An epidemic of obesity and type 2 (non-insulin-dependent) diabetes is in progress across the world. The global burden of diabetes has been projected to rise, with an increase in the total number of people with type 2 diabetes from about 120 million in 1997 to about 215 million in 2010 (1). The obvious remedy for this development is to combat overweight and obesity, and to counteract the sedentary lifestyle of modern society. The basis for these actions must be a population strategy of prevention. However, an equally important mission, not least from an ethical standpoint, is to find and engage those individuals that are in most need of help (high-risk strategy). The screening procedure is used to identify these high-risk individuals. Screening in this chapter refers to prescriptive screening, whose aim is to use early detection and early treatment to control the outcome of the disease. In epidemiological surveys, the principal aim of the screening is to explore the prevalence and natural history of the variable in question and not to bring patients to treatment.

PRINCIPLES OF SCREENING

Screening may be defined as the examination of apparently well or asymptomatic people in order to find out if they are likely or unlikely to suffer from disease. They can then, if they are likely to have the disease, be placed under treatment early in the natural course of the disease. The goal of screening is to detect and treat the disease as early as possible and thereby reverse or retard the disease process. Sometimes the object of the screening procedure is to find people at high risk of getting a disease. By identifying precursors of disease and correcting these, the disease may be postponed or at best prevented. There is no sharp line between a risk factor and a disease (2).

The screening procedure must always be followed by a treatment programme offering treatment to those found to have a disease or an increased risk of getting the disease. A screening programme can thus be divided into a diagnostic and a therapeutic component. In 1968, an increased interest in screening inspired the WHO to publish a Public Health Paper with the title 'Principles and practice of screening for disease' (3). This presented basic principles of screening together with practical and ethical considerations (Table 5.1). Launching a screening programme is a complex task, which if not done appropriately may lead to serious consequences. Several questions of an ethical and practical nature must be considered. By using certain screening principles, the chance of success will increase and the risk of serious adverse consequences will diminish.

The Importance of the Problem

The importance of the health problem needs to be regarded from the point of view of the individual as well as of the community. An uncommon condition with serious consequences for the individual, such
Table 5.1 Principles of screening

<table>
<thead>
<tr>
<th>Principle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The condition sought should be an important health problem</td>
</tr>
<tr>
<td>2. There should be an accepted treatment for patients with recognized</td>
</tr>
<tr>
<td>disease (condition)</td>
</tr>
<tr>
<td>3. Facilities for diagnosis and treatment should be available</td>
</tr>
<tr>
<td>4. There should be a recognizable latent or early symptomatic stage</td>
</tr>
<tr>
<td>5. There should be a suitable test</td>
</tr>
<tr>
<td>6. The natural history of the condition, including development from</td>
</tr>
<tr>
<td>latent to manifest disease, should be adequately understood</td>
</tr>
</tbody>
</table>

Modified from Wilson and Jungner (3).

as phenylketonuria, may warrant screening measures just as much as a more common but individually less serious condition.

The Necessity of an Accepted Treatment and Resources for its Implementation

Perhaps the most important criterion for a screening programme is to have an accepted treatment for those screened positive. It must be admitted that there are many difficulties in evaluating the outcome of a screening programme. Often, months or years must pass before the gains may be measurable. It is vitally important to determine whether earlier treatment really does give a better prognosis. If this is not the case, then there is no advantage in alerting the patient of the risk condition by early detection. No screening programme should be implemented without first having ensured that there are adequate resources in personnel and equipment for all individuals in need of treatment to get it. The responsibility is clearly on the health care organization that has initiated the screening examination and urged the individual to respond.

A Latent or Early Symptomatic Stage of the Disease

The disease must have a recognizable latent or early stage that can be detected by the screening test. The interval from this detection to the time when diagnosis ordinarily would have been made due to symptoms, which would make the person seek medical attention, is known as the lead time. In other words, lead time is the amount of time by which treatment may be begun earlier due to the screening programme. To summarize, if early treatment is not especially helpful, then there is no point in early detection.

Characteristics of the Screening Test

The validity of a screening test is measured by its sensitivity and specificity. ‘Sensitivity’ is the ability of the test to classify people as positive when they have the disease or the risk factor under study. ‘Specificity’ is defined as the ability of the test to classify people as negative when they do not have the disease or the risk factor under study. Having or not having the disease or risk factor in question should ideally be determined by a test that is a part of the diagnostic procedure. A diagnostic test may take more time and be more expensive to perform, and may have a lower degree of safety, but it is essential that it has the highest degree of accuracy. Consequently, an estimate of sensitivity should be regarded as the sensitivity of one test (the screening test) relative to another (the diagnostic test). The same kind of argument may be applied to the use of specificity. In reality, it is often impossible to use the diagnostic test on all screenees to verify the result of the screening test. For instance, the diagnostic test in cancer screening might be extensive surgery.

False positives are people who tested positive but do not have the disease or risk factor under study and false negatives are people who tested negative but do show the disease or risk factor under study. The ‘positive predictive value’ is the ability of the screening test to predict that there is a state of early disease or a high risk. The positive predictive value will depend in part on the screening test characteristics (sensitivity and specificity) and in part on the prevalence of the disease or risk situation. The reliability of the test is its capacity to give the same result on repeated measurements. Ideally, a screening test should be valid, safe, simple to perform, acceptable to the subject and inexpensive. The sensitivity of the test may be increased or decreased by changing the level at which the test is considered positive. An increase in the sensitivity will decrease the specificity and vice versa (Figure 5.1).
Adequate Understanding of the Natural History of the Target Disease

Whether a screening programme will be useful to a given population or not depends to a large extent on the natural history of the target disease. A main question is: Does early detection and treatment affect the course and prognosis of the disease? In order to answer that question well-planned and preferably randomized experimental studies must be conducted. In many cases, these clinical trials must be started as soon as possible. If not carried out speedily enough, the time trend may change the practice of treatment and treating the latent stage of the disease may be regarded as normal practice. In such a situation, it would no longer be considered ethical to perform a randomized clinical trial. As a result of this, scientific evidence, showing that the early detection and treatment really changes the natural course of the disease and improves its prognosis, may be lacking.

