

WEEK 4 SUPPLEMENT

HEART HEALTH

A Beginner's Guide to Cardiovascular Disease

CARDIOVASCULAR RISK FACTORS

Cardiovascular risk factors are things that have been associated with an increase in the probability of developing a cardiovascular disease. Some risk factors are non-modifiable (you can't change them) eg. age or gender, whilst other risk factors are known as modifiable risk factors (you can choose to try and change them) eg. Smoking status, cholesterol level or obesity.

ASSOCIATION VERSUS CAUSATION

Risk factors are things that are associated with an increased risk. This means that studies have shown that when a cardiovascular risk factor is present, people seem to have a greater chance of getting cardiovascular disease – but this doesn't mean that the risk factor directly causes it. For example, skids on the road are associated with car accidents but they don't cause them.

Trying to identify which risk factors are correlative (associated) and which ones are causative is an interesting part of scientific investigations in this area.

CARDIOVASCULAR RISK CALCULATORS

Risk is all about probability or chances. We've learnt on this course that for each of us the probability of dying of a cardiovascular disease is 1 in 3, but this doesn't actually tell us a lot as it is the same for everyone. A more useful calculation is the probability of a specific individual having a cardiovascular event within the next 10 years, in other words, a calculation that takes into account some of our individual circumstances such as the non-modifiable and modifiable risk factors.

Many GP practices now use computer programmes to calculate a person's risk of cardiovascular disease. This week as you learn about the different risk factors for cardiovascular disease you can explore how much they influence a person's risk by using one such risk calculator, the QRisk Cardiovascular Disease Risk Calculator www.qrisk.org.

NON-MODIFIABLE RISK FACTORS: AGE AND GENDER

Non-modifiable risk factors are things that we can't change, such as our age, gender, ethnicity and family history. Each of these factors is known to influence a person's risk of developing cardiovascular disease. The British Heart Foundation publication *Coronary Heart Disease Statistic 2012* explores many of the risk factors for cardiovascular disease. You can find this publication at www.bhf.org.uk/research/heart-statistics.aspx.

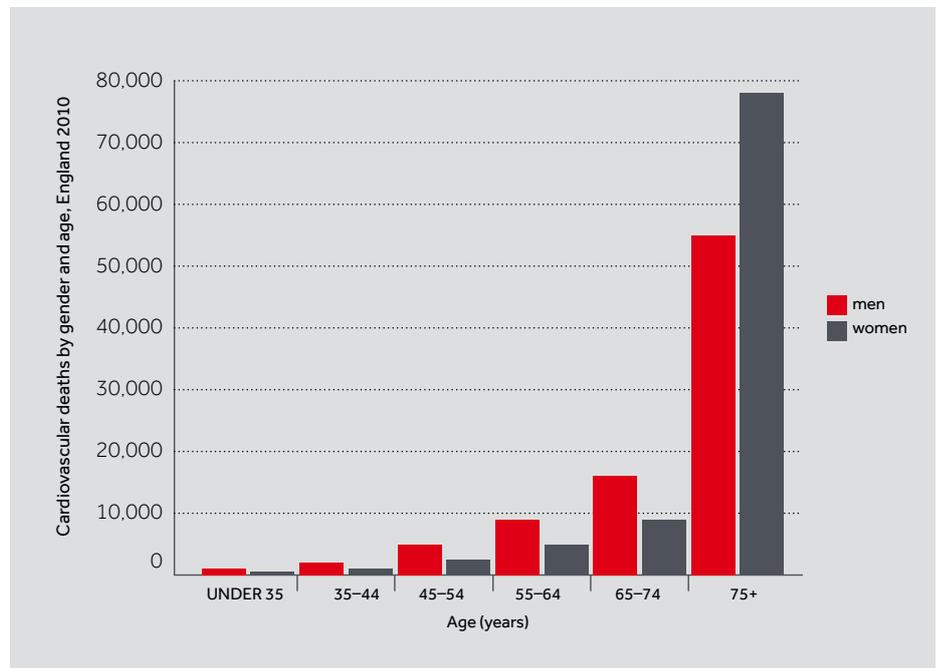
FIGURE 1

The absolute numbers of men and women dying of cardiovascular disease at different ages. We can see that most people who die of cardiovascular disease are over 75. We can also see that more men than women die of cardiovascular disease under the age of 74, but over 75 more women die of cardiovascular disease (because women outnumber men over the age of 75).

