vegetable consumption will reduce the risk of breast cancer. These cancers combined represent about 18% of the cancer burden in men and about 39% of the cancer burden in women in the UK, so even a small reduction in relative risk can have important public health benefits in terms of the reduction in the absolute numbers of people affected. The data generally show a graded reduction in risk associated with higher fruit and vegetable consumption. The overall picture supported the hypothesis that the consumption of fruits and vegetables protects against the development of some cancers. On the basis of their conclusions, the COMA Working Group recommended that fruit and vegetable consumption in the UK should increase. They did not specify by how much, but said that any increase would be expected to carry benefits.

Table 1.6 Summary of the conclusions of the WCRF/AICR and COMA reports on the possible effect of fruit and vegetable consumption on decreasing cancer risk

Cancer site	Committee on Medical Aspects of Food and Nutrition Policy, UK, 1998	World Cancer Research Fund/American Institute of Cancer Research, 1997	World Cancer Research Fund/ American Institute of Cancer Research, 2007 (fruit)	World Cancer Research Fund/ American Institute of Cancer Research, 2007 (non-starchy vegetables)
Mouth and pharynx	Weakly consistent for fruit, inconsistent for vegetables	Convincing	Probable	Probable
Larynx	Moderately consistent, limited data	Probable	Probable	Probable
Oesophagus	Strongly consistent	Convincing	Probable	Probable
Lung	Moderately consistent for fruit, weakly consistent for vegetables	Convincing, particularly for green vegetables and carrots	Probable	Limited–suggestive
Stomach	Moderately consistent	Convincing, particularly for raw vegetables, allium vegetables and citrus fruit	Probable	Probable, limited–suggestive for pulses
Pancreas	Strongly consistent, limited data	Probable	Limited–suggestive, probable for foods containing folate	Probable for foods containing folate
Liver	Not included in the review	Possible for vegetables, not fruit	Limited–suggestive	–
Colorectum	Moderately consistent for vegetables, inconsistent and limited data for fruit	Convincing for vegetables, limited and inconsistent data for fruit	Limited–suggestive	Limited–suggestive

Breast	Moderately consistent for vegetables, weakly consistent for fruit	Probable	–	–
Ovary	Insufficient data	Possible	–	Limited–suggestive
Endometrium	Insufficient data	Possible	–	Limited–suggestive
Cervix	Strongly consistent, limited data	Possible	–	Limited–suggestive for carrots
Prostate	Moderately consistent, especially raw and salad type for vegetables	Possible for vegetables	Probable for foods containing lycopene and foods containing selenium	Probable for foods containing lycopene, foods containing selenium and for pulses
Kidney	Not included in the review	Possible for vegetables	–	–
Bladder	Moderately consistent, limited data	Probable	–	–

Note: According to WCRF's assessment process, judgements of 'convincing' (none found for these foods) and 'probable' usually generate public health goals and recommendations for individuals. Other categories such as 'limited–suggestive' (i.e. limited amounts of information that can only be regarded as suggestive of a causative relationship) are not considered sufficient.

Sources: DH (1998); WCRF (1997, 2007).

Table 1.7 Summary analysis of the meta-analyses on fruit and vegetables and the risk of some cancers in case control and cohort studies

	Vegetables		Fruits	
	Case control	**Cohort**	**Case control**	**Cohort**
Mouth and pharynx	NS	?	↓	?
Larynx	NS	?	↓	?
Oesophagus	↓	?	↓	?
Breast	↓	NS	NS	NS
Lung	↓	NS	↓	↓
Bladder	NS	NS	↓	↓
Stomach	↓	NS	↓	NS
Colorectum	↓	NS	↓	NS

↓ Significant protective effect; NS, non-significant protective effect; ? inconclusive.
Source: Riboli and Norat (2003).

One of the weaknesses of the evidence base at the time the COMA and the first WCRF reviews were conducted and published was the relative reliance on case-control data and the relative lack of cohort studies for some cancer sites, the latter being viewed as a more robust study design, although it is still subject to measurement errors. Where cohort data did exist, they typically seemed to be weaker than those derived from the case-control studies (Table 1.7). Over the intervening years, more cohort studies have been completed and perhaps as a result the evidence base supporting a role for fruit and vegetables in cancer prevention has been somewhat weakened in some cases, as summarised in Table 1.6 (the column referring to the more recent WCRF review; i.e. a reduction for some cancer sites from convincing to probable).

A meta-analysis by Riboli and Norat (2003) discusses the relatively limited supportive evidence from cohort compared to case-control studies and they report that cohort studies do not support the hypothesis of a protective effect of fruit and vegetable consumption on colorectal cancer risk and suggest that the most promising way of reducing risk is to increase physical activity levels and avoid overweight. Indeed, the recent update from WCRF on colon cancer has provided support for this approach (WCRF and AICR 2010). However, Riboli and Norat (2003) do not discard the possibility that the lack of significance could be indicative of a lack of statistical power of the published cohort studies because of random error in the measurement of diet rather than because of the lack of a biological association.

Furthermore, over recent years, data has become available from the unique European Prospective Investigation into Cancer and Nutrition (EPIC), which has investigated dietary and other determinants of cancer and other diseases in nine European countries. The study began in 1992 and involves 406 303 subjects including two cohorts in the UK (Oxford and Norfolk). In the EPIC-Norfolk cohort of the study, additional data have been collected to enable assessment of determinants of chronic disease. Data from the study suggest that plasma ascorbic acid is inversely related to cancer mortality in men but not women (Khaw et al. 2001). Findings for fruits and vegetables are shown in Table 1.8.

