16
Cardiovascular Disease: Answers to Common Questions

16.1 Epidemiology of Cardiovascular Disease

Q1. Does the UK have a high death rate from cardiovascular disease compared to other countries?

Cardiovascular disease is the major cause of death, particularly in the Western world, but increasingly so elsewhere. Rates have been rising steeply in low- and middle-income countries which are likely to bear the brunt of cardiovascular disease in the years to come. Although deaths from cardiovascular disease have fallen significantly in many high-income countries since the 1980s, rates remain high, particularly in those with ageing populations, such as the UK. In Europe, countries in Eastern and Central Europe, where mortality from cardiovascular disease rose rapidly until the beginning of the twenty-first century, have higher rates than the UK. The lowest rates of cardiovascular disease among developed countries are found in Japan and the Mediterranean countries, such as France, Spain, and Italy.

Q2. Are cardiovascular disease rates falling around the world?

Cardiovascular disease is the leading cause of death worldwide, accounting for around 17.3 million deaths each year (31% of all deaths globally). On a global scale, the burden of cardiovascular disease is growing at an alarming rate. By 2030, it is expected to account for more than 23 million deaths globally. Mortality from cardiovascular disease is rising rapidly in developing countries as they become increasingly industrialised and urbanised, and their large populations adopt more Westernised diets and lifestyles. This trend is particularly serious for low- and middle-income countries that already have to tackle the dual problem of infectious disease and undernutrition.

Countries such as the USA, Canada, Israel, Australia, and New Zealand have seen large falls in premature cardiovascular disease mortality rates since the 1970s, while Western European countries, such as the UK, Belgium, and Norway.
have seen smaller reductions. For example, in the UK, death rates from coronary heart disease fell by over 80% among those dying before 75 years of age over the last half-century.

However, the number of people suffering from cardiovascular disease in the UK (e.g. those with angina or having a heart attack) is rising, particularly in older age groups. This is probably associated with increased life expectancy and with improvements in treatment procedures and better medication (see Section 1.5.2).

Q3. Are there specific groups within the UK that are at high risk of cardiovascular disease?

Heart disease is more common in men than in women, but the prevalence increases with age in both sexes so that the difference reduces after the age of around 50–60 years. Within the UK, mortality rates from heart disease are higher in Scotland and the North of England than they are in the South of England. They are also higher in manual than in non-manual social classes.

Certain ethnic groups are particularly prone to cardiovascular disease. People from the Indian subcontinent are more likely to suffer from coronary heart disease than the White British population, while people of African and Caribbean descent living in the UK appear to suffer greater risk of stroke. Other ‘at risk’ groups include people with diabetes, people with serious mental illness that requires treatment with antipsychotics, and people with chronic renal disease and rheumatoid arthritis.

Q4. Why are men at greater risk of heart disease than women?

Young men are more likely to die from heart disease than young women in most industrialised countries. Although hormonal factors (i.e. female oestrogens) may play a part, diet and lifestyle are also important. Men’s elevated risk may arise because they store more fat in central abdominal regions than do women. This suggests they may have more to gain from improving their lifestyles, in particular, by stopping smoking and increasing levels of physical activity, to prevent heart disease and type 2 diabetes. However, they are often less likely than women to seek medical advice or respond to health promotion activities.

Q5. So, is heart disease a man’s disease?

Heart disease is far from being solely a man’s disease. It is a leading killer of women in the UK. One in eleven women currently die from heart disease, which is twice as many as those dying from breast cancer.

16.2 Main Factors Influencing Cardiovascular Disease Risk

Q6. How can individuals reduce their risk of cardiovascular disease?

The likelihood of an individual developing cardiovascular disease is influenced by some factors that are outside their control, such as genetic make-up, gender, race (see Chapter 1) and perhaps their early growth pattern (see Chapter 2). However, some of the detrimental effects can be counteracted by changes in behaviour, such as taking more exercise, stopping smoking, maintaining a healthy bodyweight, and eating a varied and well-balanced diet.

Q7. Why has advice to reduce the risk of cardiovascular disease focused so much on fat in the diet?

Dietary fats are important determinants of cardiovascular disease because of their effects on blood cholesterol levels. Human intervention studies have shown that blood cholesterol can be influenced by the balance of different types of fatty acids in the diet; blood levels of low-density lipoprotein cholesterol are lowered when some saturates (e.g. myristic and palmitic acid) are replaced by monounsaturates, polyunsaturates, or complex carbohydrate. Fatty acids may also affect cardiovascular disease risk via other mechanisms (e.g. by influencing the tendency of blood to clot). Current recommendations advise people to cut down on the amount of saturates in the diet (principally found in butter, full-fat dairy products, fatty meat products, and confectionery such as biscuits and cakes).

While blood cholesterol is an important risk factor for heart disease, it has been suggested that even if everyone in the UK population managed to reduce their cholesterol levels below 6.5 mmol/l,
there would only be around a 10% reduction in heart disease because it is a multifactorial disease. Thus, advice to reduce risk of cardiovascular disease must also include advice to change other aspects of the diet (e.g. to eat more fruit and vegetables, cut down on free sugars, reduce salt intake, and eat more fibre and wholegrain foods), as well as stopping smoking, taking more exercise, and maintaining a healthy weight.

Q8. What is the most important risk factor for cardiovascular disease?

The risk of cardiovascular disease cannot be predicted from a single risk factor. Cardiovascular disease is a multifactorial disease, which arises out of the joint effects of combinations of different risk factors. The effect of different risk factors is also, to a greater or lesser extent, dependent upon individual susceptibility.

The ‘classical’ risk factors for cardiovascular disease include smoking, raised blood cholesterol, raised blood pressure, physical inactivity, obesity, and diabetes; these are discussed in more detail in Chapters 1, 3, 12, and 13. However, these cannot explain all cases of heart disease and this has led to a search for other risk factors, many of which have been discussed in detail in earlier chapters.

Q9. What might the more novel risk factors described in this report add to what we know about cardiovascular disease?

Although cigarette smoking, elevated blood pressure, and cholesterol account for many cases of cardiovascular disease, there is reason to believe that other risk factors may account for some of the differences in cardiovascular disease rates within and between populations. A better understanding of the role of these additional risk factors may help to identify other ways of predicting individuals at risk and identifying additional approaches for treatment and prevention.

Q10. Are changes in diet and lifestyle becoming less important as treatment for cardiovascular disease and its risk factors improves?

A number of highly effective drugs (such as lipid-lowering agents, aspirin, ACE inhibitors, beta blockers, and other anti-hypertensive drugs) are available in developed countries, such as the UK, that have had a substantial impact on reducing cardiovascular disease mortality. However, the treatment of cardiovascular disease by drugs or medical intervention has important cost implications. In 2013, more than 307 million prescriptions were dispensed for cardiovascular disease in England alone, which was six times higher than in 1981. The National Health Service in England spent around £6.8 billion on cardiovascular disease in 2012/2013, the majority of which came from spending on secondary care. Encouraging changes to diet and lifestyle can prevent heart disease without the side effects associated with surgery and drug therapy. Being physically active and eating a balanced diet can also tackle several cardiovascular risk factors simultaneously. Thus, lifestyle changes remain critical to reducing the prevalence of heart disease and stroke.

16.3 Nutrition During Pregnancy and Fetal Growth

Q11. Are small babies at greater risk of developing cardiovascular disease in later life?

Yes – this has been shown consistently in a large number of cohort studies. A baby weighing 2.5 kg at birth is approximately 20% more likely to die from cardiovascular disease in adult life than a baby weighing 3.5 kg. There are two main reasons for being born small: one is a failure of fetal growth so that the baby is ‘small for gestational age’ and the other is being born too early (preterm) before intrauterine growth is complete. The former is more important as a risk factor for later cardiovascular disease, but there is some evidence that preterm babies also carry an increased risk. Birthweight in itself is not thought to be the cause of cardiovascular disease; rather, the lower birthweight is thought to be an indicator that the fetus experienced sub-optimal nutrition, or was exposed to other factors in utero, which either impaired or damaged cardiovascular development or altered the individual’s metabolism, making cardiovascular disease more likely. Interventions that simply increase fetal growth may not address the problem, and we need to develop a better
understanding of how cardiovascular disease is related to lower birthweight. It is also important to say that babies who are born excessively large, and have a high birthweight, because their mothers were obese or had diabetes in pregnancy, have an increased risk of cardiovascular disease and type 2 diabetes (see Chapter 2).

