Obesity and overweight

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This section will evaluate the contribution of increased weight and diet to the disease burden of CVD, including both morbidity and mortality. As discussed in section 1.1.1, morbidity leads to an additional burden of disability with enormous implications for society.

This section differs in approach from the other scientific reviews in this paper because obesity is both a condition in itself and a risk factor for cardiovascular disease. This chapter, therefore, examines the latest evidence on the complex inter-relationships between obesity, cardiovascular disease, cardiovascular risk factors, dietary factors and physical activity.

1.1.1.1 Obesity and overweight in Europe

1.1.1.1.1 Measures of obesity and CVD predictors

Body mass index (BMI), waist-hip ratio (WHR) and waist circumference (WC) are all used as predictors of cardiovascular diseases (CVD). However, which measure more accurately reflects CVD risk has been the focus of many investigations. One issue that emerges seems to be that different interpretations can be made depending on whether the study is conducted in a single population with predominantly similar population or across many societies with people of very different build.

The multinational WHO-sponsored MONICA study of 32,000 men and women aged 25-64 yrs from 19 populations participating in the second MONltoring trends and determinants in CArdiovascular disease (MONICA) survey from 1987-1992 found considerable variations in waist circumferences and WHR between different populations. Waist circumference and WHR, were both used as indicators of abdominal obesity but the waist circumference seemed to reflect well the degree of overweight whereas the WHR did not.

In the other major international studies—the INTERHEART[1] and INTERSTROKE analyses of 52 and 22 different countries respectively and spanning, as in the MONICA study, Asians as well as Caucasians—the question was what produced the most consistent prediction of cardiovascular disease. It rapidly became evident that BMI was only a crude measure of risk and that measuring the waist circumference as an index of abdominal fat distribution was more predictive of heart disease but the best measure was the WHR.[2] The proportion of the variance explained by taking the ratio of the waist to hip was not great so the simplicity of using just the waist measure is appealing although the body build of an individual from different ethnic groups can vary substantially so when

comparing across ethnic groups the ratio can be useful. Similar results were obtained in the Asia-Oceania Obesity Collaboration.[3]

The waist measure in these international studies was more closely associated than BMI with cardiovascular disease, presumably because it reflected the greater hazards of abdominal obesity and took account of the varying propensity to abdominal obesity in different societies. The WHR, however, allowed for very different proportions of skeletal size in different societies.

Some single national studies give a different perspective. A Canadian study concluded that waist circumference may be the best single indicator of an individual's cardiovascular risk factors in a cross sectional study[4] whereas an Australian study[5] found that WHR had the strongest correlations with CVD risk factors before adjustment for age. All three obesity measures performed similarly after adjustment for age.

These studies are all cross-sectional and therefore assess the best correlations between indices. A comprehensive study by van Dis and colleagues however, compared the absolute risk, hazard ratio and population attributable risk of non-fatal and fatal CVD for BMI and WC in a large prospective cohort of over 20,000 men and women aged 20-65 years and with an average follow-up of 10 years in the Netherlands.[6] Overall the study concluded that the associations of BMI and WC with CVD risk were equally strong. Overweight and obesity had a stronger impact on fatal CVD than on non-fatal CVD. This then limits the criticism involved in the use of the BMI as a predictor of risk, but it does not necessarily apply to all 53 European countries in the European region (as defined by WHO). Indeed there seems to be evidence that populations emerging from poverty have a particular propensity to selective abdominal obesity where the use of waist circumference or WHR may be particularly valuable.[7]

In light of all these studies it is recommended that health professionals, in addition to measuring BMI, should incorporate the use of waist circumference as a simple additional measurement in their routine clinical examination of adult patients.

1.1.1.1.2 The prevalence of overweight and obesity in Europe

New analysis by the International Obesity Task Force (IOTF) of the prevalence of overweight and obesity in Europe in comparison with other regions of the world is shown in Table 9**.** This reveals that in Europe, the Americas and Middle East more than half of all adults are either overweight or obese and in some parts of Europe more than three quarters of older adults are affected, with Eastern Europe having the greatest problems. The usual pattern is for more women to be obese than men but the prevalence of overweight in men is greater.

The data on children are also alarming as over a quarter of them are overweight with about 5% of the entire European child population being obese with all its long-term adverse health consequences. There is emerging evidence of a potential levelling off in the prevalence of obesity in children in recent years in some European countries. Rokholm and colleagues[8] reviewed 52 studies in over 25 countries and found evidence of

stability[1] or a levelling off of the epidemic in children and adolescents. Of the 21 studies in children in 11 European countries reviewed, 20 reported a levelling off, stability or a decrease in prevalence of obesity. Of seven studies in adolescents in seven European countries, all reported a decrease, stability or levelling off in adolescent females, and five for adolescent males. While these results give cause for hope, the authors point out that, in general, the prevalence of obesity still remains higher than ever before and previous stable phases in the epidemic have been followed by increases.

[1] Stability refers to no statistically significant changes, while a levelling off refers to a clear change in the trend from an increase towards stability or a clear slowing down in the increase.

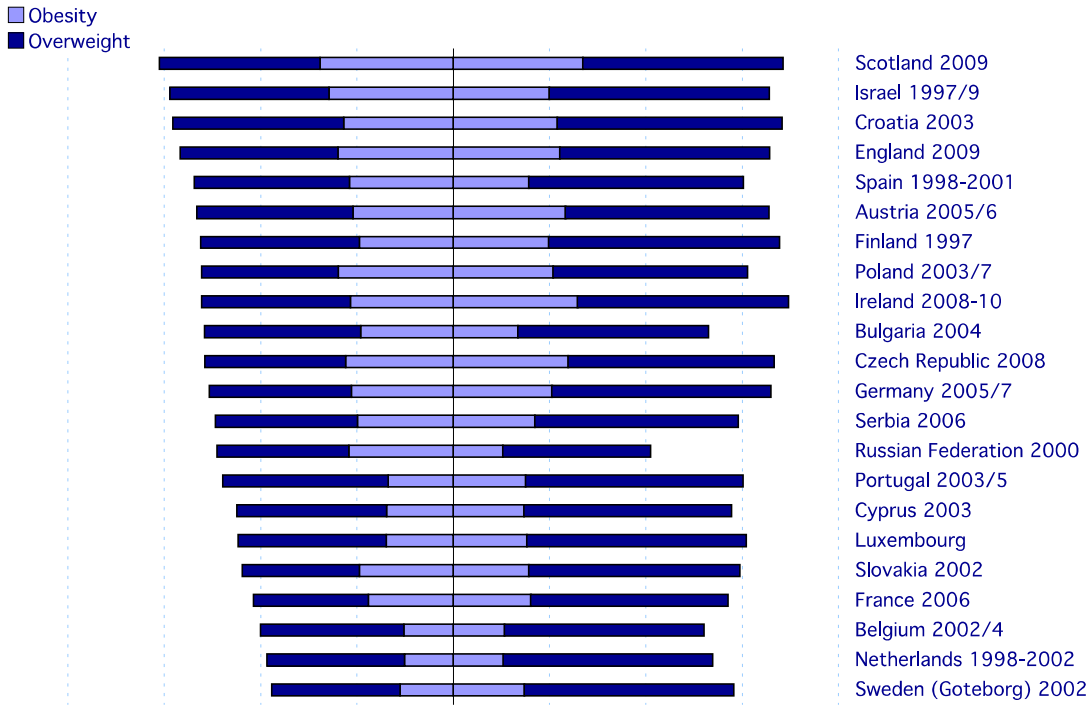
Table 1 Prevalence of overweight and obesity by age group for men and women in different WHO regions