Table 1.8 Findings from EPIC for plant foods and cancer, by main cancer site

Cancer site	Publications	Main results
Prostate	Key et al. (2004)	No association of fruits and vegetables with prostate cancer risk.
Lung	Miller et al. (2004)	Inverse association with fruit intake. No association with vegetables.
Colon and rectum	Bingham et al. (2003) Bingham et al. (2005) Jenab et al. (2004)	Inverse relation of dietary fibre with colorectal cancer incidence with the greatest protective effect in the left colon, and least in the rectum. No individual food source of fibre is significantly more protective than others. Confirmation of the above after adjustment for folate and longer follow up. Inverse association with nuts and seeds in women, but not men.
Breast	van Gils et al. (2005) Grace et al. (2004) Keinan-Boker et al. (2004)	No statistically significant decreased risks for fruits and vegetables. One study found positive association with isoflavones in EPIC-Norfolk cohort. But no association was found with these phytoestrogens in the EPIC-Utrecht cohort. Further analyses with pooled data are on-going.
Ovaries	Schulz et al. (2005)	No protective effect overall but some evidence of an effect of garlic/onions.

The recent update from WCRF on colon cancer risk concurred with the 2007 WCRF report that the evidence that fruits and non-starchy vegetables protect against colorectal cancer risk is limited (WCRF 2010).

Some pooling analyses have also been indicative of a weakening of the evidence base regarding the impact of fruits and vegetables on cancer risk. A pooled analysis of cohort studies suggests there is no significant association between breast cancer risk and fruit and vegetable consumption (totals and subcategories) (Smith-Warner et al. 2003), a finding that is supported by data from EPIC (van Gils et al. 2005). A similar study of 12 cohort studies found no significant association between fruit and vegetable intake and ovarian cancer (Koushik et al. 2006).

Inverse associations between fruit and vegetable consumption and lung cancer have been consistently reported. A recent analysis pooling eight prospective cohort studies indicates that the modest reduction on cancer risk that remains once smoking is taken into account is largely attributable to fruit, not vegetables (Smith-Warner et al. 2003). EPIC has also demonstrated a significant inverse association between fruit consumption and lung cancer (the hazard ratio for the highest consumption quintile relative to the lowest being 0.60). Again there was no association with total vegetable intake or consumption of vegetable subtypes (Miller et al. 2004). The primary focus remains the reduction of tobacco use.

Legumes and nuts

Very few studies have specifically investigated the relationship between the consumption of legumes or nuts and the risk of cancers, and the evidence is often difficult to interpret. The WCRF Report (WCRF, 1997) identified 58 epidemiological studies that reported results for pulses and cancer risk, either for specific pulses or pulses in general. There was no clear picture: 50% reported a reduced risk of cancer, 38% reported an increased risk and 12% reported no association. The 2007 report concluded that the evidence for pulses (in relation to stomach and prostate cancer specifically) is no more than limited-suggestive (WCRF 2007). Very few studies have looked specifically at the association between nut consumption and cancer risk and WCRF concluded that there was no evidence to suggest that nuts might protect against some cancers (WCRF 1997).

Foods containing fibre

The evidence for a role of dietary fibre in cancer protection has strengthened in recent years. The 2007 WCRF Panel concluded that such foods probably reduce the risk of colon cancer, and for oesophageal cancer the evidence was considered limited-suggestive. Recently, an update by WCRF of colon cancer risk, taking into account recently published studies, has concluded that the evidence for a protective effect from foods containing dietary fibre is now convincing (WRCF and AICR 2010). A meta-analysis revealed a 10% decrease in colorectal cancer for each 10 g of fibre consumed (12% for men and 8% for women). Intakes in Britain are currently 14.9 g/day in men and 12.8 g/day in women (Department of Health, 2011) and so fall short of the 18 g/day recommendation. A statistically significant 10% decrease in colorectal cancer risk with cereal fibre intake was found in meta-analysis. The reduction in risk with other sources of fibre was in the same direction but did not achieve statistical significance. For wholegrains, there was a 21% decreased risk per three servings a day for colorectal cancer and 16% decreased risk for colon cancer (WCRF and AICR 2010). Fibre exerts various effects in the gastrointestinal tract (such as increasing transit time and providing substrates for short chain fatty acid production via fermentation) but the specific mechanism of effect in cancer protection is still not understood. Fibre intake is also strongly correlated with folate intake but the WCRF update found that adjustment for folate did not typically affect the risk reduction attributed to fibre.

Vitamins

Case-control and prospective studies have consistently shown an inverse association between intake of carotenoids and risk of lung and stomach cancer (Department of Health 1998). Some prospective nested case-control studies have also shown an inverse association between plasma level and risk of lung cancer, with levels in the range 0.34–0.53 μmol/L conferring the lowest risk (National Academy of Sciences 2000). However, this association was no longer significant after adjusting for beta-cryptoxanthin. A recent pooling project of seven studies of beta-carotene and lung cancer failed to reveal a significant association (Mannisto et al. 2004). WCRF regards the evidence as probable for an

inverse association between carotenoids and cancers of the mouth, pharynx, larynx and lung; between beta-carotene specifically and oesophageal cancer; and between lycopene and prostate cancer (WRCF 2007).

Vitamin C intake from food alone has been shown to be associated inversely with lung cancer risk in a pooling project of eight studies (Cho et al. 2006) but there was no association with total vitamin C intake. Most observational studies have also reported an inverse association between vitamin C status and cancer risk, particularly for the non-hormone-dependent cancers, and two large studies (NHANES II and EPIC) have found an inverse association between plasma vitamin C and cancer risk in men but not in women (Loria et al. 2000; Khaw et al. 2001). WCRF reported a probable inverse association between vitamin C intake and risk of oesophageal cancer (WRCF 2007).