**Q12. Are small babies more likely to become obese in adult life?**

No – adult body mass index (BMI) is positively related to birthweight; in other words, smaller babies are more likely to have a low adult BMI, and larger babies to have a high adult BMI. Since obesity is defined by BMI, smaller babies are less likely to become obese. However, for any level of adult BMI, there is evidence that smaller babies have less lean (muscle) tissue, and that they also distribute their fat differently, developing relatively more abdominal fat, which is known to be more harmful in terms of cardiovascular disease risk than peripheral fat (on the arms and legs), than heavier babies.

**Q13. What is the ‘fetal origins of adult disease’ (or ‘thrifty phenotype’) hypothesis?**

The ‘fetal origins of adult disease’ hypothesis was first suggested by epidemiologist David Barker in 1989, as an explanation for the association between lower birthweight and higher risk of adult cardiovascular disease. He proposed that if a fetus experiences undernutrition during ‘critical periods’ of the development of key organs and tissues, either because the mother is undernourished or because there is a problem with the ‘supply line’ to the fetus (uterine circulation or placenta), the fetus adapts its growth, organ development, and metabolism in order to survive, and these changes are permanent, making it more vulnerable to developing cardiovascular disease in later life. There is strong support for the hypothesis from animal experiments; it is possible to make animals hypertensive or diabetic by undernourishing their mother during pregnancy. The hypothesis is now generally known as the ‘developmental origins of health and disease’, because it is thought that nutrition during early postnatal life, as well as during fetal development, can also have such permanent effects.

The ‘thrifty phenotype’ hypothesis is another name for the same phenomenon, but has a slightly different nuance. This name comes from Neel’s ‘thrifty genotype’ hypothesis, which proposed that in the past, when poor nutrition was commonplace and the food supply was intermittent, mankind evolved ‘thrifty’ genes that enabled us to store energy efficiently during times of plenty, to use in times of hardship. Neel proposed that these genes helped us to survive in the past but cause diabetes in the modern age, in which food is plentiful. The ‘thrifty phenotype’ hypothesis suggests that a fetus exposed to undernutrition makes adaptations (such as reduced insulin secretion) which make it thrifty, and enable it to survive in utero, but also make it vulnerable to diabetes in later life.

**Q14. Is growth during childhood important in terms of cardiovascular disease risk?**

Yes, excessive gain in weight or BMI in childhood is important. Studies have consistently shown that children whose BMI increases relative to population growth curves (in other words, children who cross the centiles upwards) between the ages of about 5 and 18 years have an increased risk of developing high blood pressure, type 2 diabetes, and coronary heart disease in adult life. The reason we frame it in these terms, rather than simply saying ‘fatter kids’ are at greater risk of later disease, is because crossing upwards, just as much as a high absolute BMI, appears to be important. In India, for example, cohort studies have shown that children who had a BMI well below the level that defines obesity, but who crossed BMI centiles upwards (becoming obese relative to themselves rather than obese in absolute terms) had an increased adult risk of hypertension and diabetes. In contrast to BMI, we do not see consistent associations between the height growth of individuals and later risk of cardiovascular disease. Indeed, tall stature is protective for heart disease and stroke in adult life.

**Q15. Do we know which aspects of a mother’s diet are associated with low birthweight?**

The honest answer to this is no, in the sense that we don’t yet know if there are specific foods or nutrients that are more important than others. Several randomised controlled trials of nutri-
tional interventions in pregnancy have shown that providing mothers with adequate protein, energy, and a range of micronutrients improves fetal growth, but we do not yet know if they improve cardiovascular outcomes in the offspring in later life. The trials carried out so far have either been too small, or have an inadequate follow-up time to answer this question. Another problem with most existing trials is that the nutritional interventions usually started only once the mother knew she was pregnant, and therefore started towards the end of the first trimester of pregnancy, thus missing crucial early developments such as organogenesis, placentation, and major epigenetic changes in the early weeks of gestation. From our understanding of fetal programming of adult cardiovascular disease, these trials may not alter long-term outcomes. At present, we would advise women to aim for a healthy, balanced diet from three or four months before, and throughout, pregnancy and breastfeeding, aiming to enter pregnancy with a normal bodyweight (BMI 18.5–25 kg/m²) and eating adequate, but not excessive intake of energy and protein, and adequate micronutrient intakes. There are a number of reliable sources of general information on diet before and during pregnancy. Guidelines in most countries recommend that mothers take 400 μg of folic acid daily in the periconceptional period to help prevent neural tube defects, and 10 μg of vitamin D daily if at risk of low sunlight exposure (e.g. between October and March in the UK). The World Health Organization also recommends routine iron and folic acid supplements throughout pregnancy to prevent anaemia on a global scale, although routine iron supplementation is not adopted in the UK.

Q16. Is lifestyle during adulthood still important or are early influences on susceptibility to later disease irreversible?

It is very clear that adult lifestyle is still important. Cohort studies have shown that adult risk factors such as smoking and obesity add to, and in some studies multiply, the effects of adverse early life exposures. Equally, this evidence suggests that people who are at risk because of poor intrauterine nutrition can significantly lower their adult cardiovascular disease risk by maintaining a healthy body weight, and avoiding smoking, in adult life. However, the effects on risk conferred by early life factors may not be fully reversible.

16.4 Diabetes, Obesity, and the Metabolic Syndrome

Q17. What is insulin?

Insulin is a hormone produced by the pancreas that allows glucose (obtained from foods containing carbohydrate) to be absorbed from the bloodstream into the cells. This is very important because glucose is the main source of energy that the body needs in order to function properly. Insulin is also a powerful regulator of fat metabolism and tends to lead to storage of fat.

Q18. What is diabetes?

Diabetes, properly known as diabetes mellitus, is a chronic disorder in which the body's sugar (glucose) level is too high. There are two main types of the disease. Type 1 diabetes (also known as insulin-dependent diabetes) occurs when the pancreas does not produce the hormone insulin, which is needed to control blood sugar levels. Type 1 patients usually develop the disease during childhood or adolescence. Type 2 diabetes (or non-insulin-dependent diabetes) is the most common form of the disease and occurs mostly in adults who are overweight. It arises when the body does not produce enough insulin or the body's tissues become resistant to insulin, which causes the blood glucose levels to rise (see Chapter 3).

Q19. How many people suffer from type 2 diabetes?

About 3.5 million people in the UK have been diagnosed with diabetes, with 90% of cases of diabetes being type 2, but experts estimate that a further 1.1 million have diabetes without knowing it. Worldwide, more than 350 million people are estimated to have type 2 diabetes.

Q20. What are the possible complications?

People with diabetes have a higher risk of developing heart disease, strokes, high blood pressure, circulation problems, nerve damage, and damage
to the kidneys and eyes. The risk is particularly high for patients who are obese, who smoke, or who are not physically active.

Q21. How is diabetes linked to cardiovascular disease?

People with diabetes are at greater risk of cardiovascular disease, although the reasons for this are not fully understood. It is thought that if blood insulin and glucose levels are higher than normal and not controlled, this may affect the lining of the body's arterial walls, increasing susceptibility to atherosclerosis (furring up of the arteries).

As well as insulin resistance and high glucose levels, people with type 2 diabetes tend to have central obesity, high blood pressure, and abnormal lipid concentrations. The combination of these risk factors is often called the metabolic syndrome and is associated with an increased risk of cardiovascular disease (see Chapter 3).

Q22. What are the main risk factors for type 2 diabetes?

Risk factors include increasing age, family history, and being overweight, particularly with central obesity (see Q57). People of Asian or African-Caribbean origin and women who have developed diabetes during pregnancy are also at greater risk. Low birthweight and diabetes in the mother during pregnancy have also been identified as risk factors for type 2 diabetes (see Chapter 2).

Q23. Can lifestyle changes reduce the risk of developing type 2 diabetes?

Being physically active, maintaining a healthy bodyweight, and eating a healthy diet that does not contain too much fat, particularly saturates, and free sugars, but contains plenty of fibre-rich foods, such as wholegrain cereals and fruit and vegetables, can lower the risk of developing the condition.

Q24. What is insulin resistance?

A person who is insulin-resistant has cells that respond sluggishly to the action of insulin. This means that the body's cells cannot take up enough glucose and the level of glucose in the bloodstream remains high. This signals yet more insulin to be released from the pancreas until the glucose is taken up by the cells. If the pancreas fails to sustain this increase in insulin secretion, type 2 diabetes develops. Insulin resistance is also associated with changes in blood lipid concentrations that may increase the risk of coronary heart disease.

Q25. What causes insulin resistance?