SCREENING FOR A RISK FACTOR INSTEAD OF A DISEASE

When it comes to the use of screening for a risk factor instead of a disease, two additional points may be formulated (4). The first of these defines the purpose of the screening. The intention must be to find reversible risk—not risk factors. The object of the screening procedure must be to find those persons who will benefit from an ensuing intervention. It is the effect of the intervention that may increase the individual's health and not the risk classification per se. The second point states that selected screening is more cost effective than mass screening. Simple and easily attainable information, such as age and sex, may help to select a segment of the population with a heightened risk. The screening procedure may then be done within that segment. In a situation where there is a lack of resources for advice and long-term support, it is better to concentrate the resources on those who need it most.

Obesity is a predisposing factor for type 2 diabetes and cardiovascular disease (CVD). In a screening programme focused on obesity with the aim of preventing or postponing diabetes and CVD, obesity may be regarded as a detectable but asymptomatic phase of these outcomes, i.e. a preclinical phase of CVD or type 2 diabetes. The distinction between screening for a risk factor and screening for a disease is that when a disease is the object of the screening, as in the case of breast cancer, then eventually most screen-detected cases will develop symptomatic disease. When a risk factor is the object of the screening, often only a minority will develop symptomatic disease. This has been the case in screening for hypertension, where only a minority of those screened as mild hypertensives will develop stroke or myocardial infarction.

MASS SCREENING, OPPORTUNISTIC SCREENING OR SELF-REFERRAL

A screening programme uses a screening test to detect early disease or a risk factor for future disease. This detection part of a screening programme need not to be that costly. At least, this is what is to be expected in screening for obesity irrespective whether body mass index or other anthropometric measures are used as screening tools. However, to treat those screened to be high-risk individuals, in a long-term weight management programme, will need considerable resources.

The decision to launch a mass screening programme (the whole population) for overweight and obesity must incorporate a commitment to allocating enough resources to give all high-risk individuals the opportunity to participate in a treatment programme. Otherwise such a decision would be unethical.
An alternative could be to use an opportunistic screening procedure, using all visits made by individuals to the health care centre for whatever reasons to screen for overweight and obesity. In Sweden, more than three-quarters of the population would be reached in this way within a 5-year period (5). Some minor resources would be saved by using a programme based on opportunistic instead of mass screening. However, the greater part of the costs for screening of overweight and obesity would come from the treatment programme and these costs must be the same irrespective of the screening procedure used.

In recent years, many magazines have been offering their readers a chance to calculate their own body mass index (BMI) and along with that a table is presented, prescribing treatment alternatives for different ranges of BMI. This form of magazine-initiated screening puts the responsibility for initiating a suitable treatment on the subjects themselves and not on the health care system. Some may, by self-referral, seek professional help for their weight problem. However, many individuals will appraise the situation of an increased risk, but will not have the strength or the social support to initiate a treatment on their own. Furthermore, most health care systems are not able to cope with a situation where large groups of people seek help for problems with overweight and obesity. A clear disadvantage of this magazine-related screening for obesity is that it alerts people of a risk without offering enough help, and this may create a feeling of helplessness. Probably, such a situation will enlarge the inequity in health already present in contemporary society. Another problem is the impact magazine-related screening may have on eating disorders, especially among young women.

**SELECTIVE AND MULTIPLE SCREENING**

The term selective screening is used when the screening procedure is concentrated on a special high-risk sector within a population. By using health indicators, information that is already at hand or at least is easy to obtain such as age, sex and race, costs for a screening programme can be reduced. We know that the prevalences of disease and pre-clinical disease often increase with age. One way of cutting costs in a screening programme could be to select only individuals above a certain age. In this way a larger percentage of those screened will be classified as high-risk individuals. The positive predictive value will be higher since the prevalence of pre-clinical disease is higher and this will reduce costs for the screening procedure. However, as stated above, the main costs in screening for obesity will come from the treatment programme.

The term multiple (or multiphasic) screening has been defined as the application of two or more screening tests in combination to a large group of people. From an economic standpoint it seems logical to offer more than one screening test at the same time, at least if much energy has been spent on getting a high participation rate in the screening programme. Many different pre-clinical diseases may then be examined at the same time. However, multiple screening tests may also be used to specify the high-risk group more precisely. In such a situation only screenees with a positive result in all screening tests are classified as high-risk individuals. The advantage would be that individuals in a smaller and more refined high-risk group would be able to get a more specified treatment programme, in which also more resources could be spent on each individual in the programme. A screening programme targeted to the primary prevention of type 2 diabetes might combine one screening test for obesity and one test for glucose tolerance. In that way, only participants having the combination of obesity and impaired glucose tolerance are classified as high-risk individuals. A further refinement of the programme, at least if the object is to reduce numbers-needed-to-screen to detect a high-risk individual, would be to choose a high-risk sector of the population and offer the programme only to certain age groups.

**EVALUATION OF SCREENING**

How do we know that our screening is doing more good than harm? Most screening programmes must be continuously evaluated and the evaluation of screening is often complex. Mass screening for breast cancer in women provides a good illustration of this. Despite more than a decade of screening results, the scientists still disagree on the value of these mass screening programmes for breast cancer.
and whether they should be continued or not (6). Most of the discussion is concerned with how to interpret mortality and survival rates.