Have a go at using the QRisk Cardiovascular Disease Risk Calculator (www.qrisk.org) to explore the effects of the non-modifiable risk factors of age, gender, ethnicity and family history. Complete the online form for "Mr. Reading" (our test subject) as instructed below and then try changing some of the options for non-modifiable risk factors. Do the results surprise you?

Mr. Reading is a 54 year old white male, living near the University of Reading (RG6 5SE). He is a non-smoker and doesn't have diabetes. His parents are both alive and well. He doesn't have chronic kidney disease or atrial fibrillation and he isn't on any blood pressure treatment. He recently had a health check-up and his cholesterol/HDL ratio was 4.5, whilst his systolic blood pressure was 118mmHg. He is of an average build, being 180cm tall and weighing 75kg.

Graph: Cardiovascular Deaths by Gender and Age, England 2012 © British Heart Foundation, 2015. Reproduced with kind permission of the British Heart Foundation.



NON-MODIFIABLE RISK FACTORS: GENETICS

There are different ways to study the genetics of cardiovascular diseases: linkage studies, association studies and genome wide association studies (GWAS). These are discussed in an article by Kullo and Ding (2007) www.nature.com/nrcardio/journal/v4/n10/full/ncpcardio0982.html and described below.

FIGURE 2

Linkage studies. Linkage studies are genetic studies that follow a single family, looking at diseases as they develop in that family. They try to identify genes that may predispose towards getting a cardiovascular disease by following small groups or family members who seem to have a tendency for having cardiovascular disease.

Genetic markers are followed in the family members and if the marker seems to follow the line of disease then it is likely that the marker is close to a gene that increases the risk of disease. Once a linkage is identified between the marker and the disease then this area of the genome can be explored in more detail. In this figure marker allele A is linked to the disease.

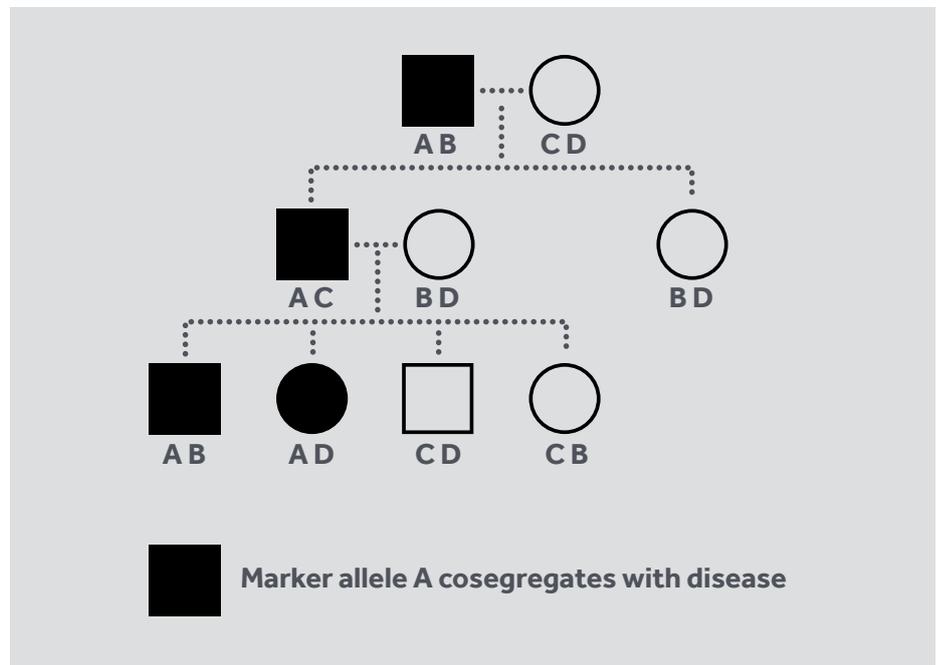
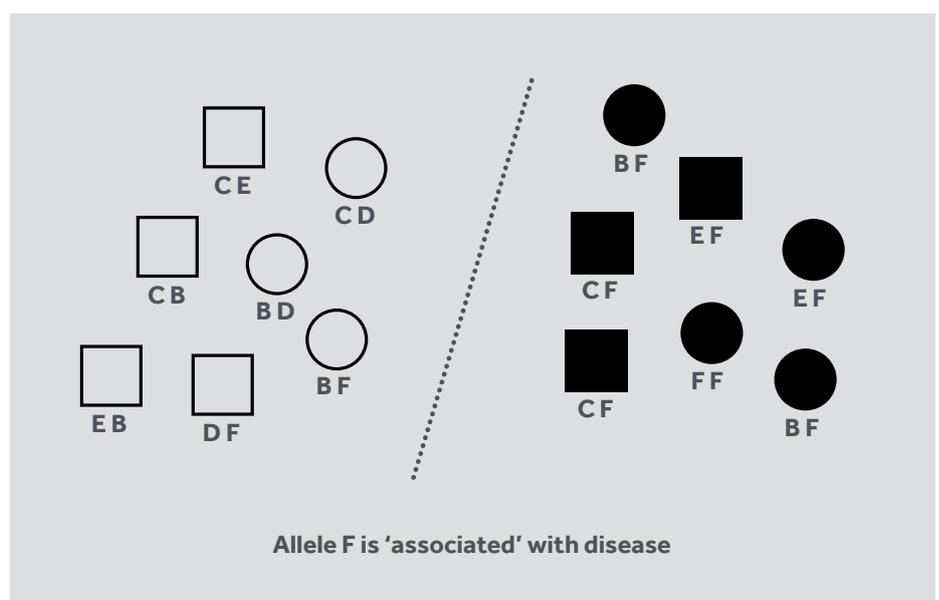


