Predicting Cardiovascular Risk

Non-modifiable Risk Factors

Modifiable Behavioural/Lifestyle Risk Factors

Modifiable Biomedical Risk Factors

Social Determinants

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The Framingham Study

The 1948 Framingham Heart Study was a groundbreaking health research project which aimed to identify common characteristics which contributed to the development of cardiovascular disease (CVD). A large number of participants who had no history of CVD were recruited and monitored over many years. This led to the introduction in 1961 of the term 'risk factor' and the identification of some of the major risk factors that we know today: hypertension, dyslipidaemia, smoking, obesity, diabetes and lack of physical activity. Since the original cohort of Framingham participants, a second and third generation of participants have been studied. The Framingham Heart Study Group continues to conduct and influence research and practice today, expanding our understanding of other factors related to CVD such as: age, gender, ethnicity and psychosocial issues (NHLBI, 2018).

Explore the 'Framingham Heart Study' website for further details:
https://framinghamheartstudy.org/

Further Reading:

Mahmood, S. S., Levy, D., Vasan, R. S., & Wang, T. J. (2014). The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective. *Lancet (London, England)*, *383*(9921), 999–1008. https://doi.org/10.1016/S0140-6736(13)61752-3

Risk Scoring Systems

Assessing short-term risk

Several risk scoring systems are available to assist clinicians in the prediction of individual risk of future CVD development or events. Examples of these include:

- Scottish Intercollegiate Guidelines Network (SIGN) ASSIGN score (SIGN, 2017). http://assign-score.com/
- QRISK3 risk calculator (used in England and Wales) (Hippisley-Cox et al., 2017). https://qrisk.org/three/
- European cardiovascular disease risk assessment model– SCORE2 (European Society of Cardiology, 2021). https://www.escardio.org/Education/Practice-Tools/CVD-prevention-toolbox/SCORE-Risk-Charts

- Framingham Risk Score (D'Agostino et al., 2008). https://qxmd.com/calculate/calculator_252/framingham-risk-score-2008

Each of these risk calculators offers either an estimated relative risk or risk percentage over a period of time, such as 10 years. However the criteria vary within each of these scoring systems and do not deliver a lifelong prediction, a key factor in progressive conditions such as CAD. Additionally, short term risk calculation is mostly governed by age (ESC, 2016). Modest increases in risk factors only have a small effect on short-term risk in men under the age of 45 and women over the age of 65 (SIGN, 2017). This can result in younger individuals and women in particular, not reaching treatment thresholds (ESC, 2016).

Assessing life-time risk

Life-time CVD risk models identify individuals at high-risk of CVD over both the short and long term. In young individuals, lifetime risk may provide more information than short-term risk. An example is the LIFE-CVD calculator (https://u-prevent.com/calculators/lifeCvd). This accounts for competing risks from other illnesses over the remaining expected time that the individual will live. In addition, the Joint British Societies (JBS3) risk calculator for 'prevention of cardiovascular disease' has the ability to estimate 10-year risk and also life-time risk of CVD events (British Cardiac Society et al., 2014: http://www.jbs3risk.com/). A life-time risk calculation is a useful way of communicating about risk factors (ESC, 2016). JBS3 (2014) guidelines recommend lifetime risk CVD calculation to assess burden of cardiac disease in a population. While intensive risk factor lowering in patients with established disease or at high risk of developing CVD is recommended, the strong message for patients is the importance of understanding the life-time consequences associated with their current life-style and the opportunity for health behaviour change. Our greater understanding of risk and multiple risk factors may in future result in a more tailored approach or individualised risk profile.

Risk scores for patients with known CVD

There are several reliable risk scoring systems that predict the likelihood of further cardiovascular events or death. These include:

- GRACE (Global Register of Acute Coronary Events) Risk Score 2.0 (Fox et al., 2014). Available at: https://www.outcomes-umassmed.org/grace/acs_risk2/index.html

- SMART risk score for recurrent vascular events (Dorresteijn et al., 2013). Available at: https://u-prevent.com/calculators
- TIMI risk score for unstable angina and non-ST elevation MI (Antman et al., 2000). Available at: https://www.mdcalc.com/timi-risk-score-ua-nstemi

Further Reading:

- **Section 3.2.4 'Communication of cardiovascular disease risk'** from the European Guidelines on cardiovascular disease prevention in clinical practice. (2021). *European heart journal, 42*(34), 3227-3337.
- https://doi.org/10.1093/eurheartj/ehab484
- **Section 3.3 'Risk Scoring Systems'** from SIGN 149 (2017). *Risk estimation and the prevention of cardiovascular disease: a national clinical guideline.* https://www.sign.ac.uk/assets/sign149.pdf

Risk Factors

Risk factors can be considered as modifiable or non-modifiable, although some risk factors do not fit into these categories (NICE,2020).

Non-modifiable risk factors include:

- Age
- Gender
- Ethnicity
- Family history of CVD

Modifiable risk factors include:

- Smoking
- Overweight and obesity
- Unhealthy Diet
- High alcohol intake
- Lack of physical activity/sedentary lifestyle
- Low blood level of HDL cholesterol
- High blood level of non-HDL cholesterol

Comorbidities that can increase the risk of developing CVD include:

- Dyslipidaemia (familial and non-familial)
- Hypertension
- Pre-diabetes/metabolic syndrome
- Diabetes Mellitus

Other factors to consider include:

- Stress
- Socioeconomic status
- Working conditions
- Social isolation/social support
- Geographic environment

(ESC, 2021; NICE, 2016; SIGN, 2017)

It is thought that **cardiac rehabilitation** produces its effects through behaviour change. In 2011 a Cochrane review (Heran et al. 2011) found that cardiac rehabilitation had a 26% reduction in cardiac mortality and a 31% reduction in hospital admissions.

The evidence of the benefits of cardiac rehabilitation has in more recent times been called into question as some believe the extensive improvements in medical intervention in CAD management has reduced the beneficial effects of cardiac rehabilitation. A further Cochrane review (Anderson et al 2016) concluded that from a total of 63 studies exercise based cardiac rehabilitation continues to reduce cardiac mortality, hospital admissions and improve quality of life in comparison to no –exercise controls.

It is important to highlight that for many individuals CAD can be 'managed' with success. This allows people to believe that control can be gained over their fate and that it is not all 'too late'. Without this hope, those living with CAD and their families can lapse into depression and have a passive approach to the condition.

Non-modifiable risk factors

Age

The population of older individuals is rising globally with it estimated that 1 in 6 people in the world will be 60 years old or over by 2030 (WHO, 2021). CAD is the largest contributor to morbidity and mortality within this population (Rogers et al., 2019). Aging has a major role in the deterioration of cardiovascular functionality which contributes to the increased risk of CVD (Yazdanyar & Newman, 2009). The greater the burden of coronary atherosclerosis in a person, the more likely that plaque rupture will occur with older people carrying a greater plaque burden than younger people (Jonas et al., 2021).

Men over 65 years old and women over 75 years old usually have a high 10-year CVD risk (ESC, 2021). Development of other cardiac risk factors including hypertension, obesity and diabetes also increase with age (Roberts et al., 2019). Additionally, frailty among older adults also contributes to an increased risk of CVD (Orkaby, 2021).

For specific information on aging and rehabilitation, please see the 'Supporting Under-represented Groups' chapter.

Further Reading: Rodgers, J. L., Jones, J., Bolleddu, S. I., Vanthenapalli, S., Rodgers, L. E., Shah, K., Karia, K., & Panguluri, S. K. (2019). Cardiovascular Risks Associated with Gender and Aging. *Journal of cardiovascular development and disease*, *6*(2), 19. https://doi.org/10.3390/jcdd6020019

Gender

CVD affects both men and women. As of 2021, an estimated 4 million men and 3.6 million females in the UK were living with CVD (BHF, 2021). CVD is the leading cause of death in women worldwide, primarily due to CHD and stroke (Mehran & Vogel, 2021). Twice as many women in the UK die from CHD than breast cancer (BHF, 2021).