There are many difficulties in the evaluation of the outcome of screening (2). Often, the gains are several months or years in the future. It is not acceptable simply to compare survival of screen-detected cases with that of cases detected by symptoms. There are two main reasons for this. A higher survival rate among screen-detected cases could be explained by the fact that the diagnosis was made earlier (lead time). Another explanation could be that a screening programme tends to detect more benign cases (prognostic selection bias). We know that the clinical course of a disease may vary substantially, even if two patients are diagnosed at the same time. A long clinical course, a sign of a more benign disease, is often preceded by a long pre-clinical phase. The probability of detecting a given case in a screening procedure increases as the length of the pre-clinical phase increases.

Comparing overall mortality rate or disease-specific mortality rate would be unbiased in this respect. A lower mortality rate in the screened group would suggest a beneficial effect of early treatment. In general, it is appropriate to compare the rate of development of advanced symptomatic disease between screened and unscreened groups (2).

What is more, even if a reliable evaluation does establish that we are doing more good than harm with our screening programme, we still have to reflect on the alternative use of the resources spent on the screening programme. What would the result be if the resources instead were to be allocated to another sector of the health care system or perhaps to a sector outside the health care system? What would that mean in terms of public health? The strategy of prevention and the balance between preventive and curative work to improve health are two additional issues that have to be included in answering whether screening is worthwhile or not.

**BENEFICIAL AND ADVERSE EFFECTS OF SCREENING**

Who will gain and who will lose on participating in a screening programme? Since the evaluation of screening programmes is often complex, especially when screening for risk factors, no simple and clear-cut answers can be given. In part, it will depend on the ability of the chosen screening test to correctly separate those that will become ill from those that will continue to be healthy. In part, it will depend on whether the instituted early treatment on those classified to be at high risk is effective or not. In other words, whether the early treatment really prevents or postpones the target disease of the screening programme.

As mentioned earlier, screening for early disease has some advantages compared to screening for a risk factor. In screening for disease, e.g. breast cancer in women, most of the true positives and perhaps some of the false negatives will develop symptomatic disease. This makes it possible, even though not easy, to evaluate on an individual level the gains and losses that are at stake.

In screening for a risk factor, as in screening for hypertension or obesity, most of those screened to be at high risk will not, during a foreseeable time period, develop the target disease of the screening programme whether myocardial infarction, stroke or type 2 diabetes. In such a situation our ability to predict the outcome on an individual level is very limited.

Those who benefit most from participating in a screening programme are individuals in whom the serious consequences of the target disease have been prevented or postponed by the early treatment. This is also the reason why we do the screening in the first place. What about those screened to be at high risk, where serious consequences of the target disease do not develop, even if followed for a very long time. Psychologically, they may be in a lose situation. They have been alerted of a serious risk, without having cause to be alarmed, and may react with anxiety and depression. How much unjustified anxiety and depression is evoked in individuals participating in different screening programmes? The question is impossible to answer in any precise manner and has not received much attention in the evaluation of screening programmes.

A study examining potential adverse psychological effects of screening for cardiovascular risk factors showed that a minority (about 20%) of those screened to be at high risk reacted with some degree of anxiety and confusion (7). Another study, also examining adverse psychological effects of screening, found a mild degree of worry in people labelled as having high cholesterol levels when compared to those labelled as normals. However, the level of
anxiety did not influence mood, participation in social activities or life satisfaction. The conclusion was that the screening did not create any adverse psychosocial consequences (8). A similar result was found in a study of screening for hypertension. Individuals with mild to moderate hypertension were compared to individuals with normal blood pressure. Assessment for psychological effects was made repeatedly during a 12-month follow-up. A self-administered questionnaire comprising general health issues was used. A diagnostic psychiatric interview was conducted if the questionnaire indicated a high risk of developing psychiatric manifestations. In the study, no support was given for the belief that the screening programme evoked psychiatric symptoms among the participants. In fact, the reverse was suggested. Based on the interviews, individuals treated for hypertension showed less anxiety than individuals not in the treatment programme. There may, of course, be several explanations for this effect. Regularly attending a clinic could be one explanation. There could also be anxiolytic side effects in the antihypertensive medications that were used (9).

What about those found to be healthy in a screening programme? As stated above, our ability to predict the outcome for an individual is very limited. On that account, there is reason to assume that some individuals classified by the screening test as normal may in fact have an increased risk of becoming ill (false negatives). A harmful effect of screening may also arise in a situation where an individual on testing is found to be without risk factors. A negative screening test may be regarded by the individual as a proof of being healthy and living a healthy life. Ideas of not overdoing things start to rankle. The next step in the chain might be a worsening in the lifestyle of that individual. This justification for an unhealthy behaviour has sometimes been called the ‘certificate of health’ effect and must be considered an adverse effect of the screening programme (7).

THE ROLE OF SCREENING IN THE STRATEGY OF PREVENTION

Whether to approach high-risk individuals or the whole population in order to improve health and to prevent disease is often a matter of opinion. Both strategies have their strong and weak points (4). Many of our most important cardiovascular risk factors, e.g. blood pressure, serum cholesterol and body weight, are measured on a continuous scale. They are often normally distributed in the population. The implication of this in risk assessment is that relatively few people have a substantially increased risk, whereas many more people have different degrees of slightly increased risk situations. A specific pattern often emerges when the relative risk of getting a disease for an individual is compared with the total distribution of the disease in the population. Most cases of the disease are derived from the large majority of the population having a slight increase in risk and relatively few cases are derived from the high-risk group. Rose called this phenomenon ‘the prevention paradox’ and stated ‘a preventive measure that brings large benefits to the community offers little to each participating individual’ (10). From this it follows that we cannot successfully control modern disease, mainly cardiovascular disease and cancer, solely by detecting and intervening on high-risk individuals. Prevention must embrace both the population and the high-risk approach. The two strategies are complementary and have their respective strengths and limitations.