Insulin resistance is thought to be caused by both genetic and lifestyle factors. Physical inactivity, a diet high in saturates and with a high glycaemic index or load, excess alcohol consumption, and increased bodyweight, high blood pressure, and a low level of the 'good' form of cholesterol (HDL or high-density lipoprotein cholesterol, see Q37) are linked to the incidence of insulin resistance, and may trigger the condition in people who are genetically prone to it. All these factors are also linked to an increased risk of cardiovascular disease, and this may be one reason why there is a high incidence of heart disease and stroke among people with type 2 diabetes.

Q26. What is the metabolic syndrome?

The metabolic syndrome (also referred to as the insulin resistance syndrome or syndrome X) refers to a combination of health problems, including insulin resistance, abnormal levels of blood fats (high triglycerides and low HDL or 'good' cholesterol), central obesity, and high blood pressure. These are all risk factors for type 2 diabetes and heart disease. It is estimated that people with metabolic syndrome are twice as likely to develop cardiovascular disease and five times more likely to develop type 2 diabetes than those without it. The more components of the metabolic syndrome an individual has, the higher their risk (see Section 3.5).

Q27. How common is the metabolic syndrome?

It is estimated that around 10% of the UK population have metabolic syndrome. It is likely that as the population ages and the problem of overweight and obesity continues to rise, the number of people with the syndrome will increase. The International Diabetes Federation suggests that there is an overall global prevalence of metabolic syndrome of 20–25%. The preva-
lence is significantly higher in the USA and the Middle East.

Q28. What can be done to prevent it?
Adopting a healthy lifestyle, which means eating a healthy diet, maintaining a healthy bodyweight, not smoking, and being physically active, can help to avoid all of the features of the syndrome. Because the conditions occur in a cluster, steps taken to bring one of them into the healthy range will probably improve the others. For example, if you’re overweight, losing up to 10–15% of your bodyweight will reduce levels of blood pressure and increase cells’ sensitivity to insulin. Similarly, being more physically active can promote weight loss and raise HDL-cholesterol levels.

Q29. How is obesity usually defined?
Obesity is generally defined as a BMI of more than 30 kg/m² (see Section 3.3.1). Waist circumference (which indicates central or abdominal obesity) is also thought to be an important determinant of cardiovascular disease (see Q57). Central adiposity, defined as a waist circumference of over 94 cm (34 in.) in men and over 80 cm (32 in.) in women, is also an independent risk factor for diabetes and cardiovascular disease. A substantial risk of disease is associated with a waist circumference of over 102 cm (40 in.) in men and over 88 cm (35 in.) in women (see Section 3.5).

Q30. Why is the worldwide increase in obesity of concern in relation to cardiovascular disease?
People who are obese are more likely to suffer from cardiovascular disease. Obesity is associated with other features of the metabolic syndrome (e.g. it increases the risk of high blood pressure, insulin resistance, and abnormal levels of blood fats). There is also a strong link with type 2 diabetes, as obesity accounts for 80–85% of the risk of developing the disease.

Q31. How much weight loss can reduce cardiovascular risk?
Studies of patients undergoing bariatric surgery demonstrate very clearly that weight loss reduces the risk of cardiovascular disease as well as type 2 diabetes and cancer. There is general agreement that sustained weight loss of 5–10% bodyweight through diet and exercise can improve a number of risk factors for heart disease (e.g. lower blood pressure, blood glucose concentrations, and cholesterol levels).

Q32. What are the health implications of being overweight during childhood?
Apart from the social and psychological problems experienced by overweight children, there are also long-term risks. Compared with normal weight children, obese children have higher blood pressure and insulin levels, and a lipid pattern that is associated with heart disease. Children who are overweight in their teens are more likely to be overweight as adults and this ‘tracking’ effect is accompanied by an increase in cardiovascular risk factors during adulthood. There is also some evidence that obese adolescents, regardless of whether they remain obese as adults, are more likely to develop heart disease.

Q33. How much weight loss can reduce cardiovascular risk?
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Q34. Why is being physically active important in reducing cardiovascular disease risk?
Regular physical activity can reduce the risk of type 2 diabetes and cardiovascular disease by improving lipid levels, aiding weight loss, and lowering blood pressure. Physical activity also has multiple beneficial effects on the emerging risk factors discussed in this report (see Section 12.4).

Q35. How much can genes influence the risk of type 2 diabetes, obesity, and cardiovascular disease?
There is much ongoing research into this very question. In some rare families, there are powerful
and dangerous genes which make it almost certain that an individual will develop type 2 diabetes, obesity, or cardiovascular disease. However, such families and genes are uncommon and in most people there are only weaker genetic effects. Present estimates are that heritability of fat mass is between 30% and 70%, type 2 diabetes is strongly genetic (if both parents have it, this increases a person’s risk by 75%) and cardiovascular disease also has a genetic component, while the rest will depend upon their lifestyle.

16.5 Lipid-Related Factors

Q36. What is cholesterol?

Cholesterol is a fatty substance (a lipid) that is found in the bloodstream and in all cells. It has an important role as part of the walls or membranes of each cell. It is also a key component in the manufacture of hormones (chemical messengers in the body) and bile acids (that promote the absorption of fat from the diet).

Some foods, such as meat, poultry, shellfish, eggs, and dairy products, contain dietary cholesterol. Organ meats, such as liver, are especially high in cholesterol, while it is not found at all in foods of plant origin. However, only a small proportion of cholesterol in the body comes from the cholesterol in food. It is made mostly in the liver and this process is stimulated by saturates (see Table 13.5 for the main sources of saturates in the UK diet).

Q37. What are ‘good’ and ‘bad’ types of cholesterol?

There are two main types of blood cholesterol, which are often referred to as ‘good’ and ‘bad’ cholesterol.

Low-density lipoprotein (LDL) is the main cholesterol carrier in the blood. If too much LDL-cholesterol circulates in the blood, it can build up in the lining of the arteries and form atheroma (or fatty deposits). These can cause the arteries to narrow in a process called atherosclerosis. An elevated level of LDL-cholesterol is associated with increased risk of heart disease. It has therefore been traditionally referred to as ‘bad’ cholesterol. However, research now tells us we also need to consider other types of ‘bad’ cholesterol, known as intermediate-density lipoprotein (IDL), very low-density lipoprotein (VLDL), and lipoprotein(a) in order to understand the risk that cholesterol poses to health.

High-density lipoprotein (HDL) is called ‘good’ cholesterol as it carries cholesterol away from the arteries and back to the liver. High levels of HDL-cholesterol help to protect against the development of atheroma (fatty deposits) in the arteries, while a low level of HDL-cholesterol may increase the risk of atherosclerosis. Recently, non-HDL cholesterol (non-HDL-cholesterol) has become a commonly used marker for a blood lipid pattern associated with increased risk of heart disease. This is the sum of all the ‘bad’ cholesterol added together (including LDL-cholesterol) and is calculated by subtracting the amount of HDL-cholesterol from a total cholesterol measure.

Q38. What is Lp(a) cholesterol?

Lipoprotein(a) or Lp(a) is a lipoprotein particle found in the bloodstream. Lp(a) levels appear to be largely genetically determined. High levels are associated with an increased risk of heart disease (see Section 4.12).

Q39. What are triglycerides and how are they linked with heart disease?

Fat in food and fat stored in the body is in the form of triglycerides. A triglyceride is a substance that is composed of three fatty acids attached to a single glycerol molecule. Triglycerides are carried in the blood bound to proteins forming very low, low, and high-density lipoproteins. Like cholesterol, triglyceride in the blood comes either from the diet or from its synthesis in the liver. High triglyceride levels are associated with increased risk of heart disease and stroke.

Q40. What are apolipoproteins?

Apolipoproteins are proteins that are mostly formed in the liver and intestine. They play an important role in the production and transport of cholesterol around the body. There are at least nine types of apolipoprotein, including apoA-1, apoB, and apoE. Each type bonds with cholesterol in the blood to form either the protective cholesterol, HDL, or the more harmful cholesterol, LDL (see Q41 and Chapter 4).
Q41. What part do they play in coronary heart disease?
High levels of certain apolipoproteins may increase risk of heart disease, diabetes, or stroke. For example, high levels of apoB are associated with higher risk of heart disease as it is the main protein in LDL-cholesterol. In contrast, high levels of other apolipoproteins can protect against coronary disease. For example, apoA‐1 is the major protein in the more protective HDL-cholesterol (see Chapter 4).