However, observational studies indicate that prior to menopause, women are relatively protected against CVD development compared to men. Women present with CVD 10 years later than men and compared to their male age-matched equivalent, premenopausal women have reduced incidence of CVD (Lorga et al., 2017). These gender differences are largely attributed to sex hormones and their associated receptors (Garcia et al., 2016). In particular, oestrogen has been recognised for its cardioprotective effect and has been directly associated with the lower incidence of CVD in premenopausal women compared to men of the same age (Lorga et al., 2017). Additionally, menopausal women are at greater risk of many CVD associated risk factors such as hypertension, diabetes and obesity which further increases CVD risk.

Oestrogens have been shown to have a physiological effect on cardiovascular health. This includes a reduction in oxidative stress and inflammatory markers, improved endothelial and myocardial function, a direct impact on calcium homeostasis and an effect on plasma lipids (Xiang et al., 2021). However, the use of hormone replacement therapy is largely controversial, as some studies show a greater risk to benefit ratio in some women (Lorga et al., 2017). There have however been reports of cardioprotective benefits in women when hormonal replacement is introduced in early menopause which suggests there may be a "critical window" for this type of therapy (Harman et al., 2014).

BHF in 2019 published a report detailing the stark inequalities in the awareness, diagnosis and treatment of heart attacks between men and women in the UK. The risk of CVD in women is often underestimated due to the misperception that women are more 'protected' than men against CVD (Maas & Appelman, 2010). In addition it is thought that presentation of CVD in women may differ from men and that women have a higher tendency to present with what may be considered atypical chest pain, dyspnoea, nausea, unexplained fatigue, and sleep disturbance. It is this atypical presentation that leads to misdiagnosis due to symptoms frequently assigned to other co-morbidities e.g. dyspnoea and respiratory disease (Keteepe-Arachi & Sharma, 2017) (see chapter "Burden of CAD" for further information on chest pain and diagnosis in women). However, research published in 2019 (Ferry et al 2019) established that women actually experience the same key symptoms as men and therefore it is important women are able to identify and act on these symptoms when they present. This raises the question as to what then leads to under or misdiagnosis of cardiac events in women.

Women have a similar or slightly higher prevalence of angina to men (Ford & Berry, 2020) and are also thought to be more likely to experience silent ischaemia and ischaemic events. Furthermore, diagnosis of angina in women may be complicated by a higher prevalence of non-obstructive disease and less defuse disease patterns which are often overlooked resulting in under treatment (Ford & Berry, 2020). NICE (2011) guideline [CG126] states that angina symptoms should not be investigated or treated differently in men and women.

Further Reading:

- Garcia, M., Mulvagh, S. L., Merz, C. N., Buring, J. E., & Manson, J. E. (2016). Cardiovascular Disease in Women: Clinical Perspectives. *Circulation research*, *118*(8), 1273–1293. https://doi.org/10.1161/CIRCRESAHA.116.307547
- Keteepe-Arachi, T., & Sharma, S. (2017). Cardiovascular Disease in Women: Understanding Symptoms and Risk Factors. *European cardiology*, *12*(1), 10–13. https://doi.org/10.15420/ecr.2016:32:1
- Lorga, A., Cunningham, C. M., Moazeni, S., Ruffenach, G., Umar, S., & Eghbali, M. (2017). The protective role of estrogen and estrogen receptors in cardiovascular disease and the controversial use of estrogen therapy. *Biology of sex differences*, *8*(1), 33. https://doi.org/10.1186/s13293-017-0152-8

Ethnicity

People from ethnic minority backgrounds form around 14.4% of the UK's population. Most of these individuals are of South Asian (Indian, Pakistani, Bangladeshi, Sri Lanka) or Black (African, Caribbean) descent with an increase in other minority ethnic groups. CVD is a major cause of death among all ethnicities. However, the presentation of CVD differs among ethnic groups.

Those from **South Asian** descent are at a higher risk for CVD, particularly CAD, and this may present earlier than individuals from other ethnic groups (Gupta et al., 2006). A large proportion of this risk can be explained by CVD risk factors including obesity, hypertension, diabetes, hyperlipidaemia, and physical inactivity In the South Asian population, a heightened susceptibility to risk factor clustering (dyslipidaemia, obesity and hypertension) may lead to the development of metabolic syndrome, another key issue in CAD. Additionally, adverse changes to lifestyle and diet upon migration to the UK also has a role in risk of CVD (Jain et al., 2017).

Black ethnic groups have a lower risk of CAD but their incidence of and mortality from stroke is much higher than the majority of the population. They are also more likely to have strokes at a younger age (Raleigh & Holmes, 2021). Hypertension appears to be the primary risk factor in this group. The type of hypertension does however differ to the Caucasian population, being of the low renin type. There is also a greater sensitivity to salt and water retention (Spence & Rayner, 2018). Similar to the associated risk factors seen in the UK South Asian population, the risk is also attributed to diabetes, obesity, lack of physical activity as well as smoking (Stroke Association, 2014).

Although findings often do not agree on an exact cause of CVD within ethnic groups, continuous research is required to further investigate and care for those at risk. Services must also offer options which are culturally sensitive to meet the needs of all those at risk of CVD within local populations.

For specific information on ethnicity and rehabilitation please see the 'Supporting under-represented groups' chapter.

Further Reading:

- Jain, A., Puri, R., & Nair, D. R. (2017). South Asians: why are they at a higher risk for cardiovascular disease?. *Current opinion in cardiology*, *32*(4), 430–436. https://doi.org/10.1097/HCO.0000000000000411
- **Section on 'Cardiovascular disease'** from: Raleigh, V. & Holmes, J. (2021). *The health of people from ethnic minority groups in England.* Available at: https://www.kingsfund.org.uk/publications/health-people-ethnic-minority-groups-england

Family History

In individuals with a family history of CVD, in a first-degree relative before 60 years of age, the risk of a coronary event is doubled (SIGN, 2017). Family history of CVD can impact on future CVD risk depending on the age and number of first-degree relatives who were affected (Kolber & Scrimshaw, 2011). An individual is considered to have a family history if their father or brother was diagnosed with CVD under 55 years or their mother or sister were diagnosed with CVD before they were 65 years (NHS, 2018). The identification and management of these individuals is particularly important considering the twofold increase in risk of those with parents affected by CAD, which is even higher in those who have siblings affected by the condition (Patel & Ye, 2011).

Familial hypercholesteroleamia (FH) is a genetic condition passed down through generations and causes excessively high LDL cholesterol levels in the blood which can be resistant to standard drug treatments, lifestyle and dietary changes. Caused by gene mutations that impact on the way cholesterol is cleared from the body results in an accumulation of cholesterol in the bloodstream, subsequently increasing risk of CAD. Diagnosed with a simple genetic blood test and assessment of family history, early treatment can improve long term risk. Drugs used to treat FH will depend on the genes affected and the response to standard treatments such as statins.

Further Reading: Kolber, M. R., & Scrimshaw, C. (2014). Family history of cardiovascular disease. *Canadian family physician Medecin de famille canadien*, *60*(11), 1016. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4229162/

Modifiable behavioural/lifestyle risk factors

Smoking/ tobacco use

Smoking is the leading cause of preventable illness and premature death in the UK, accounting for around 78,000 deaths per year (Action on Smoking and Health, 2021). Cigarettes contain an estimated 7000 chemical components, including at least 70 carcinogenic compounds. Substances such as: nicotine, tar, carbon monoxide, butane benzene, arsenic, ammonia, formaldehyde and acetone, are all found within cigarettes smoke (Prochaska & Benowitz, 2019), with nicotine being the key compound which leads to addiction. Although nicotine is the addictive component, it is the additional toxins contained within tobacco smoke which lead to health related issues (Action on Smoking and Health, 2021). Chewing tobacco products are used widely by some ethnic minority groups in the UK. This method of tobacco use, although less hazardous, remains detrimental to health (Action on Smoking and Health, 2019).