The screening procedure is a means to identify individuals at high risk of developing disease. Screening is thus a part of a high-risk strategy of prevention. The basic idea behind high-risk strategy is to concentrate the resources for advice and support on those who need it most. The high-risk approach offers a more cost-effective use of available resources and this is especially important when the needed treatment both has to be intense and must continue for a long time. This is clearly the case in the treatment of obesity. The rationale of this high-risk strategy is easy to understand and accept in the medical care system. Giving most resources to those who need it most is a principle that feels familiar to health professionals and is considered more as an extension of the ongoing curative work. This strategy also seems natural to most high-risk individuals. They have been examined and classified as being at risk for future disease. A person who appraises such a situation rationally also realizes that there is a lot to be gained from a treatment programme, and this is likely to increase motivation. Unfortunately, even if we can accurately estimate the average risk for a group, our ability to predict
what will happen to an individual is much more uncertain. This uncertainty often has a hampering effect on the individual’s motivation.

SCREENING FOR OBESITY

Although obesity should be regarded as a disease entity of its own, many of its more serious consequences are due to the strong relations that exist between obesity and some common chronic diseases. Obesity is an important risk factor for type 2 diabetes, cardiovascular disease, sleep apnoea, gallbladder disease and certain types of cancer.

Why Screen for Obesity?

The association between obesity and type 2 diabetes is perhaps the strongest of all reasons why a crusade against overweight and obesity must be initiated in the near future. The ongoing secular trends in Westernized societies are alarming. It is a healthy sign that the medical profession is showing an increasing interest in and awareness of the impact lifestyle has on health. However, many health professionals express a pessimistic view over the future with regard to many of our chronic diseases, if the ‘Westernized’ way of living continues to expand over the world. Headlines such as, ‘obesity—a time bomb to be defused’ (11) and ‘non-insulin dependent diabetes mellitus—an epidemic in progress’ (12), have been used. The global burden of diabetes has, as stated above, been projected to rise from about 120 million type 2 diabetic individuals in 1997 to about 215 million in 2010 (1).

The 1980s and the 1990s research in cell and molecular biology has presented a body of evidence that supports many years of past clinical experience. Sustained high levels of free fatty acids (FFAs) seem to affect both insulin secretion and insulin action in susceptible individuals by interfering with the glucose transporter mechanism in the pancreatic islet cells and in the muscle and fat cells. Caloric restriction and exercise training have, in animal experiments, been shown to counteract the suppression of glucose transporters, verifying on a cellular level over forty years of experience from observational and experimental studies in humans on the relationships between body weight, physical activity and glucose tolerance. The amount of body fat mass and the metabolic activity in different fat cells seem to regulate the production of FFAs and the consumption of FFAs is largely dependent on the level of physical activity. High levels of stress (cortisol and catecholamines) seem to be implicated both in the enlargement of the visceral fat depots and in boosting their activity. A long-term lifestyle change therefore seems to be the obvious remedy.

The Screening Test—Measuring Body Mass Index or Waist Circumference or Both

The purpose of screening for obesity must be to find individuals at high risk of developing future disease that is caused by a long-standing effect of obesity. Since ‘obesity’ is associated with a certain level of BMI (more than or equal to 30), the term obesity in this passage will be replaced by the term ‘excess storage of body fat’. Excess storage of body fat may be measured in many different ways. Some methods measure the amount of body fat very precisely, but are not suitable for screening purposes. They are often laborious and expensive. Ideally, a screening test should be safe, valid, rapid and inexpensive. The identification of high-risk individuals based on measuring body weight seems, at least compared to many other screening tests, relatively simple and straightforward. The measurements are easy to obtain, safe to use, and reliable. What about validity? Some studies imply that BMI correlates well with percentage of body fat (13). Other studies, using modern imaging techniques, have found significant variations in the percentage of body fat across the whole range of BMI (14). Yet, it is reasonable to believe that measuring BMI would for most subjects capture the increased risk for comorbidities that is linked to an excess storage of body fat. Furthermore, BMI is much more stable as a measurement than blood pressure or serum cholesterol, and consequently more suitable as a screening tool. Stress or anxiety can, within seconds, change the level of blood pressure but will have no effect on an individual’s BMI.

If measuring BMI is simple and straightforward, the issue of where to draw the line between a high-risk situation and a normal situation is more complex. Body mass index, like many other risk factors,
is measured on a continuous scale. However, when used as a screening test, the purpose is to divide the screened population into a minority assessed as having a high risk of developing future disease and a majority assessed as normal. A cut-off point at a low level of BMI will define our high-risk group more broadly, ensuring that practically all individuals with excess storage of body fat are classified as high-risk individuals (true positives). This is easily understood if we hypothetically choose a BMI of 20 kg/m\(^2\) as a cut-off point. The sensitivity would be high in such a situation (Figure 5.1). However, a broadly defined high-risk group would also include many individuals not having excess storage of body fat. These would be falsely regarded as high-risk individuals (false positives). Another way of expressing this is to say that the screening test does not correctly classify as negative those individuals without excess storage of body fat. The specificity of such a test would be low (Figure 5.1). Similarly, if a high level of BMI was chosen as the cut-off point, the high-risk group would be defined narrowly. This is most easily understood if we hypothetically choose a BMI of 35 kg/m\(^2\) as a cut-off point. In such a situation, many individuals having excess storage of body fat would be classified as negatives, i.e. belonging to a normal risk situation (false negatives). The sensitivity of the test would be low. However, the specificity would be high, since practically all those without excess storage of body fat would be classified as normals (true negatives).