Sub-region	Sex	5–14 yr			15–29 yrs			30–44 yrs			45–59 yrs			60–69			70–79			≥80		
		Ow	Ob	OW+Ob	OW	Ob	OW+Ob	OW	Ob	OW+Ob	OW	Ob	OW+ Ob	OW	Ob	OW+Ob	OW	Ob	OW+Ob	OW	Ob	OW+Ob
Afr D	Male	1.8	0.7	2.6	14.2	3.3	**17.4**	22.4	7.0	29.4	29.3	10.6	39.9	27.8	9.7	37.5	11.8	1.1	12.9	0.0	0.0	0.0
	Female	1.9	0.3	2.2	13.4	4.4	**17.8**	21.0	11.4	32.5	23.2	14.0	37.1	30.0	19.9	50.0	12.4	6.6	19.0	0.0	0.0	0.0
Afr E	Male	2.6	0.8	3.4	14.8	3.7	**18.5**	24.8	8.5	33.3	29.6	11.6	41.2	27.8	11.6	39.4	32.0	14.0	46.0	*0.0*	*0.0*	0.0
	Female	3.3	1.2	4.5	10.9	4.1	**14.9**	16.6	10.1	26.7	18.2	14.9	33.1	29.9	27.9	57.8	33.9	31.8	65.7	*0.0*	*0.0*	0.0
Amr A	Male	18.5	9.6	28.1	31.3	22.5	**53.8**	38.8	29.0	67.9	43.5	33.2	76.7	41.6	36.3	77.9	42.1	36.0	78.1	42.3	35.6	77.9
	Female	15.2	11.1	26.3	22.7	27.4	**50.1**	26.4	33.7	60.1	28.3	36.8	65.1	34.8	33.2	68.0	34.9	33.1	68.0	35.2	32.8	68.0
Amr B	Male	18.2	8.8	27.0	25.8	9.9	**35.8**	38.7	17.7	56.4	38.8	20.5	59.3	38.5	17.7	56.3	35.2	11.6	46.8	30.9	7.6	38.6
	Female	19.0	7.4	26.4	21.6	10.3	**31.9**	30.0	21.5	51.5	34.6	27.8	62.4	34.9	27.1	62.0	34.7	21.1	55.9	30.4	14.9	45.2
Amr D	Male	17.5	7.8	25.4	24.1	8.9	**33.0**	*38.7*	*17.7*	*56.4*	*38.8*	*20.5*	*59.3*	*38.5*	*17.7*	*56.3*	*35.2*	*11.6*	46.8	*30.9*	*7.6*	38.6
	Female	18.1	7.1	25.2	21.6	15.8	**37.4**	26.6	23.4	50.1	26.2	18.4	44.6	*34.9*	*27.1*	*62.0*	*34.7*	*21.1*	55.9	*30.4*	*14.9*	45.2
Emr B	Male	11.1	6.4	17.5	20.5	6.4	**26.9**	38.0	13.5	51.6	40.6	15.9	56.5	39.2	15.6	54.7	42.5	11.7	54.2	39.3	12.2	51.5
	Female	12.1	6.7	18.8	23.0	10.9	**34.0**	35.4	28.0	63.4	35.9	36.8	72.7	35.5	35.1	70.6	39.8	27.4	67.2	31.0	16.5	47.4
Emr D	Male	8.4	6.4	14.8	12.9	5.0	**17.8**	21.8	8.4	30.2	23.1	11.1	34.3	13.8	3.1	16.9	12.5	4.1	16.5	13.6	4.5	18.1
	Female	9.3	6.7	16.0	16.0	7.9	**23.9**	21.1	22.6	43.8	20.8	29.3	50.0	17.0	9.1	26.2	13.9	6.5	20.4	27.3	9.1	36.4
Eur A	Male	16.6	5.5	22.1	26.9	9.0	**35.9**	44.8	18.1	62.9	48.6	26.3	74.9	50.2	30.7	80.9	51.7	25.6	77.3	51.5	26.7	78.2
	Female	17.4	5.5	22.8	17.3	8.7	**26.0**	25.3	17.1	42.4	34.1	27.6	61.7	39.3	35.1	74.4	39.0	31.4	70.4	40.0	32.3	72.3
Eur B	Male	14.6	4.1	18.6	20.7	4.1	**24.9**	40.9	15.0	55.9	42.7	23.4	66.1	45.8	25.0	70.8	44.3	22.6	66.9	34.7	16.5	51.1
	Female	12.6	2.6	15.1	12.5	3.8	**16.3**	27.7	15.9	43.6	35.1	30.2	65.3	37.8	38.2	76.0	36.7	37.7	74.4	36.5	28.0	64.5
Eur C	Male	20.2	6.0	26.2	20.2	1.6	**21.8**	36.7	8.5	45.2	41.1	13.5	54.6	39.1	13.4	52.6	40.5	9.8	50.3	33.8	8.5	42.3
	Female	17.4	4.2	21.5	16.7	5.6	**22.3**	33.4	22.1	55.5	37.0	35.1	72.1	38.0	36.1	74.1	36.8	27.0	63.8	31.8	16.6	48.4
Sear B	Male	11.7	2.5	14.3	5.4	1.6	**7.0**	12.6	2.0	14.6	14.2	2.8	17.0	8.2	1.7	9.9	14.8	1.7	16.5	17.5	7.5	25.0
	Female	7.1	0.0	7.1	9.3	2.7	**12.0**	36.3	6.9	43.2	24.1	6.3	30.5	14.2	4.2	18.4	20.4	5.5	25.9	21.9	9.4	31.3
SEAR D	Male	11.7	2.5	14.3	4.9	0.9	**5.8**	11.6	1.9	13.5	13.4	2.3	15.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Female	7.1	0.0	7.1	6.0	1.3	**7.3**	14.5	4.4	18.8	16.6	5.9	22.5	2.4	0.0	2.4	9.1	0.0	9.1	0.0	0.0	0.0
Wpr A	Male	13.2	4.5	17.7	17.7	7.8	**25.5**	26.7	5.8	32.5	28.9	6.8	35.7	23.6	5.5	29.1	20.5	4.0	24.5	15.9	2.9	18.7
	Female	13.2	4.0	17.2	10.4	5.2	15.6	16.3	5.6	21.8	25.4	7.5	32.9	28.6	7.6	36.2	25.9	5.6	31.5	21.3	4.2	25.5
Wpr B	Male	6.5	3.4	9.9	14.0	1.2	15.2	24.2	4.7	28.9	27.0	6.4	33.4	27.9	7.4	35.3	9.7	0.0	9.7	15.9	2.9	18.7
	Female	5.3	1.7	7.0	10.4	1.8	12.2	18.4	6.4	24.9	22.2	4.7	26.8	22.1	9.8	31.9	28.9	3.2	32.1	21.3	4.2	25.5

Within each region there are obviously clear national differences as illustrated in Figure 1 where it becomes clear that the Southern Mediterranean countries have a surprisingly high prevalence of adult overweight and obesity rate with women again showing a propensity to obesity.