Nicotine can induce pleasure as well as producing effects which control stress and anxiety. Nicotine acts on nicotinic acetylcholine receptors (nAChRs) that are found throughout the nervous system. Stimulation of these receptors releases a variety of neurotransmitters within the brain including dopamine, which is known to signal a pleasurable experience or sense of reward, reinforcing the behaviour. However, tolerance develops to many of the effects of nicotine which can lead to the pleasure experienced from smoking a cigarette to disappear. As nicotine levels reduce, withdrawal symptoms develop, reversing the positive effects of nicotine. This typically leads to a cycle during which nicotine levels rise in the blood, substantial tolerance develops, and smoking occurs to relieve withdrawal symptoms (Prochaska & Benowitz, 2019).

Smoking and cardiovascular risk

Smoking is a major cause of CVD and causes approximately one of every five deaths from CVD (WHO, 2020). Smoking increases the risk of CVD in many ways:

- Damaging the lining of the arteries, including the coronary arteries.
- Releasing various free radicals which increase oxidation of LDL cholesterol causing foam cells to develop.
- Cholesterol levels are often elevated with the HDL to LDL ratio being decreased.

- Smooth muscle proliferation increases under the endothelium, extending the atheroma plaque.
- Fibrinogen increases along with platelet aggregation, increasing the risk of clot formation.
- Causes blood vessels to constrict which leads to high blood pressure and a reduction in blood supply to the heart.
- Carbon monoxide saturates haemoglobin reducing oxygen supply to the myocardium.

(Action on Smoking and Health, 2021).

Smoking-related CVD risks are highest in current and recent smokers, compared to those who have never smoked and those who have quit in the distant past. Risk also rises with increasing duration of use and with greater intensity of smoking, as measured by the number of cigarettes smoked per day (Pirie et al., 2013). Smokers are twice as likely to experience a heart attack compared to non-smokers. The mortality rate during MI is also greater for those who smoke with around 60% of smokers dying. The risk is even higher in heavy smokers at around 80% (Scarborough et al., 2010). The risk of cardiovascular death in younger individuals is often minimised due to age. However, it is important to be aware that those under the age of 40 who smoke, are 5 times more likely to experience an MI than non-smokers of the same age, with those who commence smoking at a young age being at greatest risk (Mahonen et al., 2004).

Smoking cessation

The Office of National Statistics (2020) reported that around 14.1% of the adult population currently smoke. In 2019, more than half of UK adults who smoked said they wanted to quit smoking and 62.5% of those who had ever smoked reported that they had stopped. There was an increase of 22% in smoking quit attempts in 2020 compared to 2019 for those living in England with an increase in the quitting success rate from 14% to 23% (PHE, 2020).

Smoking cessation causes a variety of withdrawal symptoms with the main ones including: nicotine cravings, increased appetite, depression, restlessness, poor concentration, irritability, disturbed sleep and light-headedness (Action on Smoking and Health, 2020). These feelings are temporary and will fade once the individual has become used to no longer smoking.

Smoking cessation significantly reduces the risk of developing CVD including heart attack and stroke (Carreras et al., 2015). Those who stop smoking after an MI at 50 years or younger reduce their risk of mortality by 70% compared to those who continue to smoke (Biery et al., 2020). Even in heavy smokers (20 or more per day), risk of CVD is reduced within 5 years of stopping smoking (Visseren et al., 2021). Some of the positive effects of stopping smoking occur rapidly while others take longer to achieve (Table 4).

Table 4. Health benefits of smoking cessation (Action on Smoking and Health 2020).

Cessation Time	Health Benefits
20 minutes	Pulse rate returns to normal.
8 hours	Oxygen levels return to normal, and carbon monoxide levels in the blood reduce by half.
48 hours	Carbon monoxide is almost eliminated from the body. Lungs start to clear out smoking debris. The ability to taste and smell improves
72 hours	Breathing feels easier. Bronchial tubes begin to relax, and energy levels increase
2 – 12 weeks	Circulation improves
3 – 9 months	Lung function increases by up to 10%, improving coughs, wheezing or breathing problems
1 year	Excess risk of a heart attack reduces by half.
10 years	Risk of death from lung cancer falls to about half that of a continuing smoker
15 years	Risk of a heart attack falls to the same as someone who has never smoked.

One of the most significant factors which may predict successful smoking cessation is motivation (Perk et al., 2012). Effective communication by health care professionals can help to enhance the desire to stop. Motivation is often particularly strong after a sudden event such as MI or life changing interventions such as revascularisation. Smoking cessation commenced during hospital stays must be followed up to increase longer term success. Additional factors which contribute to successful smoking cessation are: living and working in a smoke free environment, being over the age of

35 years, having experienced a higher level of educational provision, being married or living with a partner and having only had one previous attempt at smoking cessation (Lee & Kahende, 2007).

NICE (2021) guideline [NG209] provides guidance for preventing tobacco uptake, promoting quitting and treating dependence. This is available at: https://www.nice.org.uk/guidance/ng209/resources/tobacco-preventing-uptake-promoting-quitting-and-treating-dependence-pdf-66143723132869

Additionally, the use of Nicotine Replacement Therapies (NRTs) such as patches, gum, lozenges, nasal sprays, inhalers, sublingual tablets and medications like Varenicline or Bupropion have been shown to increase the success of quitting smoking and aiding long-term smoking cessation (Hartmann-Boyce et al., 2018; Visseren et al. 2021). As with any medication, side-effects should be monitored closely. As of November 2021, Varenicline was unavailable in the UK due to supply disruption (NICE, 2021).

Electronic Nicotine Delivery Systems (ENDS) or "e-cigs"

Electronic cigarettes were designed to mimic the action of smoking, including delivering nicotine, by heating and transforming a liquid into an aerosol which is then inhaled. The liquid (often known as e-liquid), usually comprised of propylene glycol and glycerol, with or without nicotine and flavours, is stored in refillable cartridges or a reservoir (tank) (McRobbie et al., 2014). Blood nicotine levels are increased by 5mg/ml within 5 minutes of use, which is comparable to oral nicotine replacement therapy (NRT), although levels over time can equate to that of smoking cigarettes in experienced tank/cylinder users as seen in Diagram 1 (PHE, 2015). These devices have grown in popularity and are now the first choice of over the counter (OTC) nicotine replacement aid and are used by an estimated 1 in 20 adult smokers in England (PHE, 2015).

Diagram 1. Range of Electronic Nicotine Delivery Systems (ENDS) or ‘e-cigs’. (FDA, 2017)

Are e- cigs safe?

The use of e-cigs is likely to be considerably less harmful than smoking (NICE, 2021). The known harm from smoking is primarily caused by the toxins produced from the burning of tobacco (ASH, 2016). Although e-cigs do often contain nicotine and can still be addictive, they have been considered less harmful for this reason (ASH, 2016).

However, despite being less harmful to health than normal cigarettes, growing evidence suggests that e-cigs are not completely risk free. Whilst the long-term effects of e-cigs have yet to be determined, recent studies suggest that e-cigs are associated with an increased risk of cardiovascular morbidity and mortality (when compared to no smoking) (Puig-Cotado et al. 2020; Raja et al. 2020). It has also been suggested that e-cigs still generate harmful substances usually found in conventional cigarette emissions (Puig-Cotado et al., 2020; Walley et al., 2019). These components are generally present at significantly lower levels, varying depending on the device and the e-liquid (WHO, 2016) but there is still potential to cause similar adverse effects on the cardiovascular system (WHF, 2021).

The risk of e-cigs to bystanders is yet to be determined. There is some evidence which supports the idea that e-cigs can affect indoor air quality and cause bystanders to breathe in aerosols and their components in some capacity (Glantz & Bareham, 2018; Qasim et al., 2020).

Are e-cigs effective in smoking cessation?

Currently, e-cigs are not medically licensed by the Medicines and Healthcare products Regulatory Agency (MHRA) as a smoking cessation tool. Thus, they are not available commercially in the UK but are regulated by the Tobacco and Related Products Regulation (2016) (NICE, 2021).

Some sources have indicated that e-cig users may be less likely to stop smoking (Glantz & Bareham, 2018). Many individuals who quit conventional cigarette smoking become chronic e-cig smokers due to the addictive nature of nicotine (Middlekauff, 2020). Data suggests that up to 60% of e-cig users also smoke ordinary cigarettes thus becoming dual users (PHE, 2015). As a result, it has been suggested these types of users may increase their risks of developing CVD (WHF, 2021).