The findings of intervention trials, which have the potential to identify causative relationships, have been summarised by Stanner et al. (2004). Beta-carotene supplements seem to offer no protection against cancer and may actually increase risk among smokers. There is no published evidence from randomised controlled trials of a role for high-dose vitamin C in cancer prevention, perhaps because dietary supply has been adequate in the subjects studied. There is also little evidence for a beneficial effect of vitamin E supplementation. However, there is some evidence to suggest that an adequate supply of selenium is important for cancer prevention, based on an association between increased risk of cancer at several sites in subjects with low baseline plasma selenium status in a selenium supplementation trial. WCRF reported a limited-suggestive inverse association between vitamin E and risk of oesophageal and prostate cancers and between selenium intake and risk of stomach and colorectal cancers. The inverse association between selenium and prostate cancer was considered probable (WRCF 2007).

COMA (Department of Health 1998) and authorities in the USA (see Krinsky and Johnson 2005) recommended the avoidance of beta-carotene supplements as a means of protecting against cancer and the need to exercise caution in the use of high doses of purified supplements of other micronutrients as they cannot be assumed to be without risk.

Since publication of the COMA report, several studies have been published showing inverse associations between cancer risk and higher folate consumption (Kim 2006), for example in relation to colon (Giovannucci et al. 1998) and breast cancers (Sellers et al. 2001). A significantly lower risk of colorectal cancer was reported in the highest versus lowest category of food folate intake in a metanalysis of seven cohort studies, although the trend was non-significant for total folate (i.e. including folic acid supplements) (Sanjoaquin et al. 2005). Similar relationships also exist for folate status (although the results are not totally consistent) and reduced colorectal cancer risk, and data from intervention trials suggest that supplementation can improve surrogate endpoint markers for colorectal cancer (Kim 2006). Animal studies are also generally supportive but emphasise that the timing is critical and provision once cancer development is underway can promote the process (Kim 2006). These findings have been interpreted as suggestive of a dual modulatory role for folate. However, there is little evidence for other cancer sites, for example a pooling project on lung cancer found no association (Cho et al. 2006).

This subject has been reviewed recently by the UK's Scientific Advisory Committee (SACN 2006). SACN concluded that prospective studies suggest a trend towards a protective effect of folate intake on colon cancer risk, in particular, but noted that some studies did

not adjust for all likely confounding factors, such as fibre. The association was typically less strong for total folate intake (including folic acid from supplements). WRCF concluded that an inverse association between folate intake and pancreatic cancer was probable and was limited-suggestive between oesophageal and colorectal cancers (WRCF 2007).

Other plant-derived substances

Some of the more promising data comes from studies of glucosinolates. Alongside a variety of bioactive substances, these compounds are found in cruciferous (including brassica) vegetables such as sprouts, broccoli and cabbage. When these vegetables are chewed, crushed or sliced, isothiocynates and indoles are formed from the glucosinolates (they can also be formed less efficiently by the gut flora) and these have been shown in animal studies to inhibit chemically-induced colon cancer but recent prospective cohort studies have been inconsistent (see Lynn et al. 2006). Indeed, a series of seven cohort studies summarised by Lynn et al. revealed little evidence of a protective effect of cruciferous vegetable intake, although habitual intakes were low and measurement by a food frequency questionnaire may have led to poor assessments of intake. It has been suggested that there may be gene–nutrient interactions, and clinical studies have confirmed a possible effect in some subsets of the population, dependent on glutathione-S-transferase genotype (Seow et al. 2002). Possible mechanisms for the effects of cruciferous vegetables have been reviewed recently (Lynn et al. 2006) and include modulation of drug metabolising enzymes, induction of apoptosis (controlled cell death), cancer cell cycle arrest and anti-oxidant effects.

Several studies have investigated associations with flavonoids. There was no association found between the intake of five major flavonoids and mortality from total cancer, lung cancer, colorectal cancer or stomach cancer in an analysis of data from the Seven Countries Study after 25 years of follow-up (Hertog et al. 1995), or with mortality from cancer at all sites (Hertog et al. 1994) or epithelial cancer sites (Arts et al. 2001b) in the Zutphen Elderly Study. Sacks et al. (2006) concluded that the efficacy and safety of using isoflavones to prevent or treat cancer of the breast, endometrium or prostate is not established; evidence from clinical trials is meagre and cautionary with regard to possible adverse effects. Therefore, despite plausible mechanisms, there is little observational evidence for a beneficial effect of flavonoids against cancer. WCRF has reported a limited-suggestive inverse association between quercetin and lung cancer risk (WRCF 2007).

Conclusions for cancer

According to the comprehensive analysis by WCRF, the only convincing inverse association is between dietary fibre intake and reduced risk of colorectal cancer. This association has been strengthened in the light of recently published cohort studies (WRCF and AICR 2010). In addition there are a number of inverse associations between plant foods and cancer risk that are probable. Contrary to the view 10 years ago, the evidence linking fruit and non-starchy vegetables with cancer risk education has weakened and the relationship is now considered to be limited with regard to colorectal cancer, though probable for cancers of the upper gastrointestinal tract (fruit and vegetables) and lung (fruit).

As with CVD, in contrast to popular belief and despite considerable effort, it remains unclear whether antioxidants in fruits and vegetables are responsible for the apparent protective effect of these foods for some cancers. Not all work has focused on the direct antioxidant properties of components present in these foods and evidence is accumulating to support other potential mechanisms as discussed earlier in the context of CVD. It has been suggested that plant-derived substances may be able to protect against genomic damage resulting in aberrant gene expression, either by up-regulating repair of the damage or resulting in the removal of damaged cells via apoptosis (see Mathers 2006).