Figure 1 Prevalence of overweight and obesity in some European countries

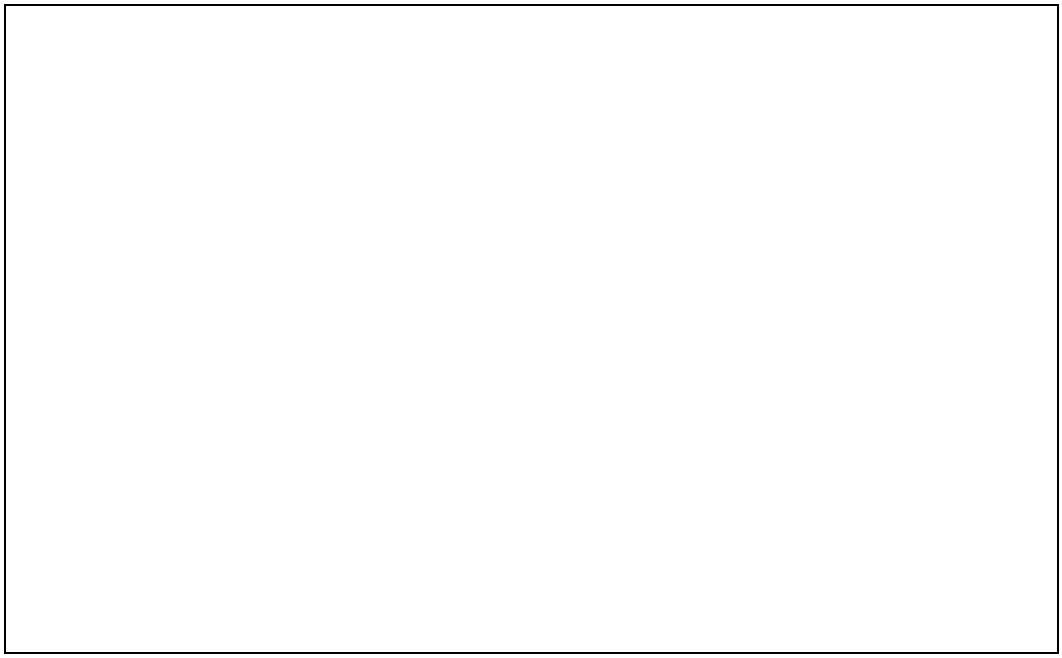
Note: Men and women shown separately. Prevalences are from non-age-standardised surveys with



measurements (not self-reported data) and relate to studies made since 2000. Some of the prevalences are based on sub-national surveys. Sources and references are available from IASO.

This geographical difference is also evident in children as shown in Figure 2.

Figure 2 European prevalence rates of overweight and obesity in children aged 7-11 years



It is recognised that there are significant differences and inequalities in the risk factors for cardiovascular health within and between EU Member States (see Section 1.1.2), and that differing obesity levels play a role in these differences. The challenge, therefore, is how best to assess the contribution of obesity to the overall differences between countries and the different rates of change in cardiovascular mortality.

1.1.1.2 Diet, physical activity and excess body weight

Given that there is strong evidence that excess body weight is associated with adverse levels of blood pressure, blood cholesterol and glucose levels,[9] the issue is whether it is the obesity itself or the way in which excess weight amplifies the cardiovascular risk factors which is really responsible for cardiovascular disease in Europe. Alternatively, perhaps it is the dietary factors promoting obesity which also independently cause increases in blood pressure, blood cholesterol, higher blood glucose and lower HDL cholesterol levels. If there are independent mechanisms then altering the diet may prevent and deal with both cardiovascular disease and obesity at the same time. Delineating the exact contribution of weight gain *per se* from its accompanying features—namely, low physical activity and a poor diet—is, however, difficult because all these factors are so interdependent that cause and effect is hard to establish. Nevertheless some evidence is emerging to clarify the field.

1.1.1.2.1 Dietary fat and obesity

Dietary fat does not appear to have a selective metabolic effect on total energy balance. This is illustrated by the fact that an additional reduction in bodyweight does not occur when obese adults reduce selectively the proportion of calories from fat in their diet, if their precise energy intake is controlled.

Dietary fat can have an impact on energy balance, however, by increasing the energy density of the diet which when dense readily allows individuals to unconsciously overeat and put on weight. In other words, if people tend to eat the same amount of food, as the fat content of the food increases their energy intake will increase. Research by Stubbs showed that when individuals eat a high fat diet, rather than a modest or low fat diet of identical appearance and taste, an individual unconsciously consumed their usual amount (mass) of food. However, individuals were unaware that the higher the content of the fat in the diet the more energy they accumulated over the subsequent days. When sedentary they only maintained energy balance on a 20% fat diet and were in positive energy balance on the common European intake of 40% fat. If the adults were more physically active then their spontaneous intake of diets with different fat contents was the same in the short term. Thus when they took more exercise from walking and cycling they just achieved energy balance on 40% fat. However, individuals readily went into positive energy balance and gained weight when fat intakes increased further. Thus there is interplay between the amount of fat in the diet and the degree of exercise: the less exercise is undertaken the lower the fat content of the diet must be.[10,11] Stubbs also showed that increasing the energy density of the diet by increasing the refined carbohydrate content has the same effect as fat induced energy dense diets. Thus it is not necessarily a specific factor in fat that induces overeating—it seems to be simply a question of dietary energy density as concluded by WHO.[12]

1.1.1.2.2 Dietary fat, weight gain and weight loss

The short-term intervention physiological studies described above chime with the observations of the impact of the extraordinary nutrition transition which has affected most poor societies in the world over the last 25 years where the fat content has escalated in association with economic improvements from about 5-15% up to 30-35%.[13] This marked increase in dietary fat content has been accompanied by an explosion in the development of obesity,[14] so that now 80% of noncommunicable diseases occur in the low and middle income countries of the world rather than the affluent West.

Studies that attempt to specify the effect of fat on the development of obesity need to be distinguished from studies based on the assessment of slimming diets. It is now well recognised that as adults gain weight there seems to be a progressive adaptation in the brain—at the post leptin receptor level—which adjusts the normal brain responses to changes in energy balance and comes to resists the impact of attempts to lose weight.