However, there is some evidence to support the use of e-cigs in aiding smoking cessation completely and in helping to reduce cigarette consumption, even in those not intending to stop (PHE, 2015). At the time of writing, the NHS and BHF strongly support the use of e-cigs as a smoking cessation tool. NICE guideline [NG209] (2021) recommends that individuals are advised of e-cigs as a successful short-term smoking cessation tool when combined with behavioural support and that clear up-to-date guidance is provided regarding use of e-cigs. It further advises discussions around ceasing tobacco use when using e-cigs, the length of time that e-cigs will be used and ceasing use of e-cigs when ready to do so.

More studies on the long-term effects of e-cigs are needed (Buchanan et al., 2019; NICE, 2021). The potentially dangerous impact of e-cigs on the cardiovascular system should also be taken into account. The World Health Organisation (2020) recommends that the safest approach is to use neither tobacco products nor e-cigs.

Further Reading:

- (NICE). (2021). *Tobacco: preventing uptake, promoting quitting and treating dependence NICE Guideline [NG209].* Available at: https://www.nice.org.uk/guidance/ng209/resources/tobacco-preventing-uptake-promoting-quitting-and-treating-dependence-pdf-66143723132869

- World Heart Federation (WHF). (2021). *E-cigarettes: a new threat to cardiovascular health*. A world heart federation policy brief. Available at: https://world-heart-federation.org/wp-content/uploads/E-cigarettes-Policy-Brief.pdf

Overweight/obesity

Being overweight or obese are terms used to define having abnormal or excessive body fat accumulation which may lead to impaired health. The rise in clinical obesity is considered a global epidemic. In 2016, more than 1.9 billion adults were considered overweight or obese, with over 4 million people dying each year as a result (WHO, 2021). In the UK, the obesity rate has almost doubled since the early 1990s with an estimated 28% of adults who are obese and 64% who are overweight (BHF, 2021).

Obesity is primarily a result of an imbalance between calorific intake and calorific expenditure, although genetics play an important role in the development of obesity. Both overweight and obesity are associated with CVD risk (BHF, 2021). Body fat or adipose tissue may be found under the skin as subcutaneous fat, around organs as visceral fat, within bone marrow as yellow bone marrow and in breast tissue. Adipose tissue is known to be a metabolic organ capable of synthesizing and releasing various compounds into the body (Perk et al,. 2012). Obesity may affect the cardiovascular system in many ways due to its influence on known risk factors such as hypertension, dyslipidaemia, insulin resistance (glucose intolerance and diabetes type 2), inflammatory markers and pro-thrombotic state (Powell-Wiley et al., 2021).

A cardiac imaging study (Marciniak et al 2021) of children in the Netherlands aged approximately 10yrs established that cardiac remodelling can happen in childhood, potentially leading to adult left ventricular dilatation and hypertrophy. This remodelling occurred in obese children with a BMI above 19 (equivalent to adult BMI of 25) due to increased demand on the heart. It is hoped that understanding these structural and functional changes of the heart during childhood may aid the future detection and stratification of risk in adulthood.

The NICE (2014) clinical guideline [CG189] on the identification, assessment and management of obesity includes recommendations on lifestyle, behavioural, dietary and pharmacological interventions and physical activity. This is available at: https://www.nice.org.uk/guidance/cg189/resources/obesity-identification-assessment-and-management-pdf-35109821097925

Intentional and appropriately managed weight loss in those who are overweight or obese can improve or prevent many of the weight related risk factors associated with CVD (Brown et al., 2016).

Body Mass Index

Weight is primarily assessed by calculating the individuals Body Mass Index (BMI). The BMI is calculated by dividing the weight in kilograms by the square of the height in meters (kg/m2). Those with a BMI of 25 or more (or > 23 for those of South Asian ethnicity) are classified as overweight, while those with a BMI of 30 or over are classified as obese. Obesity is sub-classified incrementally as class I, II and III with increasing BMI (NHS, 2019). Various tools are available to ease the assessment process (Figure 2). The American Heart Association estimate that the optimum BMI for adults aged between 18 and 85 years is 23-25 for white people and 23-30 for black people (Poirier et al., 2006). The use of BMI should however be used with caution in some groups such as those of Asian ethnicity and older people, where comorbidity risk factors may be of concern at low (South Asian's) or higher (elderly) than normal measurements (NICE, 2014).

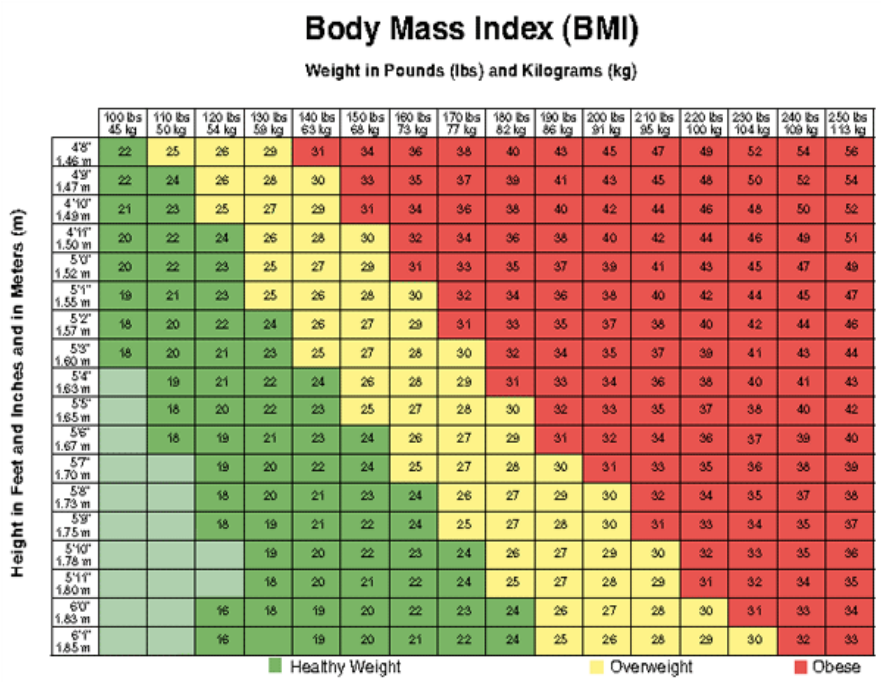

Figure 2. BMI chart
(U.S Department of Health and Human Services and National Institutes of Health, 2008)

Other Measures

Although increasing BMI is associated with CVD risk, a great deal of work has been done to assess the importance of adipose tissue distribution and comparing fat and

lean mass. Measurements include the use of **waist-to-hip circumference ratio** (WHR) and **simple waist measurement**. WHR measures the proportion of body fat stored around the hips and the waist. This is done by measuring the hips at the widest point over the buttock and then measuring the waist at the narrowest circumference around the natural waistline. The ratio is obtained by dividing the waist measurement by the hip measurement. In healthy women the ratio should be < 0.85, while in men the ratio should be higher, < 0.90 (World Health Organisation, 2008). Many studies have based their measures primarily on Caucasian participants. However, as the world's population is so diverse, there is a need for broader measurements which are more anthropologically sensitive and include different races and ethnicities. Additional factors which may influence cut off points for the clinical measures may also include different health factors which are highly influenced by abdominal obesity, this includes those at risk of or diagnosed with CVD, metabolic syndrome and type 2 diabetes.

The highest indicator of risk in relation to body fat for people with CVD or diabetes is a higher level of **central obesity**, which can be determined by simply obtaining the waist measurement. This is achieved by measuring under clothing. The anatomical waist is found by measuring half way between the base of the rib cage and the superior iliac crest. Measurements should be taken at the end of normal expiration in the standing position with the body weight evenly distributed. Greatest accuracy is achieved following overnight fasting and when the individual is in a relaxed enough state to reduce abdominal tension. Measurements should be taken twice with any difference less than 1cm the average should be calculated (WHO, 2008).

Although useful in enhancing clinicians understanding of obesity and its effect on health, the use of WHR and waist circumference do not appear to have enough evidence to support their replacement of BMI measures within practice. Instead, their **use should be to complement the use of BMI** in those with a BMI <35, in order to develop a greater understanding of CVD risk (Ross et al., 2020).