Many different considerations have to be taken into account when deciding which cut-off point to use in a screening test. All individuals found to have a high risk are entitled to a treatment programme. If obesity is to be treated successfully on a long-term basis, a lot of professional support is needed. In this way, the amount of resources allocated to the treatment component of the screening programme will have a major impact on how broadly or narrowly the high-risk group is to be defined. Of course, a cut-off point that is already generally accepted by the medical profession, and represents a level of BMI above which the risk curve for comorbidities rises more steeply, would seem natural. A BMI of more than or equal to 30 kg/m\(^2\) would define between 10 and 25% of most Western populations as high-risk individuals (15).

As mentioned earlier, intensive research in cardiovascular disease and type 2 diabetes, over more than two decades, has pointed to visceral fat accumulation and free fatty acids as key factors in the aetiology of these diseases. This clearer understanding of the mechanisms by which obesity contributes to cardiovascular disease and type 2 diabetes may also imply that waist circumference, abdominal sagittal diameter or waist-to-hip ratio are more accurate measures of the risk of future disease than BMI and should therefore be preferred as screening tests. Abdominal obesity has in prospective studies independently, after controlling for BMI, been associated with the incidence of cardiovascular disease (16) and type 2 diabetes (17). However, the picture is not entirely clear-cut. In the Health Professionals’ Follow-up Study, although waist circumference was shown to be a good predictor, a high BMI was the dominant risk factor for type 2 diabetes (18).

The new techniques for measuring body fat introduced during the 1980s and the 1990s, such as computed tomography and magnetic resonance imaging (MRI), have the ability to determine accurately not only total body fat but also the body fat content in different compartments. This makes it possible to measure the amount of visceral fat in a more precise manner (14). Several studies have already been performed using these new techniques to measure the amount of visceral fat. The visceral fat content has been linked to different anthropometric indices and to the presence of cardiovascular and metabolic risk factors. Pouliot and colleagues showed, by using computed tomography, that waist circumference and abdominal sagittal diameter correlated better than the more commonly used waist-to-hip ratio with both the amount of visceral fat accumulation and the different metabolic risk factors (19). From the data in this study it was suggested that a waist circumference of above 100 cm, or an abdominal sagittal diameter of above 25 cm, would indicate an increased risk situation for the development of cardiovascular disease and/or type 2 diabetes. However, since the sagittal diameter in the study was measured indirectly using an abdominal scan obtained with computed tomography, further studies need to be performed where the abdominal sagittal diameter is measured clinically, before the method can be recommended for clinical purposes.

The use of waist circumference has also been advocated. In this context, it should be pointed out that the relationship between waist circumference (or waist-to-hip ratio) and abdominal visceral fat accumulation may be age-specific. Older subjects
seem to have more visceral fat for each given value of waist circumference (or waist-to-hip ratio) than younger adults (20). From a public health point of view, it might be argued that measuring waist circumference on large subgroups of a population, and then using age-specific threshold values to identify individuals at risk, would present no major problems. In a study from Glasgow, the waist circumference was found to relate closely to both BMI and waist-to-hip ratio. By using a combination of these two measures of adiposity as a ‘gold standard’ and calculating sensitivity and specificity with respect to waist circumference, two action levels for waist circumference were suggested. A waist circumference of more than or equal to 94 cm in men and 80 cm in women (lower action level) identified with a sensitivity of 96% and a specificity of 97.5%, subjects having either a BMI more than or equal to 25 kg/m², or a waist-to-hip ratio that was high (≥ 0.95 for men and ≥ 0.80 for women). The higher action level was defined as a waist circumference of more than or equal to 102 cm for men and 88 cm for women. These levels identified, with the same degree of sensitivity and specificity, subjects with either a BMI of more than or equal to 30 kg/m², or a high waist-to-hip ratio. The conclusion was that waist circumference is a suitable tool to use in health promotion programmes to identify, i.e. screen for, individuals who might benefit from weight management programmes (21). It was also suggested that individuals identified to be above the lower action level should acknowledge being in an increased risk situation and take action to avoid weight gain, and that individuals above the higher action level should seek professional help to lose weight and maintain a lowered body weight.

From samples within the Nurses’ Health Study and the Health Professionals’ Follow-up Study, the validity of self-reported body weights and waist and hip circumferences has been explored. The self-reported measurement was compared to a measurement conducted by a specially trained technician in the study. An especially high degree of correlation was found for body weight (0.97) and waist circumference (0.95 in men and 0.89 in women) (22). Recently, national guidelines for the management of obesity in Scotland were presented by the Scottish Intercollegiate Guidelines Network (23). Their report recommended the use of BMI and waist circumference as screening tests for obesity.

A point of caution is warranted if using these new action levels of waist circumference on populations other than Caucasian. A study comparing the prevalence of glucose intolerance in Chinese and Europid men and women showed similar age-adjusted prevalences in men (13%) but higher prevalence of glucose intolerance in Chinese women (20%) compared to Europid women (13%), despite the fact that the study found mean BMI and waist circumference to be lower in Chinese men and women than in Europids. Furthermore, the mean waist-to-hip ratio in Chinese women was higher than in Europid women (24).

Taken together, total body fat measured as body mass index and body fat distribution measured as waist circumference seem to supplement each other in indicating a cardiovascular or metabolic risk situation for an individual. They seem both to be suitable as screening tests and should preferably be used together in health promotion programmes. The action levels that have been suggested are based on our present knowledge of using simple proxy measures to assess total and visceral fat accumulation. However, as stated earlier, the choice of cut-off point in screening programmes must be determined by the level of resources allocated to take care of those identified to be at high risk. Alerting without offering advice and support is harmful. It goes without saying that different degrees of risk may need different levels of treatment programmes. It is crucial that every high-risk individual feels that the screening programme offers something they experience as beneficial.