Type 2 diabetes

The US Health Professionals' Follow-up Study of 42 504 men has shown that a 'prudent' dietary pattern was associated with a marginally decreased risk of type 2 diabetes (van Dam et al. 2002). The prudent dietary pattern was characterised by high consumption of vegetables, legumes, fruit, wholegrains, fish and poultry. Another US cohort study found that low consumers of fruits and vegetables were more likely to develop diabetes (Ford and Mokdad, 2001).

A recent meta-analysis of six cohort studies revealed a 14% reduction in risk of type 2 diabetes in association with a greater intake of green leafy vegetables (Carter et al. 2010). Similar associations were found in the US Nurses' Health Study for leafy green vegetables and also fruit (Bazzano et al. 2008).

Results from the 10-year follow-up of US Nurses showed that women who were in the top fifth for wholegrain cereal intake had a 38% lower risk of developing diabetes than women in the lowest fifth for intake; the effects were not explained by dietary fibre intake or intake of magnesium or vitamin E (Liu et al. 2000b). Also, in the Health Professionals' Follow-up Study cohort, the relative risk of type 2 diabetes was 0.58 in the highest compared to the lowest quintile of wholegrain intake (Fung et al. 2002). The association was reduced to 0.7 when adjustment was made for BMI, but remained highly significant. A similar protective effect was reported in Finland (Montonen et al. 2003).

It is well known that people with diabetes are vulnerable to oxidative stress. There have been a number of short-term clinical trials to assess whether isolated flavonoid compounds could influence lipoprotein vulnerability to oxidation. Results have been mixed, with some studies showing an effect (e.g. Lean et al. 1999) and others not (e.g. Blostein-Fujii et al. 1999). There have been many studies that have assessed the hypoglycaemic effect of compounds found in many different foods; the relevance of these studies to humans is not clear.

Age-related macular degeneration and cataract

Age-related macular degeneration (AMD) and cataracts are eye disorders that are increasingly common among older people (Fletcher 2009). Macular degeneration is the leading cause of irreversible blindness in people over the age of 65 years. The macula is the central part of the retina and in the early stages of the disease begins to accumulate lipid deposits known as drusen, ultimately resulting in atrophy associated with

distortion and finally loss of vision (especially in the central area of vision). Cataracts result from glycosidation of lens proteins, which leads to opacities forming within the lens. Although the aetiology of cataracts varies and they can develop at any stage of life, the vast majority develop in elderly individuals and so are sometimes referred to as senile cataracts.

The tissues of the lens and the retina are subject to oxidative stress throughout life as a result of the combined exposure to light and oxygen. It has been proposed that antioxidants may prevent cellular damage by reacting with free radicals produced during the process of light absorption (Christen et al. 1996). Indeed, laboratory and animal studies have demonstrated the important role of antioxidants in the lens and retina. Epidemiological studies have also suggested that dietary antioxidants (e.g. vitamins C and E, carotenoids and, more recently, lutein and zeaxanthein) may provide protection against cataracts and AMD (see Fletcher 2009). Although there is less consistency for individual antioxidants, the data from both animal and human studies suggest that vitamin C, carotenoids, lutein and zeaxanthein play a critical role.

This evidence supports general dietary recommendations concerning the importance of fruits and vegetables, especially citrus fruit and other rich sources of vitamin C, and vegetables rich in lutein and zeaxanthein, such as spinach, broccoli, kale, lettuce and red and orange peppers. For example, a 10-year study of almost 40 000 female subjects found a modest but significant reduction in cataract risk of 10–15% when the highest quintile of fruit and vegetable consumption was compared with the lowest (Christen et al. 2005). In contrast, evidence is lacking that the use of vitamin supplements is of proven benefit in the prevention of age-related eye disease (Fletcher, 2009).

In summary, the evidence is suggestive that increased fruit and vegetable intakes are associated with a lower risk of AMD and with cataracts in older people. It is not yet clear which components and which vegetables are protective; confounding cannot be ruled out in explaining some of the associations previously reported.

Age-related cognitive decline

A prospective cohort study of almost 4000 subjects over 65 years of age has suggested that high vegetable consumption, especially leafy green vegetables (median 2.8 servings per day), but not high fruit intake, was associated with a slower rate of cognitive decline (Morris et al. 2006). Similar results were observed in the Nurses' Health Study (Kang et al. 2005). An interesting finding was a significantly reduced risk of Alzheimer's disease associated with the consumption of fruit and vegetables juices, especially among ApoE4 carriers (Dai et al. 2006), a genotype reported to be potentially influential in several other studies (see Gillette-Guyonnet et al. 2007) in which higher intakes of fruits and vegetables (and fish) were associated retrospectively with reduced risk of cognitive decline or dementia. Nevertheless, several recent reviews have reported inconsistent associations or a lack of an association between various aspects of diet and cognitive decline (Nooyens et al. 2011, Plassman et al. 2010). This is likely to be due, at least in part, to study design to date and the need for prospective studies of adequate duration, appropriately rigorous collection of dietary data and RCTs that are appropriately focused.

Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is an all-inclusive and non-specific term that refers to a defined set of breathing-related symptoms, characterised by airflow obstruction. Asthma is defined as a chronic inflammatory airway disorder. The criteria used to define COPDs in general have not always been applied in the same way in all epidemiological studies, making interpretation of data more difficult.