High levels of apoE can affect the removal of cholesterol in the blood, and also influence the progression of heart disease, depending on the subtype of the apolipoprotein. ApoE2 appears to play a protective role as it is associated with lower LDL levels, while apoE4 slows the removal of LDL from the circulation, and is associated with higher risks of heart disease.

Q42. What causes high cholesterol?
There are several factors that may contribute to high blood LDL-cholesterol and/or low HDL-cholesterol levels. These include a diet that is high in saturates and refined carbohydrates, lack of physical activity, family history, being overweight, drinking alcohol excessively, and smoking. Rarely, high blood cholesterol can also be caused by a condition that runs in the family called familial hypercholesterolaemia.

Q43. Do low-fat diets have beneficial effects on blood lipids?
Consuming a diet that is low in fat can lower blood levels of total and LDL ('bad') cholesterol. As diets that are low in fat, particularly those that are high in complex carbohydrate, are usually lower in energy (calories) than high-fat diets, they can also improve bodyweight (see Chapter 13). However, it is now widely believed that the type of fat is of even greater importance for cardiovascular disease than the total amount of fat in the diet. In particular, lowering the amount of saturates in the diet is important in reducing blood cholesterol levels (see Q49 and Section 13.4.3). A moderate-fat diet which is rich in unsaturates also promotes cholesterol lowering.

Q44. What sorts of fats are in foods?
Fat in food is composed mainly of triglycerides, which contain two main types of fatty acids: saturates and unsaturates. Saturates are predominantly found in animal fats, such as butter, full-fat dairy products and fatty meat products. Unsaturates can be either polyunsaturates or monounsaturates (see Sections 1.7 and 4.5.1). There are two main types of polyunsaturates: n-6 fatty acids obtained predominantly from the seeds of plants, such as sunflower oil or soya oil, and n-3 fatty acids, some of which are predominantly from seeds (e.g. rapeseed and linseed), and others that are present in large amounts in fish oils and have attracted particular attention. All foods contain a combination of saturates, polyunsaturates, or monounsaturates, but the proportion of each varies greatly with different foods (for example, see Figure 13.5 for the fatty acid composition of oils).

Q45. What effects do these fatty acids have on blood lipids?
Saturates in our diets raise blood cholesterol levels more than anything else, including trans fatty acids (see Q46) as they are consumed in greater quantities than trans fatty acids. n-6 polyunsaturates lower total cholesterol levels primarily by lowering LDL-cholesterol levels associated with coronary heart disease. Monounsaturates have also been found to help lower the amount of LDL-cholesterol in the blood (see Table 4.1 for dietary sources).

One of the ways in which the long-chain n-3 polyunsaturates found in oil-rich fish may protect against heart disease is via their ability to lower blood triglyceride levels. There is also some evidence that high intakes of these fatty acids may additionally protect against heart disease by positive effects on other blood lipids (e.g. by lowering small, dense LDLs, and reducing remnant lipoproteins; see Chapter 4). Their effect on blood cholesterol levels, however, is less clear, and it may be that individuals react differently to these fatty acids. The extent to which the n-3 fatty acids present in seeds (e.g. flaxseeds, walnuts, and hempseeds) can simulate the effects of those from oil-rich fish remains to be clarified. However, the available evidence suggests that fish oil supplements (marine-derived omega-3 fatty acids) have no beneficial effects on risk of heart disease.
Q46. What about trans fatty acids?
Trans fatty acids are produced during the process of hydrogenation of unsaturated fats and are principally found in manufactured products (e.g. biscuits, cakes, and chocolates) and some ready meals. They have a particularly adverse effect on lipoproteins [they increase LDL-cholesterol and Lp(a) and decrease HDL-cholesterol], and have been shown to increase risk of heart disease. In the UK, however, they contribute a relatively small proportion of total energy compared with saturates, and current average intakes are now below the dietary reference value (see Section 13.9.2).

Q47. Is eating between meals a problem?
While there is little evidence to date that snacking has negative metabolic consequences or any effect on bodyweight after controlling for total energy intake, more research is needed to clarify the effects of meal frequency on blood lipids and bodyweight (see Section 4.8). Nevertheless, some highly palatable snack foods are high in fat and sugars and energy-dense, which may encourage overeating. Irregular eating habits can also create difficulties for those trying to control their weight.

Q48. How does exercise affect blood lipids?
Exercise has a number of beneficial effects on the blood fats, cholesterol and triglycerides. Regular exercise is associated with an increased ability to clear fat particles from the bloodstream after meals. This is because the exercised muscles need more energy from fat and thus use the fat quickly so that it is cleared from the bloodstream. Exercise also affects blood cholesterol levels by increasing HDL-cholesterol (‘good’ cholesterol) levels. Long-term exercise programmes may also reduce LDL-cholesterol (‘bad’ cholesterol) concentrations. In addition, being physically active can help to control weight, diabetes, and high blood pressure, all of which would reduce the risk of heart disease (see Chapter 12).

Q49. Can the effect of different diets on blood lipid levels vary between individuals?
Yes, genetic make-up can have a large effect on blood lipid levels and the way in which the body deals with different diets. For example, two healthy individuals eating the same food and with similar lifestyles can have quite different blood cholesterol levels. Also, some individuals may experience greater benefit from changing their diet and lifestyles than others (see Section 4.14).

16.6 Inflammation
Q50. What is inflammation and what effect does it have on the risk of heart disease?
There are two types of inflammation: acute and chronic. Acute inflammation is a normal process whereby white blood cells are recruited into tissues in response to an injury, infection or an allergen. This is accompanied by the common signs of acute inflammation – pain, swelling, redness, and heat. These symptoms are caused by blood vessels dilating around the affected area, bringing substances involved in the inflammatory process to dispense or disperse the damaged tissue or bacteria.

If inflammation becomes chronic, this is problematic. This occurs when the body’s inflammatory response is prolonged beyond normal and can occur because the immune system becomes overstimulated, overactive, or fails to switch off its response (or any combination of the three). This type of inflammation can be detrimental as it may injure body tissues; it has been implicated in the aetiology of inflammatory diseases, such as rheumatoid arthritis, psoriasis, and inflammatory bowel disease. It has also been suggested that prolonged inflammation of the arteries may be one of several factors that contribute to atherosclerosis (narrowing and hardening of the arteries) (see Chapter 5). The result is that the arteries become constricted, their elasticity and flexibility are compromised and the volume of blood able to travel through them at any given time is reduced. This ‘hardening’ can lead to elevated blood pressure and increase the risk of a heart attack or stroke (see Section 1.4.1).

Q51. What causes the type of inflammation associated with increased risk of heart disease?
It is not yet known exactly what causes the inflammation that might increase risk of cardiovascular disease. Some researchers suggest that
inflammatory cells are recruited to the sites of developing atherosclerotic plaques in response to deposits of cholesterol or oxidised lipid products on the artery wall. Fat (adipose) tissue, particularly abdominal fat (see Q57), is believed to be a source of inflammatory substances (see Q55), which is why obesity has been suggested to be a state of low-grade inflammation. Other possible factors that may cause an inflammatory response in the body are smoking, uncontrolled diabetes, and high blood pressure. Others suggest that infection, possibly caused by a bacteria or a virus, might contribute or even start the narrowing process. Possible infectious bacteria include Chlamydia pneumoniae and Helicobacter pylori (see Chapter 5).

Q52. Can markers of inflammation be used to identify people at risk of heart disease?

Levels of some markers of inflammation (e.g., C-reactive protein, fibrinogen, and lipoprotein-associated phospholipase A2) have been linked with risk of cardiovascular disease. For example, researchers have found that people with high blood levels of C-reactive protein, which indicates underlying levels of inflammation, are more likely to develop heart disease and stroke than those with lower levels of this protein. This increased risk has been shown to be independent of other risk factors, such as high cholesterol levels, smoking, high blood pressure, and obesity. As sensitive tests for C-reactive protein are now available, measurements of C-reactive protein are used to identify those at high risk of developing a first heart attack or stroke (it is likely to be of limited value in secondary prevention as a heart attack increases C-reactive protein levels). However, it is not yet known whether C-reactive protein is a causative agent or a consequence of heart disease, or whether reducing circulating levels of this protein can actually lower cardiovascular disease risk (see Section 5.6.1).

Whether markers of inflammation, such as C-reactive protein, add anything of value over conventional markers of heart disease as yet remains unclear. The best marker of inflammation to measure is also still being debated. However, giving drugs to reduce inflammation to heart attack patients has been shown to protect them from a stroke or second heart attack.