In the UK, health risk assessments should be based on both the BMI as well as the waist circumference (Table 5). This provides the opportunity for risk to be discussed more fully in terms of the potential for long term health problems. Using this approach also allows the specialist clinician to discuss the level of intervention required, from the use of first line strategies focusing on behavioural interventions, diet and physical activity advice to more intensive interventions such pharmacological therapy and surgery. The clinical approach should be adjusted according to the individual's health

related needs and the potential benefits of losing weight, with the level of intervention potentially being higher for those with comorbidities (NICE CG189, 2014).

Table 5. BMI and waist circumference targets (NICE, 2017)

BMI Classification	Waist circumference		
	Low	**High**	**Very High**
Overweight	No increased risk	Increased risk	High risk
Obese I	Increased risk	High risk	Very high risk

For men, waist circumference of less than 94 cm is low, 94–102 cm is high and more than 102 cm is very high.

For women, waist circumference of less than 80 cm is low, 80–88 cm is high and more than 88 cm is very high.

Note: for Asian men and women, a waist circumference of > 90 cm or >80 cm respectively would automatically denote the higher risk category.

Diet

Diet is known to influence the development and progression of CVD. This may be associated with the effect of diet on known risk factors such as serum cholesterol, blood pressure, diabetes or body weight, but also due to other physiological responses that occur (Perk et al., 2012). Research to date has looked at not only specific nutritional components but also at dietary patterns such as the consumption of a Mediterranean diet. A Mediterranean diet contains a high fruit and vegetable intake mixed with legumes, whole grains, fish and unsaturated fatty acids. A small intake of alcohol, particularly red wine, is also accepted as part of this diet. It is thought that the greater the adherence to a balanced diet consuming foods within the Mediterranean food groups, the greater the benefit conferred (Cena & Calder, 2020). It is also often easier for patients to understand dietary advice in terms of whole food groups such as the Mediterranean diet rather than being giving advice purely on individual nutrients. It is important therefore practitioners are able to understand the nutrient variations in whole food options, especially in how they are prepared or cooked.

In respect to nutrients, research is generally focused primarily on fats or fatty acids, fibre, vitamins and minerals.

Fats

The impact of fats on the cardiovascular system has been studied for many years, with the composition of fats, triglycerides, tri-esters, glycerol and fatty acids, being of greatest interest. Fatty acids are divided into types: saturated, polyunsaturated and mono-unsaturated. Further areas of interest are n-3 fatty acids, also known as omega 3 fatty acids.

The general guidance is that fat should account for less than 30% of the bodies total energy intake, with 7% or less being saturated in origin (NICE CG126, 2016). Saturated fatty acids are primarily obtained from animal sources such as: cheese, cream, ghee, butter and fatty meat, although vegetable sources include coconut oil and palm kernel oil. Monounsaturated fatty acid foods include olive oil, rapeseed oil, avocados and some types of nuts such as peanuts. Sources of polyunsaturated fatty acids include nuts, particularly walnuts, seeds and oily fish. It is many of these poly and monounsaturated fats that are advocated as part of a Mediterranean diet. Fat intake from good quality and natural sources are recommended, while avoiding processed and convenience foods, cakes, pastries etc. where possible. When eating meat, avoid processed meat. It should be lean, trimmed of visible fat and chicken should have the skin removed. Preparing and cooking food should be done with as little fat as possible. Food should be steamed, poached, grilled, baked, micro-waved, and casseroled or lightly stir fried instead of deep frying.

Fats and CVD risk

Eating higher amounts of saturated fat is associated with increased low-density lipoprotein (LDL) which increases the risk of CVD (Boren et al., 2020). A systematic review and meta-analysis of randomised controlled trials (15 studies) by Hooper et al (2020) concluded that cutting down on saturated fat led to a 21% reduction in CVD risk. NICE (2016) guideline [CG126] recommends that people at high risk of or with CVD are advised to reduce their saturated fat intake and increase their mono-unsaturated fat intake.

Omega-3 fatty acids

The three main omega-3 fatty acids found in foods are alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). NICE (2020) guideline [NG185] does not advise recommending the consumption of oily fish for the

sole purpose of preventing a further MI. It also advises that omega-3 fatty acid capsules or supplemented foods should not be offered or recommended to individuals to prevent a further MI. If individuals wish to increase their consumption of fish or take omega-3 fatty acid supplements, there is no evidence of harm from doing so.

Fruit and Vegetables

As with many lifestyle associated health behaviours, measuring the positive components of dietary intake is complex. The publication of meta-analysis of cohort studies such as the one conducted by Dauchet et al (2006) has provided clearer evidence in relation to the health benefits of fruit and vegetables in diet and in reducing the risk of CAD, however the exact mechanisms are as yet unclear. It has been suggested that there are a variety of nutritional components within fruit and vegetables such as: antioxidants, flavonoids, potassium, fibre and folate, which may influence CVD. It is clear however, that the benefit of fruit and vegetable consumption is related to the **amount** of fruit and vegetables taken, with those consuming at least five portions of fruit and vegetables per day experiencing a risk reduction of 17-21% (European Heart Network, 2011). However questions do remain regarding the optimal amount and type of fruit and vegetables that confer the strongest risk reduction for CVD. According to a meta-analysis by Aune et al (2107) reductions in cardiovascular mortality were observed with intake of apples/pears, citrus fruits, green leafy vegetables/salads and cruciferous vegetables. This is particularly interesting when considering the cardiovascular risk in vegetarians. In a study conducted by Appleby et al (2002) the incidence of CAD was 24% lower in lifelong vegetarians and 57% lower in lifelong vegans when compared to those who consumed animal products.

SIGN (2017) guideline [149] recommends consuming at least 5 portions of a variety of fruit and vegetables per day (400g). One portion (approximately 80g) is equal to a medium sized piece of fruit, one cup or two to three heaped tablespoons of vegetables. It is worth noting that 30g of dried fruit is the equivalent of 80g of fresh fruit. Unsweetened 100% freshly squeezed fruit juice, vegetable juice and smoothies (150ml or small glass) can only count towards 1 portion in the day. NHS Choices suggest that smoothies and fruit juices are best taken at mealtimes as blended fruits release natural sugars.

Fibre

The intake of fibre within the diet has been linked to CVD risk reduction, a further important aspect of fruit and vegetables in the diet. A systematic review of the evidence in relation to dietary fibre has demonstrated a risk reduction of around 20% in those with a high fibre diet (Threapleton, 2013). This reduction in risk may be associated with improved glucose control and reduction in total and LDL cholesterol (McRae, 2017). The recommended dietary fibre intake for adults is 30g per day (BDA, 2021).

Vitamins and Minerals

In respect to vitamins and cardiovascular health, the greatest interest has been on those with antioxidant properties; vitamin E, C and Beta carotene (a form of vitamin A). The consumption of antioxidant rich diets appears to support the intake of these vitamins in studies but the use of supplements is not recommended (European Heart Network, 2011). Other sources of antioxidants are obtained through polyphenols which are obtained primarily through plant based food stuffs. Polyphenols include flavonoids, phenolic acids and tannins. Research has been conducted on various foods including green tea, cocoa rich chocolate and red wine. Findings have been interesting but as yet are inconclusive to provide specific recommendations (European Heart Network, 2011).

Phytosterols (plant sterols and stanols) are similar in chemical structure to cholesterol. They are found naturally in vegetable oils, nuts, grains, seeds and leaves. They act directly on the gut reducing absorption and increasing the excretion of cholesterol (Baic 2006). They have been added to many foods such as spreads, milk, cheese, yoghurt and drinks as a method of reducing CHD risk by reducing LDL-C. They have little effect on HDL-C or triglycerides. A suggested daily intake of 2-3g per day may reduce LDL-C by approximately 10% (Cabral & Klein, 2017).