Bearing definition problems in mind, there have been a number of reviews of the links between nutrition and COPDs (Schunemann et al. 2001; Romieu and Trenga 2001; Trenga et al. 2001; Denny et al. 2003). Schunemann et al. (2001) concluded that the largest body of literature exists for a protective effect of vitamin C and fresh fruit and vegetable intake. The review concluded that the evidence is insufficient to recommend the use of any supplements, but the data do support the recommendation to eat more fruits and vegetables. Denny et al. (2003) concluded that people who have a diet rich in fruit and vegetables have a lower risk of poor respiratory health and a recent study reported the benefit of a 'prudent diet' (high consumption of fruit, vegetables, fish and wholegrain cereals) with regard to COPD and impaired lung function, especially in male smokers (Shaheen et al. 2010).

An analysis from EPIC, using a nested case-control approach, has shown that symptomatic asthma is associated with a low dietary intake of fruit, vitamin C and manganese, and low plasma vitamin C levels in adults (Patel et al. 2006), replicating previous findings in other groups and suggesting that nutrition might be a modifiable risk factor for asthma, the prevalence of which has increased considerably in recent years.

A population-based case-control study in South London showed that, after adjusting for potential confounding factors, apple consumption was inversely associated with asthma (odds ratio 0.84, 95% CI 0.75–0.97) (Shaheen et al. 2001). The authors concluded that there is a need for a better understanding of how flavonoids or other constituents of apples might influence respiratory health. Shaheen et al. (2001) also found that a higher intake of selenium was inversely associated and the authors commented on the declining intake of selenium in the UK population, which they speculate may be expected to lead to an increased prevalence of asthma in the future.

Currently, it would be premature to attribute causality to any particular food or food constituent.

Osteoporosis and bone health

There is epidemiological data that suggests that a diet rich in plant foods is also beneficial to bone health (see Lanham-New and Loveridge 2007). Further support comes from the DASH trials (Lin et al. 2003), which are suggestive of conservation of calcium at least in part by a high potassium intake. A recent systematic review concerning fruit and vegetable intake and bone health in women aged 45 and over reported that any benefits remain unclear (Hamidi et al. 2011). The findings of studies investigating the ability of soya to slow postmenopausal bone loss are inconsistent (Sacks et al. 2006).

Plant foods and health: overall conclusions

Eating patterns characterised by an abundance of fruit, vegetables and other plant foods are associated with a moderately reduced risk of chronic disease (e.g. CVD – especially stroke – and cancer), and to a much lesser extent of other conditions such as age-related eye defects and possibly cognitive decline. Researchers from Harvard (Hung et al. 2004) suggested some years ago that the benefits of fruits and vegetables may have been over-stated, and this now seems to be the case, especially for cancer. Much of the supportive evidence derives from case-control studies, which are potentially affected by methodo-logical biases such as recall bias and selection bias. Selective reporting and publication may also have exacerbated the situation. Evidence from prospective cohort studies, regarded as more robust in design, has typically been less strong. However, these findings do not preclude the benefits of specific plant foods.

One possible explanation for the lack of association with cancer risk in some studies is that the category 'fruits and vegetables' is too broad to capture effects exerted by specific constituents found only in subclasses of fruits and/or vegetables. It is also important to recognise that the methods used in large-scale studies, such as food frequency question-naires, can be relatively ineffective in providing a precise measure of the intake of specific foods, and this can lead to an underestimation of the strength of associations.

The search for the active components in these foods has met with limited success. Research initially focused on the antioxidant vitamins C and E and beta-carotene, although a few studies have also looked at other carotenoids and some of the other plant bioactives (e.g. flavonoids, glucosinolates, phytosterols). In relation to plant bioactives, promising and generally consistent results have been reported for animal studies and for *in vitro* studies, but to date convincing evidence from human intervention and epidemio-logical studies is sparse, and this is reflected in the paucity of authorised health claims emerging from the health claims process in Europe.

Evidence is now accumulating that flavonoids might exert neuro-modulatory effects that are independent of classical antioxidant capacity through interaction with various protein kinase and lipid kinase signalling cascades, which regulate transcription factors and gene expression involved in both synaptic plasticity and cerebrovascular blood flow (Spencer, 2010a, b). Recent evidence demonstrates the reversal of age-related memory deficits following supplementation of animals with anthocyanin-rich blueberry extract (Andres-Lacueva et al. 2005). Such findings, though still preliminary, are of particular importance in the context of our ageing population.

As was mentioned at the start of the section 'A summary of the evidence linking plant food intake and health', the use of health claims on foods and beverages in Europe is now regulated. So far in 2011, claims about plant stanols and sterols and cholesterol lowering and about the effect of a tomato extract on platelet aggregation have been approved by the EC. In addition, claims on walnuts and endothelial function and on beta-glucan and main-tenance of healthy cholesterol levels have received positive opinions from EFSA. However, many other claims including those on dietary fibre, soy protein, nuts other than walnuts, and plant antioxidants have received negative opinions to date (see EFSA 2011c for more details).

Recommendations and current policy on plant food intake

Fruit and vegetables

The World Health Organisation (WHO) recommends a minimum intake of 400 g of fruits and vegetables per day (WHO 2002), and this recommendation has been adopted globally in the context of ensuring a healthier dietary pattern. A joint FAO/WHO workshop in 2004 in Japan concluded that there is strongly suggestive evidence that there is potential for increased consumption of fruits and vegetables to reduce the risk of CHD, stroke and type 2 diabetes, but further research is needed to evaluate the effects of specific fruits (WHO/FAO 2005). The evidence for a role for fruit and vegetable consumption in obesity prevention, weight management and cancer prevention is weaker and further research is needed to evaluate these associations. The workshop also concluded that messages about fruit and vegetables need to be integrated into food-based dietary guidelines, to be country specific and culturally relevant, and coordinated with other messages about healthy diets. Intervention strategies need to be multidisciplinary and coordinated, and should comprise a balance of components to stimulate growth in both supply and demand of fruits and vegetables. Evaluating such projects is essential in order to learn what works and what does not and to avoid wasting time and resources on inappropriate approaches.