Q53. Can inflammation be reduced by drugs or diet?

There are a number of pharmacological agents available to reduce inflammation, but we need further research to predict their ability to reduce cardiovascular risk. Some aspects of the diet also seem to influence the inflammatory response. For example, the long chain n-3 fatty acids (found primarily in oil-rich fish) and some antioxidant nutrients (e.g., vitamin C and beta-carotene) seem to have anti-inflammatory effects, but we need more research to determine whether these nutrients influence cardiovascular disease risk in this way. However, drug treatment to lower levels of inflammation has been shown to reduce the risk of heart disease.

16.7 Factors Relating to Adipose (Fat) Tissue

Q54. Why is being obese a risk factor for cardiovascular disease?

Being overweight increases the chance of having a heart attack. This is partly due to the strain placed upon the heart by excess weight, but obese individuals are also more likely to experience a number of cardiovascular risk factors, including diabetes, high blood pressure (hypertension), an adverse blood lipid profile and abnormalities of blood clotting factors. Fat (adipose) tissue secretes a number of substances (collectively referred to as adipokines), which emerging research suggests may themselves increase the risk of cardiovascular disease. The good news is that these risk factors improve when obese people lose weight.

Q55. What are adipokines?

Adipokines are a group of substances, including enzymes, growth factors, cytokines, and hormones, which are produced in, or released into the blood from, fat tissue. Circulating levels of many of these substances are affected by obesity and have been shown to regulate, directly, or indirectly, a number of the processes that contribute to the development of heart disease, including hypertension, endothelial dysfunction, chronic inflammation, and insulin resistance. Whilst a lot more research is needed, it is hoped that a greater understanding of the role of these substances and how their levels are regulated
might help to combat obesity and cardiovascular disease in the future (see Chapter 6).

Q56. Does diet influence levels of these adipokines?

As weight loss leads to a reduction in the amount of fat in the body, it is associated with a fall in levels of several of the adipokines (with the exception of some ‘good’ adipokines such as adiponectin which increase with weight loss). Similarly, weight gain and excess energy intake are associated with a rise in many of these substances. At the moment there is insufficient evidence of the effect on adipokines of individual nutrients, but this remains an active area of research.

Q57. Does where you carry excess fat influence your risk of heart disease?

The medical risks from being overweight are increased if excess fat is distributed abdominally (i.e. around the stomach). Men and postmenopausal women tend to lay down fat around the abdomen and have an ‘apple-shaped’ distribution of fat, while pre-menopausal women tend to have a ‘pear-shaped’ distribution, with fat on the thighs and buttocks. ‘Apples’ generally carry a higher risk of developing heart disease and diabetes than ‘pears’. Measuring your waist circumference is the quickest and simplest way to estimate whether abdominal fat is increasing your risk of cardiovascular disease (see Section 3.4).

Q58. What is leptin?

Leptin is a hormone produced by the fat cells that controls appetite and regulates bodyweight via receptors in the brain. A decrease in body fat leads to a decrease in the hormone, which in turn stimulates food intake by increasing appetite. Increased body fat leads to increased levels of the hormone, which act to reduce food intake by turning off the feeling of hunger in the brain. By this mechanism, weight is usually maintained within a relatively narrow range.

Q59. Can leptin be used to treat obesity?

Around 20 years ago, researchers gave leptin to obese mice that were genetically leptin-deficient and found that they lost a substantial amount of weight. This led to great excitement both in the media and the scientific community about the possible role of leptin as a treatment for human obesity. However, researchers quickly discovered that most obese humans are, in fact, very unlikely to be deficient in leptin. While rare cases of leptin deficiency have been identified in a small number of obese children, most obese people appear to have much higher levels of the hormone than non-obese people, so giving them more would have little effect. This is not completely unexpected since obese people have more fat and so will produce more leptin, but it seems that they may be resistant to high levels of the hormone so that it does not signal effectively to the brain to eat less. We need to discover more about the functions of leptin and the role it plays in weight gain before we can estimate its potential role in helping to treat obesity.

16.8 The Role of the Endothelium

Q60. What is the endothelium and what is its main role?

The endothelium is the layer of cells lining various blood vessels of the body. It regulates the normal functioning of blood vessels and plays a role in functions as diverse as: expansion and contraction of blood vessels, repair of damage, formation of new vessels, and immune responses to infection. Due to its key position, the endothelium also forms a selective barrier between the blood and the underlying tissue, allowing oxygen and nutrients to cross, but not dangerous substances. The range of functions involving the endothelium means that if it is damaged, that can have serious consequences on the vascular system. These include the formation of atherosclerotic plaques, the build-up of fatty materials within the walls of the arteries, and potentially angina, stroke, and heart attacks (see Chapter 7).

Q61. What is endothelial dysfunction?

Endothelial dysfunction is an abnormality in one or more functions of the blood vessel lining which, when functioning properly, regulates the tone of the blood vessel, and helps prevent the process of blood vessel narrowing, and fat accumulation.
Q62. How does endothelial dysfunction affect cardiovascular disease risk?

In this circumstance, rather than preventing the process of blood vessel narrowing and thus heart disease, the lining of the blood vessels can actually contribute to this process. It may affect blood vessel tone and blood pressure. It may also be associated with an enhanced expression of molecules that permit the entry of white blood cells into the vessel wall, allowing harmful inflammatory processes to occur and more cholesterol to enter into the lining of blood vessel. In other words, when the endothelium is ‘dysfunctional’, it can actually accelerate many of the processes, leading to blood vessel narrowing and thus increasing risk of cardiovascular disease.

Q63. Does diet influence endothelial function?

Some dietary factors do appear to alter the function of the blood vessel lining. For example, long chain n-3 (omega-3) fatty acids (found predominantly in oil-rich fish), Mediterranean-style diets (rich in monounsaturates), and some vitamins (e.g. folic acid) appear to enhance the ability of the blood vessel lining to prevent heart disease. In contrast, other agents, either acutely, or chronically (e.g. high dietary fat levels, leading to elevated levels in blood), can harm blood vessel function.

Q64. Can other lifestyle factors influence endothelial function?

Yes, other lifestyle factors are important. Physical activity (see Chapter 12), moderate weight loss, and smoking cessation can all improve endothelial function.

16.9 Diet and Blood Clotting

Q65. How and why does blood clot?

Blood is usually a liquid as it is being pumped around the body by the heart, but under some circumstances (e.g. following a cut), it needs to solidify and form a clot. Blood clotting (also known as coagulation) is triggered by a protein called tissue factor (TF), found on cells in the deeper layers of the blood vessels and not normally exposed to blood until there is an injury. TF reacts with a blood protein called factor VII, and with the aid of small blood cells called platelets initiates a series of complex chemical reactions to produce a substance called thrombin. Thrombin converts a blood protein fibrinogen to fibrin at the site of the wound. These strands of fibrin trap platelets and other blood cells, forming a blood clot (see Chapter 8). This process protects the body from excessive bleeding, ensuring that a clot forms at the site of a wound or injury – either internally or on the body surface. As part of the body’s natural healing mechanism, clots are usually dissolved, and reabsorbed by the body.

Q66. What happens when the clotting mechanism goes wrong?

The clotting process (also known as haemostasis) functions as a careful balance between blood flowing and stopping, and between clotting and dissolving/reabsorbing clots. The consistency of the blood is regulated and maintained by a large number of different proteins, some of which are involved in clot formation (coagulation), while others are involved in the prevention of clot formation (anticoagulation) and dissolving of formed clots (fibrinolysis). Abnormalities in the amounts of either these coagulation, anticoagulation, or fibrinolytic proteins can cause problems. If the blood is prone to clot too little, then there is a risk of bleeding; too much and there is a risk of clots forming where they are not wanted. For example, clots that develop in an artery supplying blood to the heart or brain can cause a heart attack or stroke.

Q67. What markers suggest that the blood might be prone to clotting?

Raised concentrations of some of the factors involved in blood clotting or the removal of blood clots from the circulation predict cardiovascular disease risk. For example, high blood levels of the blood clotting protein fibrinogen are associated with increased risk of cardiovascular disease. A number of other markers (e.g. PAI-1, tPA, von Willebrand factor) have also been identified that may help in the assessment of patients at risk for coronary heart disease (see Section 8.6).
Q68. What can be done to prevent clots forming in the arteries?