FIGURE 3

Association studies. Association studies are genetic studies of a large number of people with or without a disease, to compare genetic variations between the 2 groups. Genetic variations are small changes in the genetic code that alter things like the amount of a protein produced, where and when it is produced, or its activity.

These small changes give rise to different alleles for one gene. The gene may be for protein X but one allele may code for protein X to be produced a lot, whilst another allele (or version of the same gene) may code for protein X to be produced at a lower level. In this figure allele F is associated with the disease.



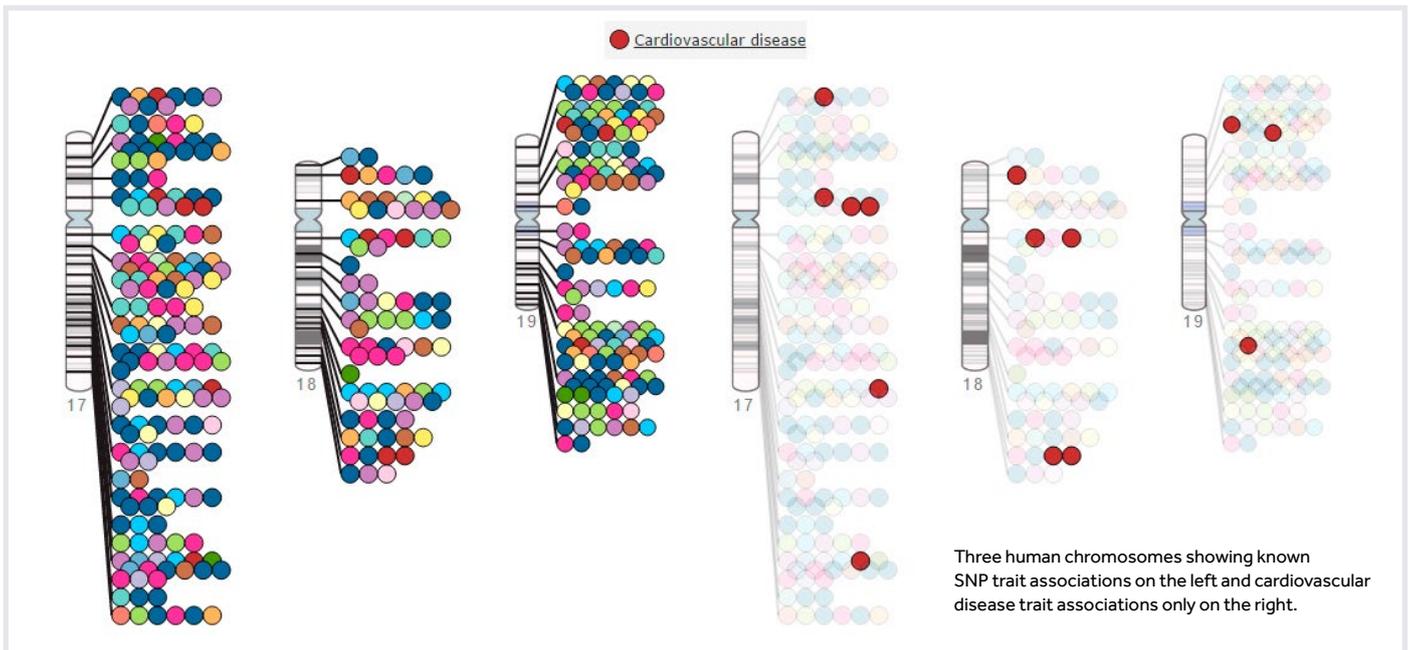


FIGURE 4

Genome wide association studies (GWAS). Genome wide association studies are genetic association studies carried out for genetic variants across the whole genome (entire genetic make-up of an organism) simultaneously, usually involving many subjects to enable the specific diseases to be traced to variations or mutations.

The National Human Genome Research Institute has produced a catalogue of all genome wide association studies, showing where markers that have been linked to different diseases are found on each of the human chromosomes (Welter et al., 2014). You can explore the human genome and where markers for different diseases can be found at www.ebi.ac.uk/fgpt/gwas. You can filter the image to show only those sites with associations to cardiovascular diseases. These vast studies have revealed 46 genetic variants that are linked to the risk of cardiovascular disease, most of which are involved in controlling lipid levels or blood pressure. Further research to unravel the genetic components of cardiovascular disease is needed.

Figure reproduced from Welter, D., MacArthur, J., Morales, J., Burdett, T., Hall, P., Junkins, H., Klemm, A., Flicek, P., Manolio, T., Hindorff, L., and Parkinson, H. (2014) The NHGRI GWAS Catalog, a curated resource of SNP-trait associations Nucl. Acids Res. 42 (D1): D1001–D1006.