There have been efforts in many countries around the world to increase fruit and vegetable intake, including many national campaigns. The first such scheme began in California in 1988 as an initiative of the US National Cancer Institute and the local health services, and preceded the WHO advice. It advised eating three to seven plant foods per day. This developed into the national US '5-a-day' scheme. The most recent advice in the USA focuses on the message to eat five to nine servings of fruits and vegetables each day and the most recent guidance, the 'My Plate' model (Figure 1.2a), shows separate categories for grains, protein, vegetables and fruits, with more emphasis placed on vegetables than fruit. There is also a UK equivalent (Figure 1.2b).

Table 1.9 lists the websites for schemes from other countries (some current, some historical). The Australian scheme, for example, specifies two servings of fruit as well as five servings of vegetables, whereas others provide a composite target figure.

Use of the UK '5 a day' logo and associated portion counter is governed by criteria that take account of portion size. Currently, the logo can only be used on fresh and frozen produce, dried fruits and pure juices, but criteria for composite foods are under development, which are expected to take into account fat, sugar and salt content. A key difference between these two schemes is that the US scheme includes potatoes whereas the UK one does not. The UK 5 A DAY scheme emphasises variety and embraces fresh, frozen, tinned and juiced fruits and vegetables, and pulses.

Most UK retailers have also developed their own logos to link with the campaign. In the UK, there is the Department of Health's '5 a day' campaign and the associated School Fruit and Vegetable Scheme, whereby in England children aged 4–6 years have been entitled to a piece of free fruit or vegetable at school each day. Related school fruit schemes have also operated in other parts of the UK. The scheme in England has now been evaluated (see www.5aday.nhs.uk). One of the findings was that over a quarter of children and their families ate more fruit at home after their school joined the scheme.
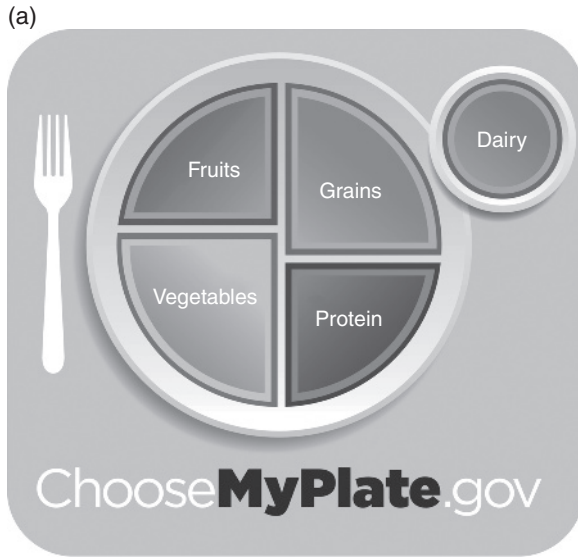
(a)

(b)
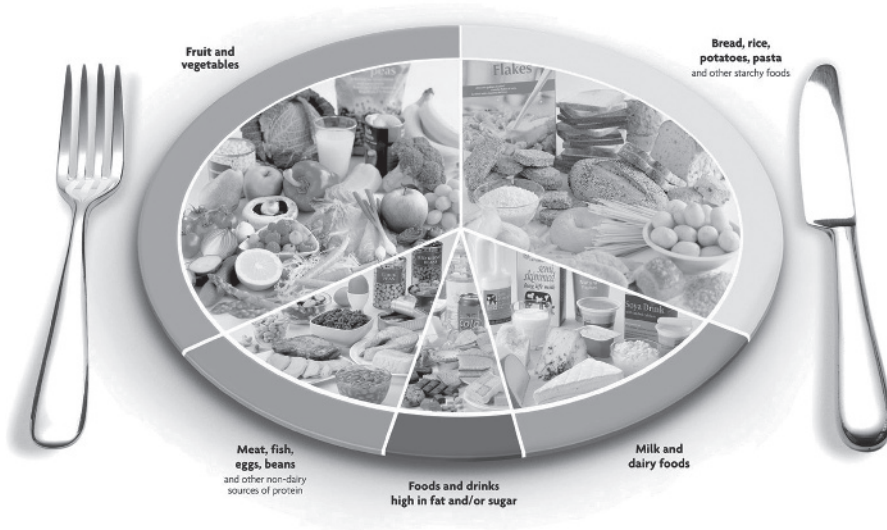
Figure 1.2 (a) US model (source: USDA 2011). (b) UK model (source: Department of Health in association with the Welsh Government, the Scottish Government and the Food Standards Agency in Northern Ireland).

Table 1.9   Worldwide schemes to increase fruit and vegetable consumption

Country	Website
UK	www.5aday.nhs.uk
Australia	www.gofor2and5.com.au
USA	www.5aday.org
USA	www.5aday.gov
New Zealand	www.5aday.co.nz
Canada	www.5to10aday.com
Germany	www.5amtag.de
Japan	www.5aday.net
France	www.10parjour.net/site/pages/home/index.php
Mexico	www.cincopordia.com.mx
Chile	http://www.5aldiachile.cl/
Argentina	http://www.5aldia.com.ar/esp_home/index.php
Spain	www.5aldia.org

Wholegrain foods

The growing body of evidence suggesting a beneficial effect of wholegrains on the risk of CVD, type 2 diabetes and some cancers (see Seal 2006) has been used in the US, in particular, to propose recommendations for daily wholegrain consumption, based on a definition from the American Association of Cereal Chemists (AACC 2005), that: wholegrains shall consist of the intact, ground, cracked or flaked caryopsis, whose principal anatomical components – the starchy endosperm, geum and bran – are present in the same relative proportions as they exist in the intact caryopsis. For composite foods, it has been suggested that the product should contain >51% wholegrain by weight (with reference to the amount typically consumed per day) in order for a wholegrain claim to be made. There has been far less interest in this type of approach at a policy level in the UK or indeed Europe.