Thus the current obesity epidemic has occurred despite so many people attempting to reduce their weight. There is strong evidence of a hypothalamic adaptation whereby obese individuals when reducing their weight by only 10% have metabolic responses which favour weight gain and are also associated with a major drive to eat. These effects can be reversed to some extent by returning the blood levels of the hormone leptin to its high level seen in the obese adults.[15] When obese individuals have lost weight, their reduced body weight maintenance needs are accompanied by a normal drive to increase energy intake above that required to maintain their reduced weight. The failure to reduce energy intake in response to the reduced energy expenditure which normally occurs on weight loss reflects both decreased satiation and the perception of how much food is eaten. Multiple changes in neuronal signalling in response to food conspire together with the decline in energy output to keep body energy stores (body fat) above a brain defined minimum. Much of this biological opposition to sustained weight loss is mediated by the fat cell derived hormone leptin.[16]

Furthermore, detailed studies of those obese adults who have forced themselves to lose at least 15kg and maintained this weight loss for at least a year find that they are constantly needing to monitor their intake, ensure that they have a lower fat intake of 20-25% and engage in marked physical activity to combat this biological drive to return to their previous weight.[17] This emphasises the importance of preventive measures to limit weight gain in children and adults, rather than relying on community-wide slimming programmes.

1.1.1.2.3 Potential selective effects of different fatty acids on weight gain

There are several studies which suggest that different fatty acids may play different roles in promoting weight gain. Astrup and colleagues have suggested that saturated fatty acids and particularly *trans* fats induce greater weight gain[18] even though short-term studies on satiety fail to show differences between saturated, monounsaturated and polyunsaturated fatty acids.[19]

1.1.1.2.4 Fat intakes and dietary energy density

On the basis of the detailed observations on fat intake it would appear sensible to consider fat intake to be a key to the development of obesity. However, Stubbs proceeded to show in his studies that if the fat content of the food was maintained but the energy density of the diet was adjusted then a high energy density diet induced by using refined carbohydrates with little unrefined fibre rich foods had equivalent effects on energy intake as high fat diets.[20] This observation is in keeping with the nature of the global nutritional transition of the last 20-30 years. This is characterised by an increase in fat intake, a reduction in physical activity and a marked increase in sugar intake with a switch from unrefined foods to fibre-poor refined carbohydrates, increasing the overall energy density of the diet.

Although some studies examining modern societies, e.g. in the US, do not find a relationship between the fat content and the subsequent weight gain of adults[21] these diets are rich in sugars and refined foods so their energy density overall is high. When analysed as a body of research the WHO, in the 916 technical report,[22]**Error! Bookmark not defined.** specified that high energy dense diets and a low fibre intake, in addition to physical inactivity, were extremely conducive to excess weight gain. Thus high fat diets do promote the development of obesity but they seem to operate through a mechanism that relates to their impact on energy density.

In addition, there are suggestions that fat intake is not as satiating as dietary protein or carbohydrates.[23] Many observations also suggest that the mouth feel induced by fat, especially in combination with sugar, is very attractive and a substantial stimulant of excess consumption.

1.1.1.2.5 Selective taste receptors for fat

Evidence of a selective taste receptor for the essential fatty acids and n-3 fatty acids[24] has now been found and more recently for longer chain fatty acids.[25] This implies that—as with sugar, salt and the umami taste receptors—there is a primeval system of taste which includes a drive for at least some specific fatty acids. This presumably originally developed in response to the fundamental need for some fat and, in particular, the essential fats, especially n-3 fats required for human brain development. These gustatory responses may then amplify the mouth feel effects of fat to promote the consumption of fat rich diets.

1.1.1.2.6 Other dietary effects linked to the development of both obesity and hypertension

International comparisons show that weight gain and the development of high blood cholesterol track each other as societies become economically more affluent, whereas hypertension occurs in poor countries before the problem of obesity emerges.[26] Studies also show that dietary changes can lower blood pressure independent of weight change. These observations reflect the fact that other dietary factors contribute to hypertension in addition to weight gain and its associated high-energy diets.

One extremely important factor is the salt content of the diet (as explored in detail in section 1.3.2). In addition to the benefits of reduced blood pressure associated with reducing salt intakes, new evidence now suggests that if the salt content of current European diets can be reduced then children will tend to drink less. With current dietary patterns, this means they will consume fewer sugar containing drinks with their weight enhancing properties.[27]

Other important factors that can affect blood pressure include fruit and vegetable consumption, fibre intakes and dietary energy density. These issues are covered separately in sections 1.3.2, 1.3.4 and 1.3.5.

1.1.1.2.7 Physical activity: effects on energy balance, obesity and cardiovascular disease

A number of mechanisms for the beneficial effects of exercise on cardiovascular health have been put forward (see Section 1.3.7). These mechanisms—which include an improved lipid profile, increased insulin sensitivity, improved vascular function and reduced inflammation—are interlinked with the effects of weight loss and changes in regional fat distribution.

Extensive analyses have shown that even short periods of moderately intense exercise improve physical fitness—and thereby insulin sensitivity—with very beneficial effects on cardiovascular disease. The major cardiovascular preventive effect of physical activity (PA) can be attained by activity such as, for example, brisk walking of 150 minutes per week. However, longer periods of physical activity (e.g. an extra 60-90 minutes of brisk walking or cycling daily) may be needed to improve the chances of maintaining body weight, given the prevailing dietary patterns in Europe.

This is particularly important because, while physical activity has been shown to be of modest benefit in weight loss, it plays a crucial part in maintaining weight loss. When there is substantial weight loss physical activity becomes much more important—as already set out in the studies by Wing and Hill on the post-obese US adults.[17] The contribution of physical activity to the degree of weight loss following bariatric surgery has also been investigated where physical activity appears to be associated with a greater weight loss of over 4% BMI in post-surgical patients.[28]

1.1.1.3 Obesity and the risk of CVD

The multi-factorial nature of cardiovascular disease is well recognised. Recent reanalyses[29] of data from the 52-country INTERHEART study[1] and the 22-country INTERSTROKE study[30] confirmed the importance of additional diet-related factors, alongside the "classic" risk factors of tobacco use, high-blood pressure and raised blood cholesterol. Abdominal obesity is identified as an important risk factor in both studies—accounting for 36% and nearly 20% of the incidence of heart attacks from which the women and men recovered respectively and 26% of strokes among male and female stroke survivors (See section 1.2 for more detail).

The two recent major international studies mentioned above have an unparalleled range and detail in their analysis of risk factors, but they rely on retrospective analyses of risk factors in those who have survived their cardiovascular episode. Two integrated analyses involving multiple cohort studies (and which do not, therefore, depend on retrospective analyses) also confirm the strength of the principal factors observed in case-control

studies. The two studies in question—the Prospective Studies Collaboration[31] of a million adults in 61 prospective studies and the Asia Pacific Cohort[32] involving over 350,000 adults in 29 cohorts—reaffirmed the need to consider these classic risk factors in Europe, where many of the studies were conducted.