SEMI-MODIFIABLE RISK FACTORS

Semi-modifiable risk factors include co-morbidities, or other medical conditions, that are often associated with cardiovascular diseases. Conditions such as hypertension, diabetes mellitus, chronic kidney disease, atrial fibrillation and rheumatoid arthritis are all associated with cardiovascular diseases, perhaps through shared origins in degeneration and inflammation. Although we can't completely negate the increased risks associated with them, with good management (life style choices and/or medications/treatment) these risks can be reduced.

MODIFIABLE RISK FACTORS

Modifiable risk factors are things that we can try to change through life style choices, such as our smoking status, cholesterol level and obesity. Each of these factors is known to influence a person's risk of developing cardiovascular disease. The British Heart Foundation publication *Coronary Heart Disease Statistic 2012* (www.bhf.org.uk/research/heart-statistics.aspx) explores many of these risk factors for cardiovascular disease.

Explore the effects of several modifiable risk factors by changing the values on the QRisk Cardiovascular Disease Risk Calculator (www.qrisk.org). Complete the online form for "Mr. Reading" (our test subject) as instructed below and then try changing some of the options for the modifiable risk factors of smoking, cholesterol level and obesity. Do the results surprise you?

Mr. Reading is a 54 year old white male, living near the University of Reading (RG6 5SE). He is a non-smoker and doesn't have diabetes. His parents are both alive and well. He doesn't have chronic kidney disease or atrial fibrillation and he isn't on any blood pressure treatment. He recently had a health check-up and his cholesterol/HDL ratio was 4.5, whilst his systolic blood pressure was 118mmHg. He is of an average build, being 180cm tall and weighing 75kg.