There are a number of widely used drugs that act as anticoagulants (which help to prevent blood clots) or clot busters (that help to dissolve blood clots), which can be prescribed to people who are at high risk of cardiovascular disease. One of the most commonly used anti-platelet drugs is aspirin. However, there are several diet and lifestyle factors that may increase the risk of a blood clot forming. Being overweight, being inactive, smoking, and consuming a diet that is high in fat (particularly saturates) increase the risk. In contrast, a moderate amount of alcohol may reduce the tendency of blood cells to stick together and form a clot. Studies have also demonstrated longer bleeding times and a reduced tendency for platelets to stick together and form a clot in subjects consuming a variety of vitamins and minerals and high doses of n-3 fatty acids, found primarily in oil-rich fish (see Section 8.8).

Q69. Are some people genetically more prone to blood clots?

A number of changes (mutations) in the genes that code for some of the factors involved in coagulation or anticoagulation have been identified, and some of these have been shown to increase the risk of blood clots forming in veins inappropriately. Individuals who inherit these mutations may have an increased risk or ‘predisposition’ to develop blood clots compared to the rest of the population.

16.10 Diet and Oxidative Stress

Q70. Why do nutritionists and dietitians promote the 5 A Day message?

There is a considerable body of evidence that has shown diets rich in fruit, vegetables, and other plant foods to be associated with a reduced risk of a number of diseases, including high blood pressure, obesity, heart disease, and stroke, type 2 diabetes and some cancers (including mouth, throat, stomach, colon, and lung cancers). In fact, it has been estimated that diet is likely to contribute to the development of one-third of all cancers, and that eating more fruits and vegetables is the second most important cancer prevention strategy, after stopping smoking. Eating lots of fruit and vegetables has also been associated with lower risk of age-related eye conditions such as cataracts and macular degeneration and chronic lung disorders. This has led to the recommendation by the World Health Organization to eat at least 400 g of fruit and vegetables every day, which has been translated by the Department of Health into advice for the UK population to eat at least five portions of a variety of fruit and vegetables each day.

Q71. What constitutes a portion?

The UK government’s recommended ‘five portions a day’ excludes potatoes and nuts, but includes pulses (e.g. baked or red kidney beans and lentils), although they collectively count only as one portion per day no matter how often they are eaten. Similarly, unsweetened fruit juice or smoothies can also constitute a portion but should be limited to 150 ml/day due to their free sugars content. Fruit and vegetables do not have to be raw to be healthy – frozen, canned, dried, and cooked versions all count towards the 5 A Day target. Fruit and vegetable-based dishes (e.g. fruit crumble, vegetable soup, stews, curry, pizza, pasta dishes) will also count as long as they contain at least one portion of fruit and vegetables per serving.

A portion is generally considered to be around 80 g (or 30 g of dried fruit). This corresponds to:

- a piece of a large fruit (e.g. half an avocado or grapefruit, a large slice of melon, a couple of rings of pineapple);
- one medium-sized vegetable or fruit (e.g. apple, orange, banana);
- a couple of small fruits (e.g. two plums);
- one cup of very small fruit (e.g. grapes);
- ½–1 tbsp dried fruits (e.g. dates, sultanas);
- 2–3 tsp cooked or canned fruit;
- three tbsp raw, cooked, frozen, or canned vegetables;
- a bowl of salad;
- three heaped tbsp beans or lentils (but only counts once per day);
- 150 ml of fruit juice or smoothie (but only counts once per day).

Q72. What is so good about fruit and vegetables?

Fruit and vegetables collectively contain a wide range of nutrients, including vitamins with antioxidant properties (e.g. vitamins C and E, and
carotenoids such as beta-carotene), folate, and other B vitamins, a wide range of minerals including potassium and iron, and dietary fibre. In addition, there are known to be tens of thousands of bioactive compounds (or phytochemicals), including flavonoids and glucosinolates, which have been suggested to have beneficial properties with respect to human health. The range of nutrients and phytochemicals present varies considerably between different types of fruit and vegetables. So, the advice with regard to consumption of these foods should focus on variety, to ensure that a wide array of nutrients and bioactive substances are consumed.

There is also likely to be a displacement effect – that is, by eating more fruit and vegetables we tend to eat less of the high fat and energy-dense foods that may increase the risk of obesity, heart disease, and diabetes.

Q73. Do antioxidant nutrients reduce the risk of heart disease?

Free radical damage has been implicated as a factor in the development of heart disease and stroke, and a number of antioxidant nutrients are important in the body’s defence systems (see Chapter 9). However, while promising and consistent results were reported from animal and in vitro studies (e.g. tissue culture), human intervention trials with vitamins E and C, and beta-carotene have not generally supported a protective role for supplementation with these nutrients against heart disease. The contribution of other plant constituents with antioxidant properties, such as flavonoids and sulphur-containing compounds, remains to be established.

Q74. Can supplements be as effective as fruit and vegetables in reducing your risk of cardiovascular disease?

Intervention trials have not supported the notion that supplements provide the same protection against chronic diseases as increasing fruit and vegetable intake. This might be because it is the cocktail effect of the many substances present in whole fruit and vegetables, including fibre, vitamins, minerals, and plant bioactives, such as polyphenols and carotenoids that confer the health properties or that the substances tested are not those responsible.

Q75. Is it true that chocolate contains substances that might be good for the heart?

There is evidence that chocolate, which contains a range of bioactive substances including flavonoids, can increase the antioxidant capacity of the blood and reduce the oxidation of LDL-cholesterol, which is a prerequisite step for cholesterol being deposited in the arterial wall. The consumption of cocoa-rich products has also been shown to have beneficial effects on other processes associated with cardiovascular disease, for example, helping to prevent blood platelets from clumping together and forming a clot, and increasing blood vessel flexibility. However, much of this work has been done in a test tube and needs to be supported by human studies. It should also be remembered that chocolate and products containing it tend to be energy-dense and contain relatively high amounts of fat and sugar, and thus should be eaten in moderation.

16.11 Vitamins

Q76. What is homocysteine?

Homocysteine is an amino acid in the blood that is produced as the body digests and breaks down protein. It is normal to have a certain level of homocysteine in the blood. In the past, researchers suspected that high levels of homocysteine might increase the risk of heart disease and stroke. However, elevated homocysteine levels are likely to be a marker of heart disease rather than being causal. Therefore, unlike cholesterol, homocysteine is not routinely measured and most people who suffer from heart disease will not have their levels measured at routine check-ups. For most people, measuring homocysteine or screening for a genetic mutation that predisposes to high homocysteine is not warranted right now. However, targeted testing is recommended, such
as for very young people who develop unexpected heart disease or stroke.

Q78. What aspects of the diet and lifestyle can alter homocysteine levels?

Several B vitamins are involved in homocysteine metabolism (folate, vitamin B6, vitamin B12, and riboflavin), and supplementation with folic acid and vitamin B12 lower plasma homocysteine levels. Homocysteine levels are higher in current smokers than in non-smokers and in people who consume very high amounts of coffee, but are lower in individuals who are moderate alcohol drinkers.

Q79. Should people take vitamin pills containing folic acid to reduce risk of heart disease?

No, taking folic acid to prevent risk of heart disease or stroke is not currently recommended. Meta-analyses of randomised controlled trials demonstrated no benefit for prevention of heart disease or stroke.

Q80. Why don’t we fortify foods with folic acid in the UK when it is mandatory in the USA?

The UK Scientific Advisory Committee on Nutrition recommends that flour should be fortified with folate in the UK in order to reduce neural tube defects. To date, this policy has not been introduced but instead women are advised to take folic acid supplements preconception and during the first 12 weeks of pregnancy. Previously, there has been some concerns that fortification of flour with folic acid for the prevention of birth defects (neural tube defects such as spina bifida) could be hazardous for older people due to delay in the diagnosis of vitamin B12 deficiency or exacerbation of either peripheral neuropathy (a disease affecting the nerves) or other neuropsychiatric complications associated with vitamin B12 deficiency. The government is to hold a consultation on mandatory fortification of flour with folic acid in the UK in 2019. Experts believe that any fortification policy should be accompanied by action to restrict voluntary fortification of foods with folic acid; measures for careful monitoring of emerging evidence on any adverse effects of long-term exposure to intakes of folic acid and guidance on supplement use for particular population groups (see Section 10.3.10).

16.12 The Gut Microbiome

Q81. What is the gut microbiome?

Our bodies provide a home to trillions of microorganisms that live alongside us. The most heavily populated area is the colon in the large intestine, which hosts hundreds of different bacterial species, most commonly referred to as the gut microbiome. The gut microbiome is a mixed community of microorganisms and is now more widely understood to have both beneficial (e.g. reducing blood cholesterol concentrations and influencing the immune response) and detrimental (such as the presence of pathogens) effects on the human body, therefore it is important to maintain an optimal bacterial community structure.