It is well known that the main causes of premature death among obese people are heart disease, coronary thrombosis and congestive heart failure and all are significantly more frequent among obese people than normal weight individuals.[33] In the integrated data from the Prospective Studies Collaborative analyses of 61 studies involving nearly a million adults it is clear that there is an almost linear relation between BMI and systolic/diastolic blood pressure.[31] High blood pressure, raised concentrations of plasma low-density cholesterol (LDL) and low concentrations of high density cholesterol (HDL) fractions are all important risk factors in cardiovascular disease and all these risk factors are amplified by weight gain. Total cholesterol has been positively associated with ischemic heart disease mortality at all blood pressure levels.[34] However, in older age groups higher blood pressures rather than greater total blood cholesterol levels are more important in determining cardiovascular deaths as shown in an extensive meta-analysis of over 55,000 vascular deaths.[35] Nevertheless, both the earlier and later meta-analysis of the role of obesity showed that weight gain amplified blood pressure and cholesterol levels, as well as increased the likelihood of increased fasting blood glucose levels and diabetes. So it is not surprising that there was a persistent effect of excess weight on cardiovascular events even in the 70-89 year-old group.[36]

Among 14 larger studies in a meta-analysis undertaken eight years ago, there was an average increase in coronary heart disease risk of 14% for each 2 kg/m^2 higher body mass[37] and this was later confirmed in the much bigger Prospective Studies Collaboration where a five unit BMI increase was accompanied by a 30% increase in total death rates and a 40% increase in cardiovascular mortality.[31] There was only limited evidence of effect modification by age, sex, ethnicity, or other variables. The authors concluded that the evidence from many studies, including randomised controlled trials, implied that the association between coronary heart disease risk and body mass index is in part or substantially mediated by the effect of weight gain on high blood pressure, dyslipidaemia, and impaired glucose tolerance. The effects of smoking and BMI were, in this predominantly European and US based meta-analysis, additive whereas in the Asia-Pacific region there was evidence that increased BMIs in smokers conferred an even greater risk than equivalent weight gain in non-smokers.[38] These studies amplify the need to quit smoking in those who are overweight.

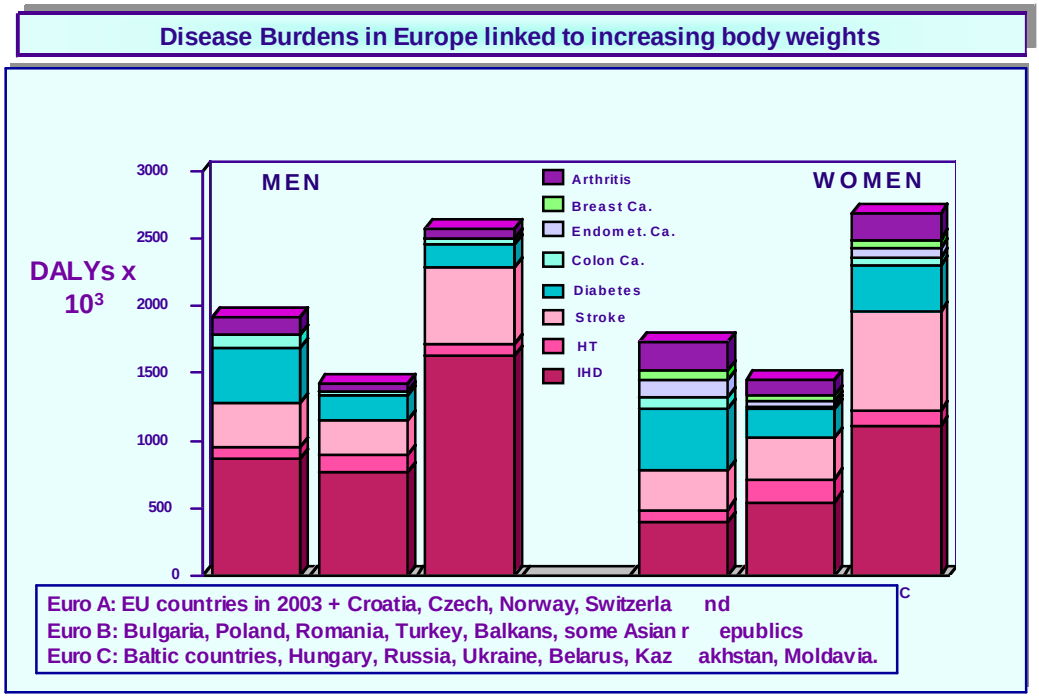
Although it is well accepted that excess body weight during midlife is associated with an increased risk of death[39] it is also known from long standing evidence from insurance statistics that the earlier the obesity occurs in adult life the greater the risk of premature death.[40] New data from Denmark demonstrates that even modestly overweight children between the ages of seven and 13 years have an increased risk of premature death from cardiovascular disease.[41]

1.1.1.3.1 Impact of excess weight gain on cardiovascular disability in Europe

It is important to consider the impact of "excess weight gain" as important in public health not just "obesity" which, using the standard WHO classification, occurs when adults have a BMI of ≥30.

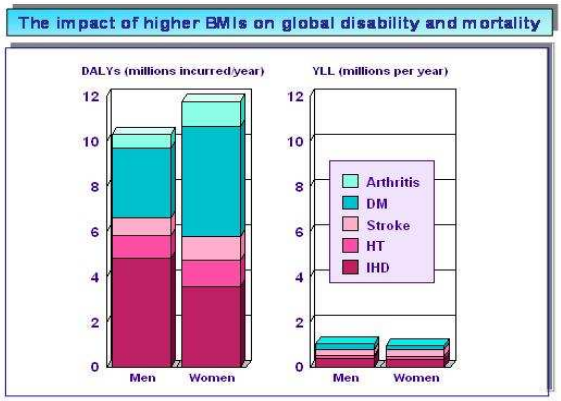
The relative impact of weight in excess of the ideal average BMI of 21 on disability and premature deaths in Europe, calculated as part of the analyses of risk factors is shown in Figure 3. The analyses show that cardiovascular diseases are the biggest contributor to the overall burden of ill-health and this is, in part, attributable to weight gain.

Figure 3 Disease Burdens in Europe linked to increasing body weights



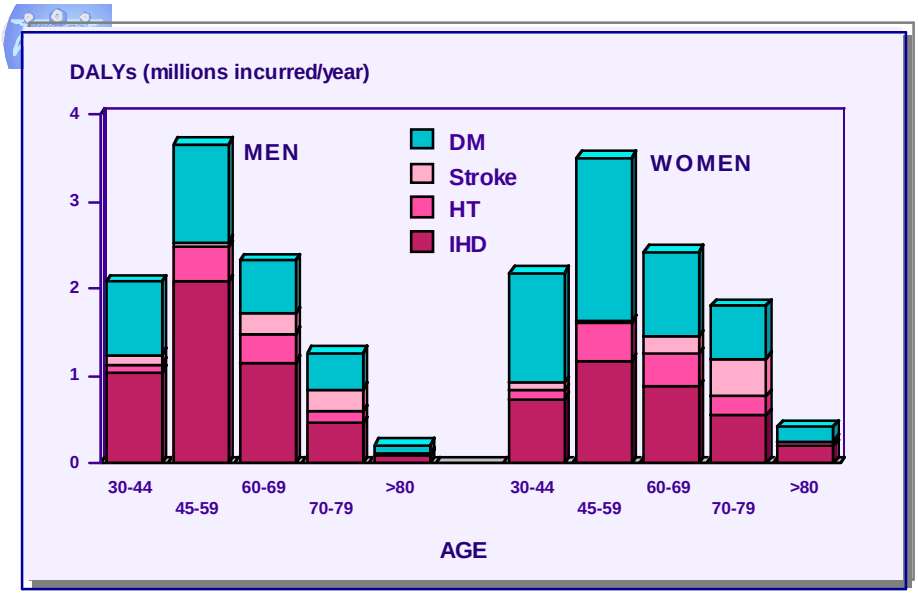
In early 2004 the greatest burden was evident in Eastern Europe. Figure 4 emphasises that the burden is dominated not by premature death (i.e. deaths<75yrs), but by the disabilities encountered by people when they have high blood pressure, diabetes, heart disease or by the handicaps of having had a stroke; this burden of disability is nearly 10 times that incurred by premature deaths.