SCREENING FOR OBESITY TO PREVENT TYPE 2 DIABETES

The primary prevention of type 2 diabetes is an urgent issue and weight control in the population seems to be the most important part of the preventive process. The drastic predictions concerning the time trends of obesity and type 2 diabetes call urgently for research aimed at finding a solution or more probably several solutions to the problem. One approach could be a mass screening programme examining the whole population for body weight and offering obese individuals the opportunity to participate in a weight management programme. Another approach could be a selective
screening procedure where only some especially high-risk segments of the population are examined.

Type 2 Diabetes and its Complications—a Serious Health Problem

People with diabetes have a substantially reduced life expectancy. Atherosclerosis is the most common long-term complication of diabetes, at least in Caucasian populations. People with diabetes are two to three times more likely to die from coronary heart and cerebrovascular disease than are people without diabetes. The relationship is even more accentuated in peripheral artery disease, which is four times more common among diabetes patients. Retinopathy develops in about 60% of those with type 2 diabetes (25) and seems to be present prior to the clinical onset of the disease in 10–30% of individuals (26). In the USA, kidney disease was 17 times more common in diabetic than in non-diabetic individuals, and diabetic kidney disease is considered the leading cause of renal disease requiring dialysis or transplantation. More than 50% of all non-traumatic lower-limb amputations conducted in the USA are associated with diabetes and the overall risk of amputation is 15 times greater in diabetic than in non-diabetic individuals (25).

Impaired Glucose Tolerance—an Intermediate Stage in the Development of Type 2 Diabetes

Both insulin resistance and beta cell dysfunction seem necessary for an individual to develop type 2 diabetes mellitus. Controversy exists about which of the two pathogenic mechanisms is the primary one. Genetic as well as environmental factors participate in the process. Using the two-step model for diabetes proposed by Saad, the diabetic process can be divided into a first step, which includes the transition from the normal to impaired glucose tolerance (IGT) and where insulin resistance seems to be the main determinant. The second step is the worsening from IGT to type 2 diabetes, where beta cell dysfunction seems to play a major role (27). In six prospectives studies the worsening of IGT to diabetes varied from 3.6% to 8.7% per year (28). In the combined analysis of all six studies, but not in all of the separate studies BMI was associated with the diabetes incidence independently of fasting and post-load glucose levels. Family history of diabetes was not associated with the progression of IGT to diabetes. It has been estimated that by the time the diagnosis of diabetes is determined according to a criterion of a fasting plasma glucose level of above 7.7 mmol/L (compare the new threshold of 7.0 mmol/L), 75% of the beta cell function has been lost (29).

A few long-term intervention studies, with the intention to prevent diabetes by treating IGT subjects, have been conducted. In the Malmö study, a combination of diet and exercise reduced the progression from IGT to diabetes during a 6-year period from 29% in the control group to 11% in the treatment group (30). The Chinese Da Qing IGT and Diabetes study showed similar results with a decrease in the incidence of diabetes in the diet and exercise treatment group of 42% compared to the control group at follow-up after 6 years (31). These two studies show that long-term lifestyle intervention may prevent or at least postpone the worsening of IGT to type 2 diabetes.

Taken together, many indications suggest that once the diagnosis of the diabetes is made, the reversibility of the diabetic state is lost, a state which probably has been present as a glucose–insulin feedback disturbance for 5–10 years (32), and what remains is to use all efforts possible to diminish further deterioration in beta cell function and diabetes disease. In contrast, lifestyle interventions have been shown to prevent the progression of IGT to diabetes. Furthermore, the effect on future macrovascular disease, due to a state of insulin resistance and hyperinsulinaemia for several years before the diagnosis of diabetes is made, must also be included in the discussion of primary prevention.

An important point that must be considered in a screening programme aimed at preventing type 2 diabetes is how the distribution of BMI in the population affects the screening procedure. In the population a majority of people will be of normal weight or have a slight excess of body fat (overweight). A few will be seriously obese. Since the number of diabetic cases that will develop is dependent on both the relative risk and the number of people sharing that risk, one may argue from a population perspective that most diabetic cases will develop among the many having a slight increase in risk and
Health Study more than 100 000 nurses participated and were followed with respect to diabetes incidence over 14 years. More than 2000 cases of diabetes were diagnosed during 1.49 million person-years of follow-up (33). In the Health Professionals’ Follow-up Study, more than 50 000 male health professionals participated. During 5 years of observation, 272 cases of diabetes were diagnosed (18). Both studies show a progressively increased relative risk of getting type 2 diabetes when groups with successively higher BMIs were compared to a group with the lowest BMI.

In the Nurses’ Health Study, the age-adjusted relative risk of getting diabetes during a 14-year follow-up was found to be more than 90 times higher if BMI was more than 35 kg/m\(^2\) compared to less than 22 kg/m\(^2\) (33). Correspondingly, the age-adjusted relative risk for diabetes after 5 years of follow-up in men was 50 times higher if BMI was 35 kg/m\(^2\) or more compared to less than 23 kg/m\(^2\) (18). It was also shown that the relative risk for diabetes already started to increase in the upper range of normal weight and became ever more pronounced as body weight increased. Nevertheless, looking at the problem from another angle, more than 85% of the subjects in the highest weight class (BMI \(\geq 35\) kg/m\(^2\)) did not develop diabetes during the observational period (14 and 5 years, respectively).