On-going interest continues in other dietary vitamins. These include the B-vitamins and their effect on homocysteine (Perk et al., 2012). There appears to be growing evidence of the benefits of lowering homocysteine levels using vitamin B therapy in the prevention of ichaemiac and subarachnoid stoke in particular (Yaun et al (2021). Low serum Vitamin D levels have been associated with an elevated risk of CVD, however a recent meta-analysis by Barbarawi et al (2019) looking at over 20 studies and 81000 individuals concluded vitamin D supplementation does not confer any cardiovascular protection.

Salt

The UK dietary recommendation for salt is no more than 6g per day (FSA, 2018). On average, adults in the UK are eating 8 grams of salt per day (PHE, 2016). High salt consumption contributes to high blood pressure and increases the risk of heart disease and stroke (WHO, 2021). Strong evidence indicates that salt reduction lowers blood pressure and reduces the risk of CVD (He & MacGregor, 2018).

Member States of the World Health Organisation (WHO, 2020) have set a target to reduce the salt intake of the global population by a relative 30% by 2025**.** NICE recommendations on national policy for diet (2021) state that further reductions in salt should be promoted with the possibility of aiming to reduce salt intake to an ambitious target of less than 3 grams per day in the UK.

Food labelling

Mandatory ("back of pack") nutrition labelling was introduced in 2016 for the majority of pre-packed foods (DOH, 2016). The following items must be included on the package or on the label:

- Energy value must be displayed in both kilojoules (kJ) and kilocalories (kcal) contained in 100g or 100ml of the food.
- The amount of fat, saturates, carbohydrates, protein and salt must be displayed as the weight in grams (g) present in 100g or 100ml of the food.

As of 2021, pre-packed food for direct sale (PPDS) labels must include the food name and a full ingredients list with allergenic ingredients within the list (Food Standards Agency, 2021). This is known as Natasha's Law.

To help consumers make healthier choices, most packaged food products will voluntarily display simple nutrition information on a label on the front of the pack. This will show information relating to energy, fat, saturates, sugars, salt (in g) (Table 6). Often traffic light indicators, such as red (high), amber (medium), and green (low) colour is given for each of the core nutrients.

Table 6. Reference Intakes for different nutrients (adults) (Food and Drink Federation 2020)

Energy or nutrient	Reference Intake
Calories (kcal)	2, 000

Fat (g)	70
Saturated fat (g)	20
Sugars (g)	90
Salt (g)	6

The Reference Intakes for an adult are based on the requirements for an average female with no special dietary requirements and an assumed energy intake of 2000 kcal.

Alcohol

Consuming alcohol can increase the risk of CVD in several ways; hyperlipidaemia, vasoconstriction, clotting instability and arrhythmia (European Heart Network (EHN), 2011). Alcohol also adds to calorific intake which can lead to obesity and hypertension. Evidence is consistent in showing that heavy alcohol consumption is associated with the highest risk of CVD and that light to moderate consumption carries a lower risk. A moderate consumption of alcohol has been suggested to produce a protective effect on CVD (Yoon et al., 2020). The Ethanol component of alcohol may be the main factor responsible for this (Perk et al. 2012). Evidence has indicated that the moderate consumption of red wine is particularly favourable. While alcohol appears to increase plasma HDL-C alcohol, the intake of polyphenols may play a key role in the reduction of T2D incidence and LDL oxidation (Castaldo et al., 2019).

Other studies have challenged the view that light to moderate alcohol consumption confers reduced risk of cardiovascular disease compared with abstaining from alcohol. SIGN (2017) guideline [149] recommends that patients with or without CVD should be advised to reduce alcohol consumption and that even light to moderate alcohol consumption may increase cardiovascular risk.

The Department of Health (2016) guidelines for men and women on alcohol consumption and associated health risks should be followed:

- To keep health risks to a low level it is safest not to drink more than 14 units a week on a regular basis.
- If you regularly drink as much as 14 units a week, it is best to spread your drinking evenly over 3 or more days.

- The risk of developing a range of health problems, including stroke and some cancers, increases the more you drink on a regular basis.
- If you wish to cut down the amount you drink, a good way to help achieve this is to have several drink-free days each week, and limit the amount you drink on any single occasion.

Here are some unit examples to help you:

- Standard glass of wine (12% ABV) 175 ml = 2.1 units
- Large glass of wine (12% ABV) 250ml = 3 units
- Pint of lager/beer (3.6% ABV) = 2 units
- Bottle of lager/beer (5% ABV) = 1.7 units
- Single shot of spirits (40% ABV) 25 ml = 1 unit
- Single large shot 35ml = 1.4 units
- Fortified wine/sherry 50 ml = 1 unit

  The Heart Manual (2016)

Physical Activity

Physical activity can protect against CAD and promotes the reduction of secondary events. Activity has a beneficial effect on many of the other cardiovascular risk factors. It improves weight control through weight loss, aids the prevention of weight gain, delays or prevents the development of hypertension, increases the bodies HDL-C concentration and reduces the risk of developing diabetes (British Cardiac Society et al., 2014).

Physical activity and exercise are discussed in detail in the physical activity chapter.

Modifiable biomedical risk factors

Lipids

Studies have shown the role that dyslipidaemia and hypercholesterolaemia play in the development of CVD. Dyslipidaemia does not always have a familial link. Secondary causes include diabetes mellitus, untreated hypothyroidism, obesity, high alcohol consumpyion and Cushing's syndrome. Some medications may also be linked to abnormal lipid profiles (Henrink et al., 2018; Yodi & Yoshida).

Cholesterol is ingested in the diet but is mainly produced by the liver. Foods high in cholesterol include animal offal, eggs, saturated fat and some shell fish. Its functions are as a structural component of cell membranes and the production of hormones and bile. Within blood plasma, lipids such as triglycerides and cholesterol are bound to various proteins (apoproteins) to form lipoproteins. There are several types of lipoproteins; those primarily involved in CVD are **low density lipoprotein** cholesterol (LDL-C) especially small dense LDL-C which is atherogenic and **high density lipoprotein** cholesterol (HDL-C) which have anti-atherogenic properties. Most cholesterol within the blood is carried as LDL's.

HDL-C has a number of anti-atherogenic properties which may slow down CVD progression. Although HDL-C has a similar structure to LDL-C, it differs in size, shape and composition. It acts by transporting cholesterol from macrophage foam cells in the arterial walls and peripheral tissues to the liver for excretion in bile. HDL-C provides additional anti-atherogenic protection including anti-inflammatory, anti-oxidation and anti-thrombotic activities.

There is a strong association between total cholesterol (TC) as well as LDL-C and the individual's risk of developing CVD (Gulec & Erol, 2020). There is strong evidence from both genetic studies and RCTs to support the role of lowering LDL cholesterol to reduce cardiovascular risk. Genetic studies provide evidence that lifelong lower LDL cholesterol results in reductions in cardiovascular events. Low-density lipoprotein cholesterol usually makes up 60–70% of total serum cholesterol and the relationship between total cholesterol level and CHD suggests that LDL cholesterol is a strong risk factor (Silverman et al., 2016). Large scale RCTs have highlighted that lowering LDL-C by 1mmol/L is associated with a reduction in cardiovascular events by about one-quarter during each year (Collins et al., 2016).

A statin is recommended as the choice of drug for lipid lowering. Please see guidelines for more information on statins and lipid-lowering:

- **Section 1.3 'Lipid modification therapy for the primary and secondary prevention of CVD** from NICE guideline (2016) [CG181]. https://www.nice.org.uk/guidance/cg181/resources/ cardiovascular-disease-risk-assessment-and-reduction-including-lipid-modification-pdf-35109807660997
- **Section 10 'Lipid Lowering'** from SIGN 149 (2017). *Risk estimation and the prevention of cardiovascular disease: a national clinical guideline.* https://www.sign.ac.uk/assets/sign149.pdf

- **Section 4.6 'Lipids'** from the European Guidelines on cardiovascular disease prevention in clinical practice. (2021). *European heart journal, 42*(34), 3227-3337. https://doi.org/10.1093/eurheartj/ehab484

Further Reading: Gulec, S. & Erol, C. (2020). High-density lipoprotein cholesterol and risk of cardiovascular disease. *E-journal of Cardiology Practice, 19*(3). https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-19/high-density-lipoprotein-cholesterol-and-risk-of-cardiovascular-disease

Blood pressure

Hypertension accounts for 13% of deaths worldwide and is the leading risk factor for cardiovascular disease and premature death (Arima et al., 2011). Due to improvements in hypertension treatment there has been a decline in the prevalence of hypertension in the UK of 11% in women and 13% in men over the last 30 years, according to figures published by the WHO 2021. However according to the BHF (2021) it is estimated that around 6-8 million adults are still living with undiagnosed or uncontrolled hypertension.