Figure 4 The relative effects of excess weight gain on disabilities rather than premature mortality from cardiovascular disease and diabetes



When considering how this burden affects adults of different ages one should recognise, as shown in Figure 5, that the burden of disease incurred by excess weight occurs to a substantial extent before retirement age. Therefore not only does this present a burden to society as a whole but the economic impact of obesity is likely to be very substantial in working men and women.

Figure 5 The age relationships of disability and premature deaths as expressed in DALYs for men and women separately in Europe in 2004



1.1.1.3.2 Metabolic changes induced by weight gain

In man the biggest reservoir of fatty acids for supplying the body's long-term energy needs is in the adipose tissue. In European countries, where the amount of fat in diets is generally high, human adipose tissue normally stores fatty acids derived from the diet rather than from fat synthesised in the body from dietary carbohydrates.

The absorbed dietary fat is stored in the liver as well as adipose tissue and as weight gain develops increasing amounts of fat are stored in muscle both within the muscle fibres themselves and in the cells surrounding the contractile fibres. It is now increasingly recognised that the storage of fat outside adipose tissue itself is particularly hazardous and affects metabolism in general as well as the function of both liver and muscle.

As fat cells expand with weight gain they respond by increasing their release of fatty acids into the plasma.[42] Hormones, in particular insulin, are a key regulator in this

process of lypolysis and insulin functions under normal conditions to restrain the hormone sensitive lipase activity in the fat cells. Fat deposited in the visceral fat area is recognised to be particularly hazardous. This is because large quantities of fatty acids are released directly into the portal blood stream where they have an immediate impact on the liver. The liver normally removes the fatty acids from the blood stream and recycles them as triglycerides which are carried by low density lipoproteins. Visceral obesity is therefore a potent source for increasing liver fat stores where they interfere with the action of insulin.[43] In addition, as the fat cells expand, there is an increase in their production of several inflammatory cytokines including tumour necrosis factor alpha (TNFα) and this induces a fall in the secretion of a crucial metabolic hormone adiponectin which not only enhances insulin action and reduces the likelihood of diabetes but adiponectin also protects the endothelium of the blood vessels from a range of inflammatory and early atherosclerosis responses. This therefore suggests a direct interplay between the expanding fat cells in obesity and the impairment of arterial vessel function as well as explaining the fundamental link between weight gain and the development of diabetes with its cardiovascular damaging effects.

There are many other complex interactions of the metabolic pathways by which visceral and intramuscular fats induce insulin resistance as a forerunner to the development of glucose intolerance and type 2 diabetes. Obesity is now well accepted as having deleterious effects on hyperglycaemia, hyperinsulinaemia and hypertriglyceridaemia. These all appear to contribute to increased arterial stiffness which interacts with insulin resistance, hypertension and endothelial function in a highly complex manner.[44] In patients with hyperinsulinaemia there are changes in the arterial wall, in particular characteristic decreases in the elasticity of the arterial wall and there is some evidence suggesting that insulin resistance precedes the onset of hypertension in high-risk patients. Improvements in insulin sensitivity improve hypertension and vessel wall function.

During the early phases of obesity, primary sodium retention occurs as a result of increase in renal tubular reabsorption. Extracellular-fluid volume is expanded and the kidney-fluid apparatus is reset to a hypertensive level, consistent with the concept of hypertension from volume overload. The plasma renin activity, angiotensinogen, angiotensin II and aldosterone values show significant increases during the development of obesity thereby explaining the retention of sodium and water.[45] As obesity develops fat cells expand and secrete more leptin. This increased circulating leptin signals to the hypothalamus and induces an increase in sympathetic nervous system activity which increases blood pressure. Obese adults have a marked increase in the spontaneous sympathetic nervous activity which therefore links to their greater propensity to hypertension.

There are many different ways of reducing weight but most if not all induce beneficial changes in insulin resistance and in hypertension. Many studies have demonstrated a positive improvement in a variety of co-morbidities on weight reduction whether this is undertaken by exercise,[46] lifestyle modifications,[47] diet,[48] drug therapy,[49] or bariatric

surgery.[50] Fat loss through dieting or exercising produces comparable and favourable changes in plasma lipoprotein concentrations.[51] Thus weight loss, particularly when there is a decrease in visceral adiposity, leads to improved plasma lipids, enhances insulin sensitivity, improves endothelial function and lowers blood pressure.

1.1.1.3.3 Obesity as an inflammatory disease promoting cardiovascular disease

Obesity has now been found to involve a chronic, sub-acute state of inflammation which accompanies the accumulation of excess lipid in adipose tissue and liver (hepatic steatosis). Evidence suggests that changes in both inflammatory cells and biochemical markers of inflammation are associated with obesity.[52] Circulating mediators of inflammation participate in the mechanisms of vascular insult and atheromatous change, and many of these inflammatory proteins are secreted directly from fat cells and adipose tissue–derived macrophages. Two of these inflammatory molecules are tumour necrosis factor (TNF) alpha and interleukin 6 (IL-6). TNF-alpha inhibits the release from fat cells of the beneficial protein adiponectin and TNF-alpha and IL-6 both induce insulin resistance and counteract the beneficial effects of adiponectin. The increased release of fatty acids from the expanded fat cells in obesity and changes in the levels of retinol-binding protein 4 (RBP-4) may also induce oxidative stress and subsequent endothelial dysfunction with changes in thrombosis and endothelial processing of lipids through the PAI-1 and ICAM-1 molecules. Thus, the combination and interactions of fat accumulation, insulin resistance, liver-induced inflammation and dyslipidaemia may all lead to the premature atherosclerotic process.

The adipocyte-specific secretory protein adiponectin has been of particular significance in this field of research. Its levels are decreased in obesity and its secretion is markedly suppressed by the inflammatory peptide, tumour necrosis factor alpha which is secreted by fat cells as they expand.[53] Adiponectin may mediate some of its demonstrated cardio-protective effects through its anti-inflammatory properties. So the fall in adiponectin levels as well as the secretion of inflammatory factors from the expanded fat cells, particularly in the abdominal area may contribute to the increased cardiovascular risk associated with obesity.