MODIFIABLE RISK FACTORS: SMOKING

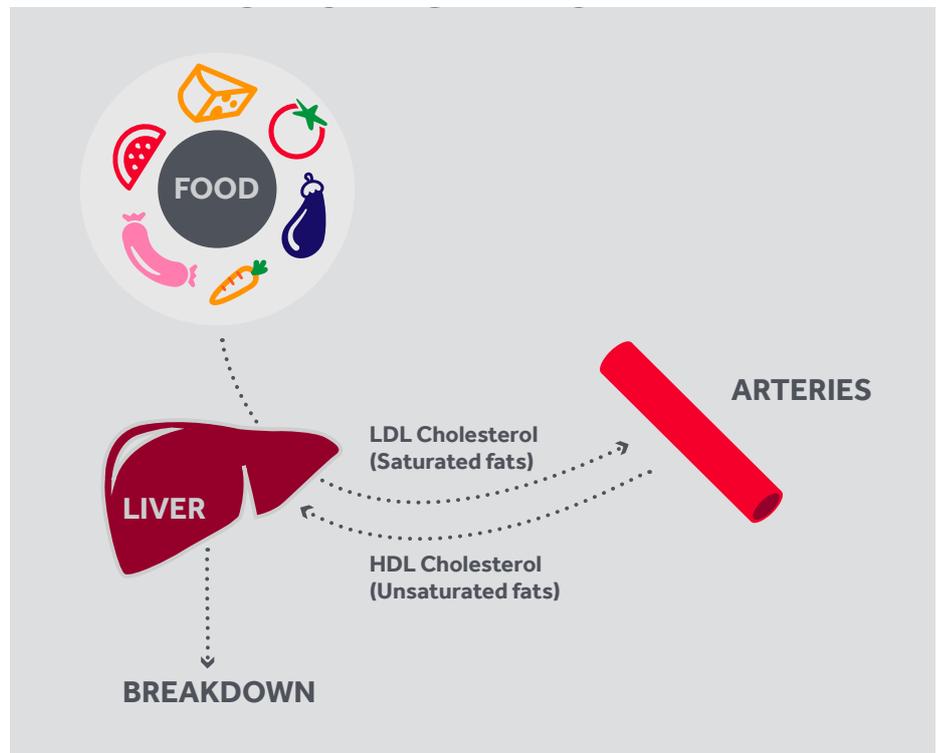
Smoking is the biggest preventable cause of cardiovascular diseases. Both active and passive smoking have been shown to increase a person's risk of cardiovascular disease, though we aren't sure exactly what the injurious compounds are. Theories include the reactive chemicals such as nicotine, carbon monoxide and free radicals, as well as the carcinogens and thiocyanate. Investigations to try and determine why or how smoking affects the risk of cardiovascular disease have shown that smoking has numerous effects on the cardiovascular system including:

- Increasing blood pressure
- Increasing platelet aggregation
- Damaging the endothelium
- Reducing HDL
- Increasing inflammation (atherosclerosis involves inflammation)
- Constricting blood vessels
- Carbon monoxide displaces oxygen from haemoglobin in the red blood cells, reducing the oxygen available to the heart muscle
- Reducing the age of menopause 2–3 years.

MODIFIABLE RISK FACTORS: CHOLESTEROL

FIGURE 5

Cholesterol is a vital lipid that is found in the membrane of every cell in the body as well as being the building block for making bile acids and steroid hormones such as testosterone and oestrogen. Cholesterol is found in foods such as animal fats, but it can also be made inside of the body, particularly by the liver. As a lipid, cholesterol isn't soluble in the blood so it needs to be carried by a protein. The lipoprotein LDL (low density lipoprotein) carries cholesterol from the liver to the body's tissues, whilst the lipoprotein HDL (high density lipoprotein) carries the cholesterol away from the tissues and back to the liver for breakdown and excretion. High levels of LDL-cholesterol have been associated with higher risks of cardiovascular disease, whilst high levels of HDL-cholesterol have been associated with a lower risk of cardiovascular disease. A better marker for cardiovascular disease seems to be the ratio of LDL-cholesterol to HDL-cholesterol.



MODIFIABLE RISK FACTORS: OBESITY

Obesity is defined as abnormal or excessive fat accumulation that presents a risk to health. Obesity is caused by an energy imbalance between energy intake (calories taken in through food and drink consumption) and energy output (calories burned by the body through physical activity, basic metabolic functions and food). Obesity is caused by the interaction of numerous environmental and genetic factors.

Obesity is a different risk factor to a lack of nutritional value in the diet.

Obesity can be measured using different criteria. Two commonly used measures are body-mass index (BMI) and waist circumference.