Current consumption patterns

The National Food Survey (NFS) collected data on UK household food purchases/supplies every year from 1942 until 2000. It was initiated to monitor household food supplies during World War II and the early years of the survey (not featured in the table) reflect the constraints of rationing. For example, in 1942, total fruit was only 197 g/person/week but potatoes were 1877 g/person/week and bread 1718 g/person/week. Household supplies of bread and potato remained high for the following decade but have gradually declined subsequently. (http://www.defra.gov.uk/statistics/foodfarm/food/familyfood/nationalfood survey/). Trends between 1954 and 1999 are illustrated in Table 1.10.

Around 2000, there was a change in methodology for the survey (Speller, 2000; Burgon, 2007, 2009) and it is now known as the Family Food Survey. Data collected between 1975 and 2000 has been adjusted to enable trends over this period to be compared

Table 1.10 Trends in plant food consumption 1954–1999 (g/person/week)

	1954	1959	1964	1969	1974	1979	1984	1989	1994	1999
Total vegetables (all types, excluding potatoes, beans and pulses)	714	807	996	807	980	1004	980	1041	968	975
Total fruit (all types excluding juice)	575	832	686	848	633	664	628	692	712	766
Fruit juice	7	12	16	15	30	63	150	214	240	284
Pulses and beans	149	86	101	112	111	125	133	135	117	119
Nuts and nut products	12	10	11	7	7	11	12	13	16	13
Potatoes (fresh and frozen products)	1792	1561	1407.3	1457	1357	1311	1234	1151	997	872
Bread	1596	1341	1190	1070	946	891	866	833	758	717
Rice	24		15	14	16	20	28	30	37	68
Breakfast cereals	45	49	57	75	81	96	117	126	134	134
Pasta	–	–	–	–	–	–	–	–	–	79

Source: DEFRA (2000); MAFF (1955, 1960, 1965, 1970, 1975, 1980, 1985, 1990, 1995, 2000).

Table 1.11   Trends in intake between 1975 and 2009. Data for 1975 and 1990 are adjusted to reflect the methodology used since 2000

	1975	1990	2000	2006	2007	2008	2009
Total fruit and vegetables (excluding potatoes)	1868	2170	2336	2454	2421	2317	2246
Total fruit (excluding juice)	738	962	1189	1313	1281	1199	1143
Fresh fruit	511	624	765	855	855	790	762
Processed fruit and fruit products	228	338	424	458	426	409	381
Fruit juices (ml)	42	225	332	366	340	325	302
Total vegetables (excluding potatoes)	1131	1208	1147	1142	1140	1118	1103
Fresh green vegetables	341	287	246	221	224	203	201
Other fresh vegetables	405	475	506	566	566	557	552
Processed vegetables excluding potatoes	385	446	395	355	350	358	350
Fresh and processed potatoes	1378	1199	1002	810	781	776	761
Rice	17	32	69	87	94	90	92
Bread	1029	859	782	692	677	659	656
Breakfast cereals	82	121	135	135	130	130	133
Pasta	15	32	73	87	92	91	91

Source: DEFRA (2010, 2011).

with newer data (Table 1.11). Over this period, fruit and fruit juice purchases have risen considerably but peaked around 2006 and have been falling since then. Total vegetable purchases (excluding potatoes) have remained fairly constant but fresh have been replaced to some extent by processed vegetables. Purchases of fresh and processed potatoes have almost halved during this period from 1378 to 761 g/person/ week, and bread has continued to fall. There have been increases in purchases of pasta, rice and breakfast cereal since 1975, reflecting changes in meal patterns.

To some extent, the trends in bread and potatoes reflect the downward trend in total energy intake that has been a characteristic of dietary patterns, and will have affected dietary fibre intakes. Current intakes in the UK are14.9 g/day in men aged 19–64 years and 12.8 g/day in women (Department of Health, 2011).

Despite the recent interest in wholegrains and health, intake remains low. For example, low intakes exist in the USA where there has been specific advice to increase intake to three servings per day and the latest advice is to 'make at least half of your grains wholegrains' (USDA 2011).

Similarly, in the UK, Lang et al. (2003) reported that about one-third of adults failed to consume wholegrains on a daily basis and over 97% consumed less than three servings per day. In studies in the USA and UK, in which careful analysis was made of absolute wholegrain intake by young people, intake was only 7 g/day (Thane et al. 2005; Harnack et al. 2003). Bread and breakfast cereals were the main contributors.

Table 1.12   Achievement of the 5-a-day target

Average daily consumption of fruit and vegetables*	Age (years)					
	Boys	Men		Girls	Women	
	11–18	19–64	65+	11–18	19–64	65+
Mean portions per day	3.1	4.2	4.7	2.7	4.1	4.2
% achieving ≥ 5-a-day	13	32	39	7	29	35

*Excludes potatoes and potato products. All fruit juice limited to 150 g/day; baked beans and other pulses consumption limited to 80 g/day; tomato puree multiplied by 5; dried fruit multiplied by 3. Children under 11 years have not been included as the 80 portion is only appropriate for older children and adults.
Source: Department of Health (2011).