1.1.1.3.4 Obesity and hypertension.

The risk of hypertension is up to five times higher among obese people than among those of normal weight[54] and it has been estimated that up to 85% of the cases of hypertension arise in individuals with BMI values above 25kg/m^2.[55] Overall the mechanistic relationship between hypertension and obesity is complex and represents an interaction of ethnic, gender, demographic, genetic, neurohormonal, and biochemical, as well as dietary factors and physical inactivity. In addition, upper body (android) obesity, especially in the presence of increased visceral fat, is more strongly associated with hypertension than lower body (gynoid) obesity.[56]

As discussed in Section 1.3.1, studies have shown that differences in total fat intakes alter blood pressure levels in people with normal blood pressure and those with hypertension.[57]

1.1.1.3.5 Blood cholesterol and obesity

It has long been recognised that the type of fat, rather than the total amount of fat *per se* in the diet, is important in the development of the increased levels of total blood cholesterol and low density lipoprotein (LDL) cholesterol levels, as outlined in section 1.3.1. Increases in LDL cholesterol induced by saturated fats can occur independently of any weight change, so reductions in cardiovascular risk can be induced even if a lower body weight is not achieved.

Nevertheless, the marked amplification of LDL cholesterol levels in association with higher body weights is remarkable and this effect is most marked in those with higher BMIs in the so-called "normal" range.[31] Thus the weight increase itself appears to be the factor which amplifies LDL cholesterol levels as there is little evidence that the percent of dietary saturated fatty acid in the diet are appreciably different in adults with BMIs of 20 compared with BMIs of 25. This suggests that obesity *per se* increases LDL cholesterol levels. Katan, in his analysis of the differences between the responses of lean and obese adults to changes in saturated fatty acid intake, notes that the obese (with their higher rates of cholesterol synthesis and higher prevailing levels of LDL cholesterol) are less responsive to lowering the saturated fatty acid intake.[58] This he ascribes to the very much bigger inflow of cholesterol to the clearance mechanism of hepatic LDL receptors. This inflow suppresses LDL cholesterol clearance so the overall LDL levels remain high and the additional benefit of lowering saturated fatty acid intake is then modest. The implication of these studies is that weight loss is also important as well as reducing the saturated fatty acid intake but achieving sustained weight loss is much more difficult than reducing saturated fatty acid intake.

The type of fat with the exception of *trans* fats—probably of both industrial and ruminant origin[59]—does not seem to impact on the levels of high density lipoprotein (HDL) cholesterol levels which are recognised to be a further indicator of the risk of cardiovascular disease. The lower the HDL cholesterol level the greater the risk of cardiovascular disease. As weight gain occurs there is a progressive fall in HDL levels and this is evident as weight increases from a BMI as low as 20.[31] The fall in HDL cholesterol levels is progressive as the BMI increases into the obesity range. Losing weight can reverse this trend in HDL levels once the weight has re-stabilised at the lower level.

There seem to be, therefore, real advantages in not only modifying the type of fat in European diets but also lowering the intake of total fat to reduce the likelihood of weight gain and to promote some weight loss which will then induce favourable increases in HDL cholesterol levels.

1.1.1.4 Weight loss and its potential benefits

In light of the evidence that obesity is harmful to cardiovascular health, weight loss is often recommended as a therapeutic goal to patients. The data suggest that modest weight loss in hypertensive patients reduces systolic blood pressure.[60,61] In addition, non-surgical weight loss for extreme obesity results in significant improvement in many metabolic parameters and blood pressure.[62] It also has a well-recognised beneficial effect in markedly reducing the likelihood of those with glucose intolerance developing diabetes. This was first suggested in Swedish studies[63] and confirmed in a meticulous Finnish intervention trial[64] as well as in other studies in the US,[65] China[66] and India.[67] Thus one would predict a marked effect on cardiovascular morbidity and mortality with weight loss in obese subjects.

Studies examining weight loss in the general population have found an equivocal association between weight loss and mortality.[68,69,70] However, this approach requires further examination of the underlying causes of the weight loss. The primary limitation of the observational literature on weight change and mortality is the lack of information about an individual's intention to lose weight.[71,72] The weight losing population includes a mixture of individuals losing weight on purpose and those who lose weight unintentionally. Unintentional weight loss is frequently associated with poor health. Thus, it is difficult to draw strong conclusions on the impact of weight loss on mortality from such studies.

Intentional weight loss

In a prospective study to assess intentional—as distinct from unintentional—weight loss among individuals with diabetes, those who intentionally lost up to ~20lb had a 25% lower all causes and cardiovascular disease mortality.[73] The modest intentional weight loss is associated with improved blood pressure, lipid concentrations, insulin sensitivity and glycaemic control[74] so reducing these risk factors. Weight loss may also reduce the high risk of vascular complications and death among individuals with diabetes.[75]

Even the intention to lose weight is associated with reduced mortality, regardless of whether weight loss has occurred.[76] Individuals who reported trying to lose weight had a 23% lower mortality rate than those not trying to lose weight.[76] These results suggest that trying to lose weight may be a marker of healthy behaviours, such as being more physically active or eating healthier foods, and these lifestyle behaviours may be more important determinants of health status than weight loss *per se*, particularly given the biological resistance to weight loss in those who are already obese.

Bariatric surgery has beneficial effects on diabetes, other cardiovascular risk factors, cardiovascular symptoms, sleep apnea, joint pain and health related quality of life.[77,78,79,80,81] The prospective Swedish Obesity Subjects (SOS) was the first study to clearly demonstrate that surgery for obesity was associated with a reduction in mortality.[82] These findings are in agreement with other surgical retrospective cohort

studies[83,84,85] and with observational prospective studies that attempted to separate intentional from unintentional weight loss occurring before the baseline examination.[86,87,88]

In the SOS study it took many years for the favourable treatment effect on mortality to be shown[89] and it also requires long follow up periods for the negative effect of obesity on mortality to become evident.[90] In the Framingham[91] and Manitoba[92] studies obesity became a significant predictor of mortality only after 26 years. Yet in the observational studies on bariatric surgery, with more marked weight loss than that seen in the SOS study, the 50% reduction in total mortality and the even greater falls in cardiovascular mortality occur within five to seven years.

Unintentional weight loss in those with cardiovascular disease

Unintentional weight loss is associated with *increased* mortality in those whose cardiovascular system is already compromised. Obesity may confer a more favourable prognosis, and an elevated BMI is an independent predictor of improved survival at one and two years in those with heart failure (HF).[93] However, this may reflect the absence of cachexia and aggressive disease in those who live longer, rather than an effect of obesity in conferring a positive health benefit.

The survival of patients with HF but without cachexia has also been reported.[94] The study concluded that BMI was a predictor of one year survival independent of exercise and left ventricular function: HF patients with a higher BMI had improved survival. However, it was also found that the survival of the lowest quintile BMI was similar to that of the cachexia patients over the first two years. These results suggest that it is difficult to find an appropriate “non cachectic” control group as BMI is directly proportional to disease status. It can be concluded that in HF patients with unintentional and involuntary weight loss mortality is high, but the converse simply indicates a less advanced or aggressive disease. Thus the so called "obesity paradox" in cardiovascular-compromised patients needs to be treated with great caution. Many inappropriate extrapolations from these studies are made to the non-diseased “general” population that obesity is “protective”.