The risk of developing CVD is associated with elevated systolic and/or diastolic blood pressure (BP). Diastolic hypertension is more common in those aged below 50 years, while systolic hypertension is more common in those over the age of 50 due to atherosclerosis and arterial stiffness (Khan et al., 2018). An elevation of 20mmHG systolic or 10mmHg diastolic BP increase above the threshold doubles the risk of death from CVD (Lee et al., 2018). In the UK, around 50% of MIs and strokes are associated with hypertension (BHF, 2021).

The clinical cause of hypertension for many is unclear; this is known as essential, primary or idiopathic hypertension. Essential hypertension affects around 90-95% of those diagnosed as being hypertensive (Vongpatanasin, 2014). The remaining 5-10% is classified as having secondary hypertension. Secondary hypertension causes include aldosteronism, renal disease and pheochromocytoma.

The pathogenesis of essential hypertension is complex and involves interactions of multiple genetic and environmental factors. Environmental factors include: obesity, excess sodium intake, elevated alcohol consumption, aging, reduced physical activity and stress (Taddei et al., 2020). Genetic risk assessment requires an in-depth

understanding of all the physiological factors which influence cardiac output and peripheral vascular resistance.
If untreated, hypertension can affect multiple organs resulting in cardiovascular disorders such as: CAD, heart failure, peripheral vascular disease, vascular dementia and stroke, as well as playing a primary role in the development of renal impairment.

NICE (2019) guideline [NG136] '*Hypertension in adults: diagnosis and management'* defines the degree of hypertension at different stages, blood pressure targets per condition and how to measure BP. This guideline also offers a clear visual algorithm of each step of the management process including guidance for pharmacological interventions specific to age and ethnic group and lifestyle interventions. This guideline is available at:
https://www.nice.org.uk/guidance/ng136/resources/hypertension-in-adults-diagnosis-and-management-pdf-66141722710213

Pre-diabetes, metabolic syndrome and Insulin resistance

Pre-diabetes is a condition in which the body's blood glucose level is higher than normal limits but is not elevated to a level which would be classified as diabetes. It has been estimated that around 13.6 million people within the UK have pre-diabetes, with men over the age of 50 years being at greater risk than women. Pre-diabetes is linked to lifestyle factors, in particular obesity and limited physical activity. Advancing age and genetic factors also increase risk, especially in those with a family history of type 2 diabetes and those of Black, Hispanic and South Asian ethnic descent. Pre-diabetes may be used to refer to several abnormalities in glucose regulation including metabolic syndrome (Diabetes UK, 2019). Pre-diabetes may result in either impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). IFG occurs when the liver releases elevated levels of glucose while impairment in early secretion of insulin is present. IFG occurs more frequently in men, while IGT tends to occur more frequently in women and with progressive age. Those with IGT generally display normal liver insulin sensitivity but have moderate to severe muscular insulin resistance (Yip et al., 2017). Research has shown that those with pre-diabetes are likely to develop type 2 diabetes within 10 years unless active prevention strategies are adopted (Diabetes UK, 2019).

Metabolic syndrome is a cluster of conditions that when they occur together increase the risk of CVD and type 2 diabetes. It is characterised by insulin resistance, abdominal obesity, impaired glucose control, lipid abnormalities, elevated

inflammatory markers and thrombotic defects (Saklayen, M., 2018). In the past metabolic syndrome has also been known as insulin resistance syndrome and syndrome X. SIGN (2017) guideline [149] utilises the American Heart Association's diagnostic criteria (2009), which defines metabolic syndrome as any three (or more) of the following:

- Increased waist circumference (≥194 cm in men and ≥80 cm in women; ≥90 cm in Asian men and ≥80 cm in Asian women), indicating central obesity
- Elevated triglycerides (≥1.7 mmol/L)
- Decreased high-density lipoprotein cholesterol (<1.03 mmol/L for men, <1.29 mmol/L for women)
- Blood pressure >130/85 mmHg or active treatment for hypertension
- Fasting plasma glucose level >5.6 mmol/L or active treatment for hyperglycaemia

The normal pancreatic response to post meal elevated blood glucose is to release insulin, allowing cellular uptake of glucose. Insulin resistance results in the body's inability to utilise insulin in a normal way. This results in poor cellular management of glucose, amino acids and fatty acids. In normal circumstances the pancreas will manage elevated glucose levels by releasing more insulin, while the liver slows the release of glucose into the blood stream. In those with insulin resistance these normal compensatory mechanisms become impaired, resulting in both elevated circulating insulin and glucose. Insulin resistance also affects the normal activity of fat cells. This results in reduced uptake of circulating lipids and increased hydrolysis of stored triglycerides, increasing circulating free fatty acids within blood plasma.

Insulin resistance is often found in those with a high percentage of visceral adiposity, fat within the abdomen. **Obesity** is currently the most 'potent' risk factor for the development of type 2 diabetes accounting for 80-85% of the overall risk of developing the condition (Diabetes UK 2019). Visceral adipose cells release a significant amount of pro-inflammatory cytokines (Rakotoarivelo et al., 2018). These have a direct impact on the normal utilisation of insulin by fat and muscle cells. Visceral adiposity also results in a condition known as non-alcoholic fatty liver disease (NAFLD). NAFLD increases the amount of free fatty acids as well as liver glucose production. These factors exacerbate insulin resistance and increase the likelihood of type 2 diabetes developing. Weight gain is further perpetuated as insulin resistance stimulates the

development of fatty tissue, resulting in continued weight gain (Dharmalingham & Yamasandhi, 2018).

Diabetes

Diabetes is a chronic, metabolic disorder which presents with high circulating blood glucose when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces (WHO, 2021). The WHO recommends that the cut off point for the diagnosis of diabetes be an HbA1C of 6.5%. At present, there are more than 4.9 million people living in the UK with diabetes. This figure has more than doubled in the past two decades. Of those diagnosed with diabetes, approximately 90% have type 2 diabetes (T2D) Diabetes UK, 2019).

T2D occurs from the body's ineffective use of insulin and is mainly the result of physical inactivity and excess body weight (WHO, 2021). It tends to occur in people over the age of 40 years but it is increasingly being diagnosed in children and young people. An estimated 7000 children and young people in the UK have T2D (Diabetes UK, 2019). In the UK, those of South Asian, black African and African-Caribbean are two to four times more likely to develop T2D than the white population (Diabetes UK, 2020). The risk of T2D within these ethnic groups' increases at a younger age and a lower BMI level.

Lifestyle factors can be closely linked to the development of insulin resistance and diabetes, in particular living a sedentary life and dietary intake.

Dietary intake not only refers to the volume of food consumed but also composition and diet quality. Diets high in trans-fats and those with a high glycaemic load, are of greatest concern for T2D, while consumption of polyunsaturated fats and high cereal fibre diets have been shown to reduce risk (Hu 2011). High sugar intake have also been linked with increased risk of developing T2D. High consumption of red meat, sweets and fried foods have also been linked to T2D due to increased risk of insulin resistance (Panagiotakos et al., 2005). Consumption of fruits and vegetables may reduce the chances of developing T2D (Sami et al., 2017).

Increasing physical activity has been shown to reduce the risk of developing diabetes, while a sedentary lifestyle is associated with increased risk (Sharif et al., 2018). 'Screen time' which includes time spent watching television, using computers or game consoles has a direct influence on an individual's ability to remain physically

active while social media sites reduce the need to actively seek social interaction. Increased screen time has been linked to T2D risk in adults and in children (Nightingale et al., 2017). The “Nurse’s Health Study” demonstrated how the amount of time spent watching television can be positively correlated with the risk of obesity and type 2 diabetes. The results showed that each two hourly increment of watching television per day increased the risk of developing type 2 diabetes by 14%. However every two incremental hours of standing or walking could reduce risk by 12% (Hu et al., 2003).