If instead of relative risk we concentrate on the distribution of new diabetes cases during the follow-up, a pattern of increasing incidence along with higher BMI emerges. However, at a point where BMI reaches 31 kg/m\(^2\) in the female study and 29 kg/m\(^2\) in the male study, the number of diabetic cases starts to fall in spite of a still increasing

### Table 5.2 Comparing the distribution of new diabetes cases at three different levels of body mass index in two populations

<table>
<thead>
<tr>
<th>Reference</th>
<th>Body mass index (%) of total</th>
<th>Person-years of follow-up (%) of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colditz (33) (^a)</td>
<td>(\geq 27) 76</td>
<td>22.1</td>
</tr>
<tr>
<td></td>
<td>(\geq 31) 49</td>
<td>8.3</td>
</tr>
<tr>
<td></td>
<td>(\geq 35) 26</td>
<td>3.1</td>
</tr>
<tr>
<td>Chan (18) (^b)</td>
<td>(\geq 27) 61</td>
<td>23.5</td>
</tr>
<tr>
<td></td>
<td>(\geq 31) 27</td>
<td>4.2</td>
</tr>
<tr>
<td></td>
<td>(\geq 35) 9</td>
<td>0.7</td>
</tr>
</tbody>
</table>

\(^a\)The Nurses’ Health Study.

\(^b\)The Health Professionals’ Follow-up Study.
relative risk for the disease. As stated earlier, at more extreme levels of BMI fewer individuals are to be found, in accordance with the normal distribution curve of BMI in the population. In the Nurses’ Health Study, there is one large exception to this pattern. Individuals having a BMI of 35 or more presented such a large risk increase that even though they were relatively few, they generated more than 25% of all the diabetic cases. This indicates that the relation between body weight and type 2 diabetes does not strictly follow the pattern of the preventive paradox.

By choosing different cut-off points in BMI, the proportion of a population that will be designated as high-risk individuals will vary and this in turn means that the number of potential diabetes cases that could be prevented or postponed will vary (Table 5.2). A cut-off value of 27 kg/m² would designate more than 20% of the population as high-risk individuals, to whom a treatment programme should be offered. According to these two prospective studies, between 60 and 70% of future type 2 diabetic cases would be involved and at best prevented or postponed. A less resourceful screening programme using a cut-off of 35 kg/m² would designate 3% of the population in the Nurses’ Health Study and 0.7% of the population in the Health Professionals’ Study as high-risk individuals (Table 5.2). As much as 26% of future type 2 diabetic cases would be involved in such a programme according to the Nurses’ Health Study. This should be compared to 9% in the male study, which also had a shorter period of observation. A screening programme where extensive treatment is to be offered to less than 3% of the population (i.e. 3% of observed person-years in the study) would be classified as high-risk individuals. Enlarging the screening programme to all individuals having a BMI ≥ 31 kg/m², and achieving the same result concerning weight management, would reduce the incidence of type 2 diabetes on a population level by 29% (628/2197 fewer cases), but in this alternative 8% of the population had to be offered the treatment programme. Of course, there are many good arguments questioning the basis for this calculation. The two most obvious would perhaps be the participation rate in the screening and the effectiveness of the treatment programme. Of course, there are many good arguments questioning the basis for this calculation. The two most obvious would perhaps be the participation rate in the screening and the effectiveness of the treatment programme.

To sum up, to achieve a large impact on public health our preventive efforts need to be concentrated on changing attitudes and behaviour in the whole population (population approach). However, it is also evident, especially from the Nurses’ Health Study, that a high-risk approach is warranted in the prevention of type 2 diabetes.

The Gain of the Game—What are the Potential Benefits?

As stated above, most would agree that a high-risk strategy certainly would be beneficial to many high-risk individuals. But the question is, may such a strategy also be justified from a public health point of view? Earlier in this chapter the prevention paradox was discussed, with its emphasis on the importance of having the whole population making small changes in lifestyle. When scrutinizing the results from the Nurses’ Health Study, looking at the association between BMI and the incidence of type 2 diabetes, a surprisingly large percentage (26%) of the incident cases was found in the highest BMI group (BMI ≥ 35 kg/m²).

What would the gain be, at best, using a screening programme to detect all individuals in the population with a BMI of 35 kg/m² or more, and offering these high-risk individuals a long-term weight management programme? Hypothetically, a crude calculation on the data from the Nurses’ Health Study can be made. Assuming that the whole population participates in the screening procedure and that the treatment programme is 100% effective in bringing down the body weight to a BMI between 29 and 30.9 kg/m². As shown in Table 5.3, the incidence of diabetes in the highest BMI group would be reduced by more than 70%. Converting this figure into its effect on the whole population in the study, there would be a decrease in incident diabetic cases in the population of 19% (414/2197 fewer cases). In this example 3% of the population (i.e. 3% of observed person-years in the study) would be classified as high-risk individuals. Enlarging the screening programme to all individuals having a BMI ≥ 31 kg/m², and achieving the same result concerning weight management, would reduce the incidence of type 2 diabetes on a population level by 29% (628/2197 fewer cases), but in this alternative 8% of the population had to be offered the treatment programme. Of course, there are many good arguments questioning the basis for this calculation. The two most obvious would perhaps be the participation rate in the screening and the effectiveness of the treatment programme. However, the point to illustrate in this calculation is that in the case of obesity and type 2 diabetes a high-risk strategy really seems worthwhile.
Table 5.3  Hypothetical calculation of reduction in number of incident diabetic cases in women during 14 years of follow-up. The assumption is that an intervention successfully achieved a weight decline to a body mass index range of 29.0–30.9 kg/m$^2$ in all individuals. The calculations are performed on data from the Nurses’ Health Study (33).