This cautionary approach is supported by a study of a large, high-risk population over a prolonged period of time (10.4 years). This analysis concluded that obesity needs to be considered an important risk factor in patients with myocardial infarction (MI) or HF with systolic dysfunction. This study also concluded that there was no evidence of any protective effect of obesity.[95]

In conclusion, there is a strong tendency towards a U shaped relation between BMI groups and hazard of death as illustrated in Figure 6 from Abdulla and colleagues.[95] A higher hazard ratio is observed in patients with a low BMI. Importantly, the previously described paradox that obese patients with HF have a lower mortality is not substantiated in this more extensive analysis.

Figure 6 The prospective analyses of all adults who were admitted initially to Danish hospitals with either myocardial infarction or heart failure

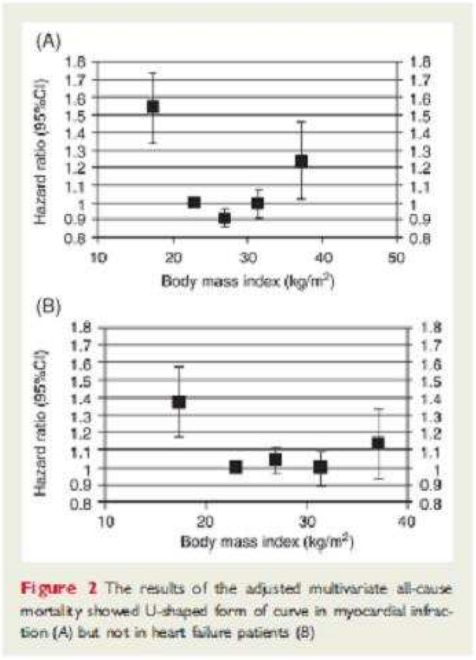


Figure 2 The results of the adjusted multivariate all-cause mortality showed U-shaped form of curve in myocardial infarction (A) but not in heart failure patients (B)

1.1.1.5 Secular changes in obesity and other risk factors associated with changes in cardiovascular disease in Europe

Despite positive improvements in coronary heart disease mortality over the past decade it could be argued that this fall would have been more dramatic if the prevalence of obesity, a major risk factor for CVD, had not tripled in the European region over the same time frame.[96]

There is evidence to suggest that the decline in CVD mortality is slowing down, particularly in the younger age groups, in a number of European industrialised countries and the continuing prevalence of obesity is a significant factor in this slow down (see Section 1.1). In England, for example, reports of improvements in hypertension management are encouraging.[97] However, in a EU comparison, women in England have been reported to have amongst the highest systolic blood pressures (systolic blood 127)[98] and the highest prevalence of obesity[2] (2007: 24.4% females BMI >30). In contrast, some EU countries where the obesity rates are lower, such as Denmark (2005: 11%

[2] www.iaso.org

females BMI >30), have amongst the lowest reported systolic blood pressure (systolic blood 115). With a wave of childhood obesity imminent (in England, for example, 17.0% of boys and 19.6% of girls are overweight according to the 2007 Health Survey England,[99] the risk factors underlying CVD in younger generations give significant cause for concern.

1.1.1.6 A prudent diet and its impact

Long-term prospective studies have shown that dietary patterns have an important impact on cardiovascular morbidity and mortality. Thus if the elderly follow a Mediterranean diet then they have lower mortality rates and lower cardiovascular disease irrespective of their obesity levels.[100] A study by Brunner and colleagues[101] also demonstrated that a healthy eating pattern significantly reduced the risks of diabetes and major coronary events. Furthermore dietary change, as a result of health promotion advice, is effective among motivated high-risk individuals[102] but tends to be modest among others.[103] These studies and others show the importance of dietary quality for population health and the reduction of cardiovascular mortality.

An analysis of Finnish data reinforces the importance of diet in CVD. When vegetable consumption trebled, and there was a substantial fall in the intake of total fat and saturated fat with a 15% decrease in total serum cholesterol concentrations[104] along with a significant decline in salt intake, there was a very marked fall in the population's blood pressure and cardiovascular disease. However, there was an increase in the average BMI of the Finnish population. Therefore, given the epidemic of obesity in Europe, with its associated increased risk of hypertension and greater blood cholesterol levels, it is still possible to reduce markedly the major risk factors for cardiovascular disease, the incidence of myocardial infarcts and strokes as well as cardiovascular mortality. This emphasises the importance of focusing on the dietary changes which are associated with obesity. Taken together, the studies suggest that dietary changes are important even if weight loss is limited. Nevertheless, preventive measures involving marked dietary improvements and increased physical activity should impact favourably on both the development of obesity and the prevention of cardiovascular disease.

WHO in its obesity report[105] suggested that the total fat intake should be as low as 20-25% and added sugar—through its effects in increasing energy density and, particularly, when consumed in drinks—is also conducive to weight gain. However, there are no goals as yet set out for the optimum dietary density of the diet. Therefore, it is clearly important to alter the diet by setting interim and longer term targets for the average fat, sugar, carbohydrate and fibre content of European diets as well as suitable targets for vegetable and fruit intake.

1.1.1.7 Population goals for body mass index

In the analyses of the impact of different risk factors on premature death and disabilities the WHO has emphasised that one should identify the ideal level of a risk factor as the optimum value for a population's average value for that risk factor in terms of its prediction of health and then consider deviations from this level as increasing risk. Therefore, WHO has emphasised that an "ideal level" of a risk factor should be set where it induces minimum health problems in a country.

For example, an individual is normally considered to have high blood pressure when the systolic blood pressure is 140+mmHg. However, the optimum average systolic blood pressure for the whole adult population has been shown to be 115mm Hg (i.e. far lower than the conventional level for diagnosing people as having the clinical disorder of hypertension). Similarly, when body weight is considered, then the average optimum body mass index (BMI) for adults was found to be 21 (i.e. far lower than the standard cut-off of BMI 25+ for specifying adults as "overweight"). Thus, as outlined earlier, it is important to consider the public health impact of excess weight gain, not just of obesity (BMI>30).

This report proposes a BMI of 23 as an intermediate target and a longer-term goal for a BMI of 21. These recommendations are in line with WHO recommendations for a population median BMI range BMI of 21-23.[106] Several Asian and African communities (with little or no adult underweight) had average BMIs in the 21-23 range in the 1980s before the onset of the nutrition transition and the westernisation of their diets. In the longer term European countries should be aiming towards the lower end of the WHO recommended range. WHO's report on obesity concluded that "*adults in affluent societies with a more sedentary lifestyle are likely to gain greater benefit from a median BMI of 21*."[105]

1.1.1.8 Conclusions

Avenell and colleagues in their Cochrane analysis could not distinguish between the effects of weight loss *per se* and the accompanying changes in diet leading to the weight loss.[107] This reinforces the important preventive health strategy of focusing on the provision of a high quality diet, high in fruit and vegetables and low in fats, sugars and salt for the prevention of cardiovascular disease in Europe.

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