Whereas the Family Food Survey provides information on household purchases, the UK's National Diet and Nutrition Survey (NDNS) provides information about the intakes of individuals rather than estimated consumption at the household level. The most recent survey, which combines years one and two of the new rolling survey, provides for the first time the contribution of fruits and vegetables from composite dishes, as a result of a project to disaggregate composite dishes in the NDNS database. Using this approach, vegetable intakes (excluding potatoes) are reported to be 189 g/day for men and 186 g/day for women, in contrast to 140 g and 159 g respectively when composite dishes are not taken into account (Department of Health, 2011). Current fruit intakes are much less affected by use of this methodology and are 99g/day for men and 103g/day for women (Department of Health 2011). This equates to fruit and vegetable intakes of 288 g/day for men and 289 g/day for women (Department of Health 2011) compared to an average of about 250 g in the 1980s (Gregory et al. 1990).

Current intakes of fruits and vegetables in Britain and other developed countries are generally lower than the five plus daily servings typically recommended (equivalent to at least 2800 g/week). Explanations for resistance to dietary advice to increase the consumption of fruit, vegetables and wholegrain cereals generally stem from issues related to taste, convenience, cost, access, cultural values and education (Buttriss et al. 2004).

At present, men in Britain are eating an average of 4.2 portions of fruits and vegetables (excluding potatoes and potato products) per day and women an average of 4.1 portions per day (Department of Health, 2011) rather than the recommended 5 or more portions (Table 1.12). Overall, 32% of men and 29% of women consumed five or more portions of fruit and vegetables per day (Department of Health, 2011). Intakes in children aged 11–18 are poorer, with only 13% of boys and 7% of girls achieving five portions a day.

The NDNS series also provides information on regional and socioeconomic differences in consumption, the most recent being from 2000–2001. In this dataset there were no statistically significant regional differences for fruit and vegetables: values ranged from 2.6 portions a day for men and 2.7 for women in the Northern region of England to 3.0 and 3.2 respectively for the South East (Henderson et al. 2002). Scotland no longer had the lowest intakes, at 2.9 and 3.0 for men and women respectively.

Men and women living in households in receipt of state benefits consumed a significantly lower number of portions of fruit and vegetables than those in non-benefit households: 2.1 portions compared with 2.8 for men, and 1.9 compared with 3.1 for women (Henderson et al. 2002). About a third, 35% of men and 30% of women, in benefit households had eaten no fruit during the 7-day recording period, and 4% and 6% respectively had eaten no vegetables. The NDNS of school age children (conducted in the 1990s) revealed that children in the lowest income groups are around 50% less likely to eat fruit and vegetables than those in the highest income groups (Gregory et al. 2000).

Conclusions

Throughout human history, communities have developed a diversity of dietary patterns, influenced to a large extent by the foods available in their locality, but usually heavily reliant on plant foods. Such foods, in combination, are capable of providing a diverse range of nutrients. More recently, they have been recognised as providers of an even wider diversity of non-nutrient bioactive substances that are speculated to have health promoting properties.

Diets rich in fruits, vegetables and other plant foods have been shown to be associated with a lower risk of diseases such as CVD (especially stroke) and some types of cancer. These associations persist after adjustment for lifestyle factors often associated with high consumption of such foods (e.g. being physically active and not smoking and having a higher consumption of wholegrain cereals), although the strength of the association is often attenuated. There is also evidence of a dose–response relationship that is consistent with the current recommendations to increase intakes of these foods. It is difficult to separate out the role of diet in general and of specific nutrients in particular, and so the causal mechanism(s) associated with this dietary pattern remain to be established. Most epidemiological research has focused on a number of individual antioxidants studied in relative isolation and it is likely that at the very least there is a complex interaction between the many plant food components and the rest of the diet, that may have an integrated effect on cardiovascular and other chronic diseases.

The strongest association between plant food intake (particularly fruit and vegetable intake) and cancer risk comes from case-control studies. The publication of data from prospective (cohort) studies, which are considered to be more robust, suggests that associations between fruit and vegetable intake and cancer risk may have been overstated. Some evidence also exists for certain eye disorders (e.g. age-related macular degeneration), chronic obstructive pulmonary disease and age-related cognitive decline.

Despite considerable research effort, the specific constituents responsible for these associations have yet to be identified. Animal and *in vitro* experiments have suggested a role in health promotion for a number of plant constituents, particularly those with antioxidant properties, but these findings have generally not been replicated in human intervention trials. The evidence that antioxidants such as vitamins E and C and beta-carotene are responsible for the beneficial effects of fruit and vegetables is at best equivocal, despite popular belief. Not all work has focused on the direct antioxidant properties of the components present in these foods and evidence is accumulating to

support other potential mechanisms. It has been suggested that plant-derived substances may be able to protect against genomic damage resulting in aberrant gene expression, either by up-regulating repair of the damage or the removal of damaged cells by apoptosis. Dietary fibre has recently been shown to be of particular importance in the reduction of colorectal cancer risk (the evidence now being described as convincing) but the specific mechanism is as yet unclear.

As a prelude to randomised controlled trials, there is a need for soundly constructed prospective studies and parallel mechanistic studies, designed to identify the active components in plant foods and their mode of action. Identification of these would enable dietary advice to be more specific. However, in the meantime, regular consumption of a diversity of fruits, vegetables and other plant foods such as wholegrains remains an important message.

Around the world, recommendations exist to increase fruit and vegetable consumption to at least five servings per day. Yet at the current time, typical intakes fall well short of this target in developed countries, meaning that there are considerable opportunities for growers and others in the food chain to encourage intake through a readily available supply of high quality products.

Acknowledgement

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