FIGURE 6

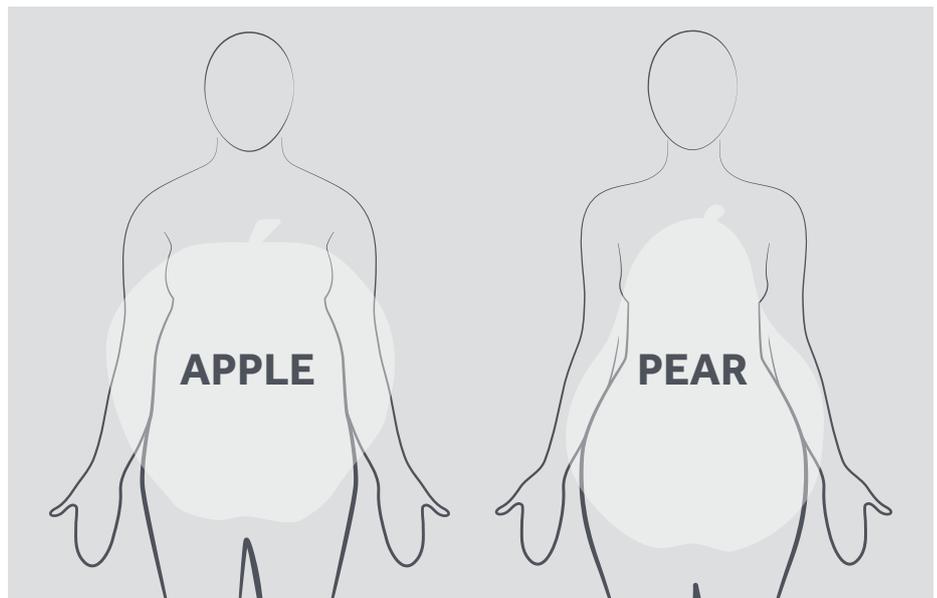
BMI is calculated by dividing a person's mass (in kg) by the square of their height (in m). A healthy BMI is between 18.5 and 25, whilst having a BMI between 25 and 30 is considered overweight and over 30 is considered obese. You can use this tool to calculate your BMI www.nhs.uk/Tools/Pages/Healthyweightcalculator.aspx

The use of BMI to assess obesity has limitations as there are variations from these numerical classifications for different ethnicities and people of an athletic build are often classified as overweight despite lower body fat measures (as muscle is denser than adipose tissue).

$$\text{BMI} = \frac{\text{WEIGHT (KG)}}{\text{HEIGHT (M)}^2}$$

FIGURE 7

Apple versus pear shapes. Depending upon where people store their excess adipose tissue they can be classified as apple-shaped or pear-shaped. Apple-shaped people tend to store their excess adipose tissue around their middle (giving a higher waist circumference) and have a higher risk of cardiovascular disease than pear-shaped people who tend to store their excess adipose tissue around their hips and thighs (and have a lower waist circumference).

**FIGURE 8**

The use of waist circumference, or waist to hip ratio may offer a better indicator of cardiovascular risk. A waist circumference greater than 94cm (men) or 80cm (women) indicates an increased risk of cardiovascular disease. Like BMI there are limitations to the use of waist circumference and different ethnicities have different target values.