Q82. How is the gut microbiome influenced in early life?

The development of the microbiota is influenced right from birth, with the types of bacteria present varying between vaginally and Caesarean born infants, as each delivery method exposes the baby to different environments (see Chapter 11). Early diet also affects the make-up of the gut microbiome, with different types and amounts of bacteria present in breastfed vs. formula-fed infants. These early colonisation configurations are believed to have significant influences on health in later life.

Q83. Which nutrients are beneficial for the gut microbiome?

Diet can have a significant impact on the gut microbiome as foods that are not digested in the first part of the gastrointestinal tract may provide the microbiome with a potential nutrient source. A main source of nutrients are undigested carbohydrates fermented by bacteria in the colon, a process that produces many end products such as short-chain fatty acids. As well as providing the brain, heart, and muscle with energy, these short-chain fatty acids make the colon more acidic, which can help limit the growth of potentially harmful bacteria, and some are involved in the regulation of lipid production and also with mediators of appetite. The types and amounts of short-chain fatty acids produced are dependent on the microbiome present, which is influenced by diet.
Q84. Is there a role for the gut microbiome in cardiovascular disease risk?
Consumption of dietary fibres is considered to induce a positive gut environment. There is strong evidence that suggests that increasing dietary fibre intake is associated with lower cardiovascular disease mortality. The mechanisms involved are unclear, however, the impact of dietary fibre on gut microbiota may make an important contribution to risk reduction. This may be due to the fact that all dietary fibres provide a potential source of carbohydrate for microbiota in the large intestine.

Q85. What is the impact of prebiotics, probiotics, and synbiotics on cardiometabolic risk?
Some probiotic bacteria (live bacteria in yogurt, other dairy products, and supplements that have a beneficial effect on host health) have been observed to have cholesterol-lowering effects, which could lead to coronary heart disease risk reduction. However, results are inconsistent and further studies are required to determine the impact of specific probiotic strains. Currently, no health claims for probiotic products have been approved for use in the European Union, generally due to issues over the classification of bacterial strains or a lack of robust evidence from human studies. In the USA, some ‘structure and function’ claims for probiotics can be made, supporting a healthy digestive system, but health claims on reducing risk of disease (which have to use the same standards for approval as pharmaceuticals) have not been approved. Alternatively, prebiotics (special fibres that encourage the growth of the ‘good’ bacteria already in the gut) can be used to specifically target limited members of the microbiome to enhance health outcomes. Prebiotics can occur naturally in several foods (e.g. leek, asparagus, banana, wheat); however, these contribute a small proportion in the UK diet. Prebiotics can also be added to a range of foods and drinks, as well as animal feeds and supplements. Findings of studies investigating the effects of prebiotics on fasting blood lipid levels have been inconsistent, but it is known that different prebiotics have varying effects. The varying findings may also reflect the different types of food vehicles used to increase the amount of prebiotic in the diet. Synbiotics are the combined use of pre- and probiotics, with the prebiotic selectively enhancing growth of the probiotic strain and/or supporting the growth of other potentially beneficial organisms already present in the gut.

Q86. What are faecal microbiome transplants (FMT)?
Faecal microbiome transplants (FMT) aim to replace the bacteria in the colon of a patient with a bacterial consortium of an individual who is thought to have a healthy gut microbiome. FMT have increased in popularity for the reduction in Clostridium difficile infection, in particular. Following a small number of initial studies in mice and humans, FMT are also being considered in the treatment of metabolic syndrome. However, consideration of pathogens and viruses within the donors’ microbiota along with more randomised controlled trials are needed before any conclusions can be made about FMT efficacy.

Q87. Do all yogurts contain probiotics?
Not all yogurts contain probiotics. In the manufacture of yogurts, two bacterial species, Streptococcus thermophilus and Lactobacillus bulgaricus, are typically used. These act to break down lactose within the milk into lactic acid, thus acidifying the product, enabling a casein gel network to be formed for the production of yogurt. Some yogurts just contain these starter cultures; while others may be heat-treated post yogurt formation and therefore contain no live bacteria. The probiotic yogurts will, however, have different probiotic microorganisms added.

16.13 Physical Activity
Q88. How much physical activity should we be doing?
It seems that there is no threshold for the minimal amount of exercise necessary to decrease cardiovascular risk, and that any increase in daily energy expenditure is beneficial. However, to gain real benefit, adults (including older adults) should take at least 150 minutes of moderate-intensity aerobic activity a week plus muscle-strengthening activities on two days or more of the week or 75 minutes of vigorous intensity aerobic activity plus muscle strengthening.
activities on two days or more of the week (or
a combination of the two). Moderate intensity
activity should lead to an increase in breathing
rate, an increase in heart rate and to a feeling
of increased warmth, possibly accompanied by
sweating. The 150 minutes total could be achieved
by doing 30 minutes of activity, five days a week
but could also be reached by doing shorter bouts
of 10 minutes or more.

Children and young people should achieve a
total of at least 60 minutes of at least moderate
intensity physical activity each day. At least
twice a week this should include activities to
improve bone health (activities that produce high
physical stress on the bones), muscle strength,
and flexibility.

Undertaking 150 minutes of moderate inten-
sity activity a week will limit risks of developing
diseases such as heart disease and diabetes. It’s
not clear how much activity is needed to prevent
the transition to overweight or obesity and this
will vary by individual but it’s likely that this
will be more than required for general health
(e.g. 45-60 minutes of moderate intensity per
day). Studies looking at people who have lost
significant amounts of weight and kept this
off have found that they tend to do 60-90 min-
utes of physical activity and it’s likely that this
higher level is needed to maintain weight after
weight loss.

Q89. What types of activities count?

All types of activity, provided they are of at
least moderate intensity, contribute towards the
150 minutes a week and different types of physical
activity benefit different body systems (e.g. aer-
obic activity for heart, or weight-bearing activ-
ities for muscles and bones). For many people,
the easiest way of increasing their daily activity
levels may be to incorporate more brisk walking,
stair climbing or cycling into their daily routine,
or to take up active hobbies such as gardening.
Others will find it easier to join a gym or to make
use of local sports centre facilities.

Q90. It’s been suggested that physical activity
doesn’t help with weight loss as people
simply eat more after exercising

Although this idea is often seen in the media, it is
not borne out by the evidence. Interventions that
include both physical activity and dieting appear
to be more effective than using diet alone and evi-
dence suggests that physical activity may become
even more important for maintaining a healthy
bodyweight following weight loss. Studies that
have looked at the effect of physical activity
on appetite have found that, for most types of
exercise any increase in food intake afterwards
does not compensate for the energy expended by
that activity – that is, more calories are burned by
the activity than are consumed in food and drink
afterwards. One exception may be high intensity
interval training where some studies have found
a relatively greater increase in appetite than that
found after more moderate exercise over a longer
period.

Q91. What is the effect of sedentary behaviour
on cardiovascular risk?

Recently there has been an increasing interest in
the role that prolonged periods of sitting, which
are typical of many twenty-first century occu-
pations and leisure pursuits, has on our health.
Accordingly, the term sedentary behaviour has
emerged. Sedentary behaviour is defined as
waking activity characterised by very low levels
of energy expenditure and a sitting or reclining
posture. Researchers have demonstrated associ-
ations between time spent being sedentary and
risk of cardiovascular disease and these effects
are mediated by adverse effects on blood lipids,
blood pressure, and type 2 diabetes. Evidence
suggests that these risks are seen even in people
who exercise regularly but spend much of their
day sitting.

16.14 Diet and Cardiovascular Disease

Q92. Does saturated fat increase the risk
of heart disease?

The relationship between saturated fat and heart
disease has been questioned in recent years. This
is because some systematic reviews and meta-
analyses of prospective studies have reported a
lack of an association between intake of satu-
rated fat and higher risk of death from heart dis-
ease. However, prospective studies, which follow
a cohort of people over a period of time, have
a number of limitations (see Section 13.4.3),
including potential errors in assessment of diet,
the choice of carbohydrate as the comparison nutrient and possible confounding by other dietary and lifestyle factors. The most direct test of the association between dietary fat and heart disease is to conduct a randomised trial to determine whether changes in diet can reduce the risk of a heart attack or well-known markers of increased risk such as LDL-cholesterol. Such studies have shown small but important reductions in cardiovascular risk when saturates are replaced by unsaturates or complex carbohydrate (see Section 13.4.3), supporting current dietary recommendations. In the UK, a draft review of saturates and heart disease by the Scientific Advisory Committee on Nutrition was published in 2018.