First line treatment for many diagnosed with diabetes is through lifestyle modification, in particular diet modification, increased levels of physical activity and tobacco use cessation. Achieving adequate control does however require drug therapy in the form of oral hypoglycaemic’s and/or insulin in many cases (WHO, 2021).

Diabetes and CVD

Diabetes is associated with a reduction in life expectancy by around 10 years. This is primarily due to the increased risk of developing CVD, including CAD and stroke as well as renal impairment. Further physiological deterioration may include neuropathy, eye disease, cognitive and sexual dysfunction (Diabetes UK, 2019). In relation to CHD, diabetes is associated with several CAD risk factors including; dyslipidaemia (↓HDL-C, ↑LDL-C, ↑Triglycerides), increased platelet aggregation and increased fibrinogen levels. People with type 2 diabetes are 2.5 times more likely to have a MI and develop heart failure than non-diabetic people.

Although glycaemic control is the main objective in diabetic stability, how tightly it is controlled may have greater significance in reducing the risks associated with micro-vascular complications than cardiovascular disease (Valensi et al., 2019) Although glycaemic control is significant in the development of CVD, the ratio between total cholesterol and high density lipoprotein cholesterol in those with diabetes appears to determine the greatest risk of CVD, accounting for around 45% of the risk. This is followed by systolic blood pressure control at 33% and HbA1c at 22% (Stevens et al. 2001). Although intensive control of blood glucose can prevent major cardiovascular events, primarily non-fatal MI, the benefits were at the expense of weight gain and increased risk of severe hypoglycaemia (McCoy et al., 2016).

Reducing the cardiovascular risks associated with type 2 diabetes, although a priority may be associated with other risks. Intense lipid control may be associated with myalgia, altered liver function, cataract formation and acute renal failure. Tight blood

pressure control can result in renal impairment, while intensive glycaemic control may induce weight gain and severe hypoglycaemia which can impair cognitive function (Opie et al. 2011). With the exception of blood glucose control, the general recommendations for the prevention of CVD appear similar for both diabetics and non-diabetics.

As CVD remains the leading cause of death in those with diabetes, the focus is on aggressive control of blood pressure and cholesterol lowering, while glucose control should be titrated to reach the optimum HbA1C target of < 7.0%. Blood pressure should be controlled within recommended limits, with regular monitoring especially if renal, visual or cerebrovascular impairment has been detected. Cholesterol levels are also associated with cardiovascular risk, with evidence suggesting that elevated levels of LDL-C are causal in atherosclerosis, and subsequent reduction in LDL decreases cardiovascular events (ESC 2021)

Social determinants

When considering risk in relation to social determinants, Lang et al (2012) suggest thinking in terms of causal chains which influence the incidence and the management of traditional risk factors. The social determinants of health are complex. What makes an individual act in a specific way is influenced by a variety of social, economic and cultural factors. These factors are not static but can change in response to the individual's physical and psychological circumstances as well as the environment in which they live. Some of the key factors in social determinates include professional factors (working conditions, social relationships, and geographic environment (Shins, Basheer, & Babu, 2017).

Socioeconomic Status

Levels of deprivation are measured in the UK using indices of multiple deprivation (IMD). The IMD for each nation of the UK are listed below:

- Scottish Index of Multiple Deprivation (SIMD) 2020. https://www.gov.scot/collections/scottish-index-of-multiple-deprivation-2020/
- Welsh Index of Multiple Deprivation (WIMD) 2019. https://gov.wales/welsh-index-multiple-deprivation
- English Indices of Deprivation 2019. https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019

- Northern Ireland Multiple Deprivation Measure 2017 (NIMDM2017). https://www.nisra.gov.uk/statistics/deprivation/northern-ireland-multiple-deprivation-measure-2017

In England, those living in the most deprived areas are almost four times more likely to die prematurely of CVD than those in the least deprived area (UKHSA, 2019). A cohort study following 1.2 million women from the UK without heart disease highlighted a relationship between deprivation and CHD (Floud et al., 2016). This association is multifaceted and is not fully explained by the higher risk of traditional CVD risk factors (Lang et al., 2016). For example, those from deprived areas have a higher prevalence of poor diet, obesity, alcohol consumption and physical inactivity (Foster et al., 2018). Additionally, those in the most deprived areas are 30% more likely to have hypertension (Public Health England, 2019). Physical activity and poor nutrition have both been linked to increased susceptibility to obesity and CAD in women from financially disadvantaged areas (Mobley et al. 2006).

For specific information on socio-economic issues and rehabilitation please see the 'Supporting under-represented groups' chapter.

Further Reading: Theocharidou, L., & Mulvey, M. (2018). The effect of deprivation on coronary heart disease mortality rate, *Bioscience Horizons: The International Journal of Student Research*, *11*, hzy007. https://doi.org/10.1093/biohorizons/hzy007

Working Conditions

Cohort studies suggest that poor working conditions (which include a mixture of high demands with a low level of control, long working hours, job insecurity and shift work) are associated with a higher risk of CVD (Meneton et al., 2017). It has been suggested that this may be due to these conditions promoting risky health behaviours such as smoking and high consumption of alcohol (Fransson et al., 2012). It had also been suggested that poor working conditions may lead to psychological stress which can have harmful effects on the cardiovascular system (Brotman et al., 2007). Work related stress has also been linked with CVD risk factors such as an increased risk of hypertension, type 2 diabetes and obesity (Chandola, 2010; Gilbert-Ouimet et al., 2014). Additionally, low income has been strongly associated with CVD mortality (Khang et al., 2017).

Further Reading:

Sara, J. D., Prasad, M., Eleid, M. F., Zhang, M., Widmer, R. J., & Lerman, A. (2018). Association Between Work-Related Stress and Coronary Heart Disease: A Review of Prospective Studies Through the Job Strain, Effort-Reward Balance, and Organizational Justice Models. *Journal of the American Heart Association*, *7*(9), e008073. https://doi.org/10.1161/JAHA.117.008073

Social Isolation/Social Support

Loneliness and social isolation have been associated with an increased risk of CAD and stroke (Valtorta et al., 2016). The quality of an individual's social relationships is a reliable predictor of lower CVD risk (Barth et al., 2010). Social support may influence wellbeing through positive behaviours while mediating the physiological response to stress which may increase risk. Social support has been linked to biological risk factors for CVD including the oxytocin system and inflammation (Uchino et al., 2020).

Further Reading: Valtorta, N. K., Kanaan, M., Gilbody, S., Ronzi, S., & Hanratty, B. (2016). Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies. *Heart (British Cardiac Society)*, *102*(13), 1009–1016. https://doi.org/10.1136/heartjnl-2015-308790

Geographic Environment

The geographic environment in which individuals live also has an impact on CVD risk. Changes in the environment due to migration to different geographical locations as well as changes in social policies and cultural practices have been linked to CVD risk (Bhatnagar, 2017). Increasing evidence suggests that seasons, exposure to sunlight and greenspace access are among features of the environment which can impact on cardiovascular health (Bhatnagar, 2017). Environmental pollution exposure has also been linked to CVD with those who have diabetes or who smoke appearing to be most vulnerable (Gold & Mittleman, 2013). The physical environment may also facilitate or impede certain health behaviours. Low-levels of urban planning may lead to reduced access to services such as supermarkets, resulting in higher use of local convenience stores with less choice and increased exposure to low cost foods with limited nutritional value. The environment can also play a role in an individual's ability to participate in

regular physical activity. This may be due to an increased sense of personal vulnerability in areas of high crime or due to lack of green space within urban areas.

Further Reading:

- Bhatnagar A. (2017). Environmental Determinants of Cardiovascular Disease. *Circulation research*, *121*(2), 162–180. https://doi.org/10.1161/CIRCRESAHA.117.306458
- **Section 5.3 'Environment, air pollution and climate change'** from the European Guidelines on cardiovascular disease prevention in clinical practice. (2021). *European heart journal, 42*(34), 3227-3337.
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