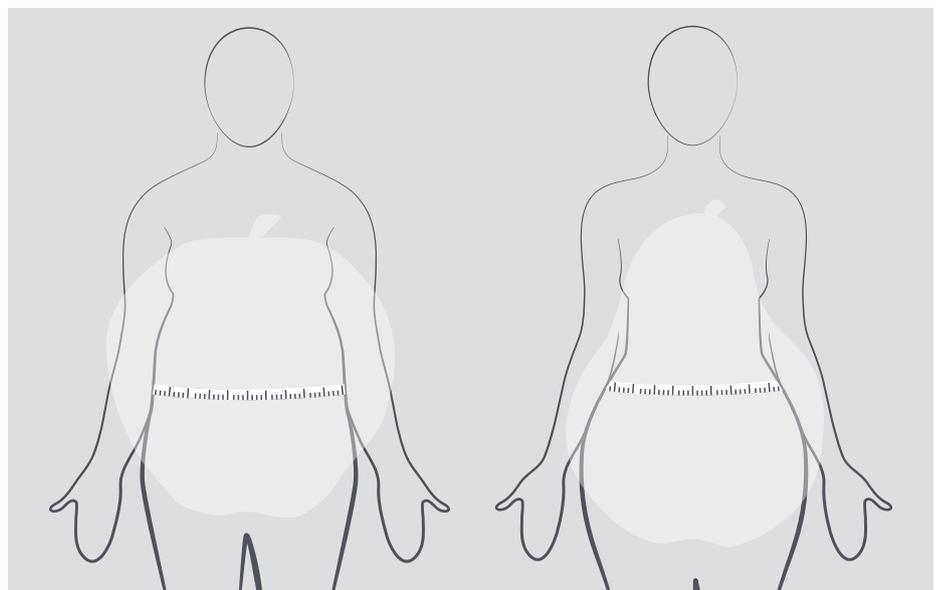
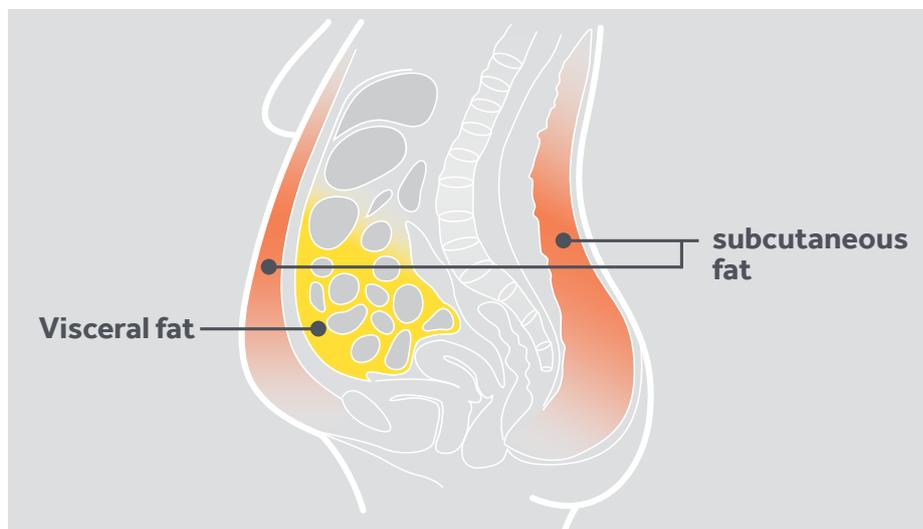


FIGURE 9

Visceral fat is the adipose tissue that surrounds the internal organs rather than the subcutaneous fat which lies just under the skin (the wobbly bits). Apple-shaped people may have more visceral fat than pear-shaped people, which may explain why they have a higher risk of cardiovascular disease.



PREVENTION OF CARDIOVASCULAR DISEASE: DIET

The food that we eat can be divided into macronutrients and micronutrients. Macronutrients include the protein, carbohydrate and fats that we eat, whilst the micronutrients include the vitamins and minerals that we eat. A healthy diet needs to provide the right balance of macronutrients for energy whilst also providing sufficient micronutrients that the cells in our body need to function.

The National Diet and Nutrition Survey (NDNS) publishes data on typical UK diets and UK recommendations for several components of the diet <http://bit.ly/1F1psJH>

The Food Analysis Worksheet summarises these values for several common dietary factors including oily fish, meats, fruit and vegetables and salt intake, enabling you to compare your own diet to the UK recommendations. If you wish to, you can also compare your diet to the UK recommendations for several other dietary factors.

If you would like to make changes to your diet it may be necessary to seek advice from your healthcare provider as dietary changes can affect and be affected by medications and various medical conditions. The NHS has lots more information on how to eat a healthy diet at www.nhs.uk/Livewell/Goodfood/Pages/eatwell-plate.aspx

PREVENTION OF CARDIOVASCULAR DISEASE: PHYSICAL ACTIVITY

Physical activity encompasses the energy expenditure through occupational, leisure and transport activity. A lack of physical activity is associated with an increased risk of cardiovascular disease. Sedentary behaviour is a group of behaviours that occur whilst sitting or lying down that require very low levels of energy expenditure (e.g. watching television, sitting at school or work, using motorised transport). Sedentary behaviour is also independently associated with increased risk of cardiovascular disease. Therefore a person who achieves the recommended 150 minutes per week of moderate physical activity can still be at an increased risk of cardiovascular disease if they spend a large portion of their time being sedentary.

The British Heart Foundation has collated and summarised data from several studies on physical activity and reports both the typical and recommended levels of activity in the UK (Physical Activity Statistics 2012). The report can be found at www.bhf.org.uk/publications/view-publication.aspx?ps=1001983.

The Activity Analysis Worksheet contains some of these values, enabling you to compare your own activity and sedentary behaviour to typical UK values and the UK recommendations.

If you would like to be more active it may be necessary to seek advice from your healthcare provider prior to starting. The NHS has lots more information on how to be more active at www.nhs.uk/livewell/fitness/Pages/Fitnesshome.aspx.