Q93. Should we be focusing on healthy dietary patterns for reducing heart disease risk rather than single foods or nutrients?

Research investigating the role of diet in health and disease has typically assessed the role of single nutrients or foods, but we do not consume single nutrients/foods on their own but in combination. Evidence has accumulated in recent years to highlight the importance of a dietary pattern approach to healthy eating advice, such as is used in food-based dietary guidelines around the world. Food-based dietary guidelines tend to have similar features, emphasising higher intakes of fruit and vegetables, legumes, wholegrain cereals, poultry, and fish (see Section 13.5, for examples). Overall there is strong evidence that risk of developing heart disease is reduced by consuming a dietary pattern characterised by being high in fibre and containing plenty of fruit and vegetables, wholegrains and calcium-rich foods; maintaining a healthy weight; exercising; not smoking, and cutting down on alcohol and salt intakes.

Q94. Should low-carbohydrate, high-fat diets be encouraged as a method of weight loss?

For those who need to lose weight, the key aspect is reducing energy intake below energy expenditure. This is best done through a combination of increased physical activity and reduced energy intake. The macronutrient source of the energy (i.e. fat versus carbohydrate) is generally of secondary importance, although it may influence adherence to different dietary regimens. The low-carbohydrate approach to dieting has attracted considerable publicity, but a systematic review of the evidence has demonstrated that weight loss while on such diets is primarily the result of a decrease in energy intake, rather than being associated with reduced carbohydrate per se. While it was previously not known in detail whether there were any possible adverse effects of very low-carbohydrate intakes, and in particular their effect in people with cardiovascular disease, dyslipidaemia, type 2 diabetes or hypertension, it is now more widely accepted that there are potential short-term benefits of low-carbohydrate diets for people with type 2 diabetes (see Section 13.6.3).

Q95. Is there a role for high-protein diets in weight loss?

When low-carbohydrate diets are adopted, intakes of protein tend to be high. High-protein diets are thought to be effective due to their high palatability and the satiating effect of protein. High-protein, low-energy intermittent fasting regimens have been found to reduce body mass index in obese adults, and result in less weight regain compared to a ‘heart healthy’ diet (see Section 13.6.3).

Q96. Does dietary fibre have a role in risk of heart disease?

The evidence supporting a relationship between a fibre-rich diet and reduced risk of heart disease and type 2 diabetes has accumulated over the past few decades since the dietary reference value (DRV) for fibre was last considered. In its review of carbohydrates and health, the Scientific Advisory Committee on Nutrition (SACN) reviewed the evidence that has since become available, and found strong evidence from prospective studies that increased intakes of dietary fibre (particularly from cereals and wholegrains) lowered the risk of heart disease, type 2 diabetes and stroke (see Section 13.4.4.3). Randomised controlled trials have also suggested that higher intake of some specific types of fibre, such as oat bran...
and beta-glucans, improve blood lipid levels. Based on this evidence, SACN recommended that the UK population’s fibre intake should be increased to an average of 30 g AOAC fibre a day for adults, from the previous recommendation equivalent to 24 g AOAC fibre per day (AOAC is the method now used for defining dietary fibre for food labelling purposes). By comparison, current intakes in adults are around 18 g per day. Targets have also been set for children (15 g/day for 2–5 year-olds, 20 g/day for 5–11 year-olds and 25 g/day for 11–16 year-olds).

**Q97. Is a low-fat diet the best approach to reduce heart disease risk?**

Current dietary recommendations in the UK advise that the population’s average dietary fat intake should be reduced to 35% of dietary energy, a level that has more or less been achieved for some time in the UK, and that intake of saturates should be reduced to 11% of dietary energy, and \( n-6 \) polyunsaturates increased to 6.5% of dietary energy. In the past, other countries have adopted even lower targets for fat intake (e.g. 30% of energy for total fat in the USA) but in several countries, including the USA, guidelines have been reviewed and there has been a move towards a range for total fat, such as 20–35%, rather than a single value (see Section 13.8.1). This strategy for dietary fat is primarily aimed at reducing LDL-cholesterol levels. However, over time, evidence has accumulated about the potential of low-fat/high-carbohydrate diets to adversely affect other blood lipid markers (e.g. triglycerides and small, dense LDL particles), and on the potential benefits of other families of fatty acids on other cardiovascular risk factors, particularly insulin resistance. This evidence points to the need for more attention to be paid to the positive attributes of the long chain \( n-3 \) fatty acids found in oil-rich fish and on replacing saturates with unsaturates (as found in vegetable oils, nuts and oil-rich fish) focusing more on changing the nature of dietary fat.

In order to include these unsaturates in adequate amounts, some experts have argued strongly for the more flexible approach to total fat recommendations, especially for subjects with metabolic syndrome, as now adopted in some countries (see Section 13.8).

**Q98. Are we meeting the current dietary targets for cardiovascular disease prevention in the UK?**

The good news is that the recommendation to adjust the population’s average fat intake down to 35% of dietary energy has more-or-less been met in both men and women, and good progress has been made towards the 11% of energy target for saturates, although there is still room for improvement (see Section 13.9.2). Furthermore, average intake of \( trans \) fatty acids (which have a particularly detrimental effect on LDL-cholesterol and also endothelial function) is now well below the 2% of energy target at 0.5% of energy in both men and women. Average salt intakes in adults are still well above the 6.0 g/day target, at 8.0 g/day, but this average has fallen from 9.0 g/day in 1994 (see Section 13.9.11). The majority of the public still fail to meet the 5 A Day fruit and vegetable target (average of four portions a day in adults; see Section 13.9.4), the recommended intakes of free sugars and dietary fibre intakes (see Section 13.9.3) and the ‘at least five-a-week’ physical activity target (30 minutes of at least moderate intensity activity on at least five days per week) (see Chapter 12). The UK government has recognised the need for a review of the evidence in relation to advice on dietary fat, and SACN published its draft recommendations for guidelines around saturated fats and health in 2018.

**Q99. What role does the food industry have to play in helping consumers reduce their intake of nutrients that may be detrimental to health if consumed in excess?**

There have been some successes in the UK in reformulating key product categories over the past decade, notably a reduction in the salt content of foods and removal of \( trans \) fatty acids from fats and spreads. As a result of this, consumers’ average salt and \( trans \) fatty acid intakes have fallen. More recently, concern about children’s intake of free sugars has led to the food industry taking action to reformulate sugars-containing foods and drinks and to reduce portion sizes of certain products (see Section 15.4.3.2). The impact of these on-going reformulation efforts will need to be monitored via future national dietary surveys.
Q100. Should we be concerned about the effect of children's diets on their future risk of heart disease?

Observational studies have linked childhood obesity and rapid weight gain during mid-childhood or adolescence with an increased risk of heart disease as an adult. It is known that the rates of childhood obesity are rising, and the development of type 2 diabetes in children is also rapidly increasing in incidence. Dietary intakes of some micronutrients also appear to be low in certain population groups, particularly teenage girls and young women, and are of concern as some of these may influence heart disease risk (see Section 13.9.9).

Q101. Do the dietary recommendations need to be revised in light of new research into the links between diet and heart disease?

Since the last comprehensive review of dietary guidelines to prevent heart disease in the UK, in 1994, a number of dietary recommendations have been reviewed and revised, including those for salt, free sugars, and fibre (see Chapter 13). A review of saturated fat and health has also recently been undertaken by the Scientific Advisory Committee on Nutrition (see Section 13.4.3).

Q102. What have we learnt about the role of diet in heart disease since the last Task Force report?

Evidence since 2005, when the last edition of the Task Force report was published, has strengthened for a number of the risk factors identified as ‘emerging’ a decade ago, both in terms of their role in heart disease risk and links with specific aspects of the diet. In particular, there is now strong evidence that homocysteine levels can be reduced by supplementation with folic acid, however, randomised controlled trials have not found any evidence that this helps prevent heart disease. So, focus has moved away from lowering homocysteine levels in this way. Evidence for a role of adverse nutrition in early life as a risk factor for heart disease later in life has also strengthened since the last Task Force report, and both over- and undernutrition during pregnancy are now believed to be linked to increased risk of health issues (such as high blood pressure, insulin resistance and type 2 diabetes) in the offspring in later life. Furthermore, interest is now growing in a number of newer risk factors, which may be as relevant to heart disease risk. These include the role of the gut microbiome and how it is influenced by the diet.