<table>
<thead>
<tr>
<th>Body mass index</th>
<th>Diabetic cases</th>
<th>Person-years of follow-up</th>
<th>Age-standardized incidence rate$^a$</th>
<th>Hypothetical number of diabetic cases$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>29.0–30.9</td>
<td>329</td>
<td>84 880</td>
<td>354.5</td>
<td>329</td>
</tr>
<tr>
<td>31.0–32.9</td>
<td>263</td>
<td>47 119</td>
<td>521.2</td>
<td>167</td>
</tr>
<tr>
<td>33.0–34.9</td>
<td>224</td>
<td>29 885</td>
<td>703.6</td>
<td>106</td>
</tr>
<tr>
<td>$\geq$ 35</td>
<td>579</td>
<td>46 636</td>
<td>1190.5</td>
<td>165</td>
</tr>
</tbody>
</table>

$^a$Age-standardized rate per 100 000 persons.

$^b$Hypothetical number of cases has been calculated by using the incidence rate among individuals in the BMI range of 29.0–30.9.

THREE SELECTIVE SCREENING PROGRAMMES FOR OBESITY—A PROPOSITION

As stated earlier, the screening procedure for obesity, whether using BMI or waist circumference or both as screening tools, will not be the expensive part of the screening programme. These measurements of obesity are easy to obtain and the measurements could be performed with a high accuracy at many different locations such as work sites, schools and primary health care centres. The expensive part of the screening programme arises when all screenees classified as high-risk individuals are to be treated. Considerable resources must then be allocated if success is to be expected in performing weight management programmes on a large scale.

Recently, the Scottish Intercollegiate Guidelines Network (SIGN) released a report on the management of obesity in Scotland (23). The report pointed out the need for earlier identification of children and adults that are gaining weight, especially if they come from overweight families. To solve this problem, the recommendation was to institute regular screening of the whole population at 3-year intervals with recording of BMI and waist circumference. Furthermore, weight management programmes were to be introduced in primary health care centres and evaluated regularly in a strict manner.

There are many reasons to involve the primary health care system in the early detection and treatment of obesity. There is one obvious question, concerning these interventions, that must be answered: ‘Do those who really need the intervention most participate in the screening programme?’ In 1985, a community intervention programme on cardiovascular disease and diabetes prevention was launched in the province of Västerbotten in northern Sweden. The programme combined a population strategy and an individually oriented strategy. The latter was mainly carried out within the primary health care system. Evaluation by comparing participants and non-participants in the intervention programme showed the social selection bias to be quite modest. The result was explained by the close involvement of the primary health care organization in the programme. The primary health care centres in Sweden seem to attract and interact with all groups in the local society, independent of social position, education, employment and income level (34).

Another observation derives from a small community in Sweden, where opportunistic screening was used to find undiagnosed diabetes. In this community, primary care was provided through a single health care centre. It was shown that as much as 75–85% of the whole population participated in the screening programme during a 5-year period of observation (5). It is important to emphasize that all screening for obesity must be evaluated on a regular basis, whether we choose to use a mass screening approach or opportunistic screening, and whether we select some sector of the population to participate or the whole population. There is a need to conduct different kinds of screening programmes for obesity and in different populations. The results from these studies may then form the basis for future planning of screening programmes for obesity.
In the light of these facts, three potentially interesting areas of screening for obesity will be highlighted, namely screening for obesity in children, for severe obesity and for the combination of obesity and impaired glucose tolerance.

The Prevention of Obesity in Children

About 30% of obese children become obese adults (35). Furthermore, obese adults whose obesity started to develop at a young age seem to suffer more serious consequences because of their excess body fat resulting in higher morbidity and mortality rates (36). It often takes years for obesity to develop, but once there it is hard to treat. A promising approach worth exploring would be to prevent childhood obesity becoming adulthood obesity. In a randomized study, obese children treated in a family-based weight reduction programme were found to have a decrease in percentage overweight (−7.5%) at follow-up after 10 years. The non-specific control group in the study had an increase at follow-up of more than 14% (37). However, two points must be emphasized when working with weight management programmes in children. First, in order to promote healthy growth and to avoid future eating disorders, a child must be fed properly, i.e. the child must receive an adequate nutrition and the meal frequency should be regular. Second, every effort must be made to counteract potential negative effects that may appear as a consequence of classifying some children as high-risk individuals and others as normals. All signs of these obese children being frozen out by their peers should be taken seriously (38).

Intensive Treatment in Severely Obese

A number of indications suggest that the treatment of severely obese people, i.e. a BMI more than or equal to 35 kg/m², should be intensified. Perhaps the most important reason is the marked increase in risk for developing diabetes that exists among the severely obese. As mentioned earlier when discussing the Nurses’ Health Study, those defined as severely obese (BMI ≥ 35 kg/m²) constituted 3% of the observed person-years but 26% of the incidence in diabetes. In the Swedish Obese Subjects (SOS) Study, it was shown that a large weight loss (about 20 kg) was associated with a 14-fold risk reduction for type 2 diabetes (39). A non-randomized study, where excess body weight in the severely obese was reduced by 50%, prevented progression from impaired glucose tolerance to type 2 diabetes more than 30-fold compared to a control group (40). The large weight loss in these studies was achieved by surgical treatment. In general surgery is today considered the most effective way of reducing weight in the severely obese. Due to the gravity of the health situation for the severely obese, immediate steps to identify and treat this group of people ought to be taken. One possibility could be to institute an opportunistic screening programme within the primary health care system. In other words, whenever an obese person makes an appointment at the primary health care centre, the routine is to measure BMI and waist circumference. Of course, different treatment alternatives, and not only surgery, must be offered to those classified as high-risk individuals in such a large-scale operation. Not everyone will or should accept surgery as the only, or as the first, treatment alternative.

Screening for the Combination of Obesity and Impaired Glucose Tolerance

Impaired glucose tolerance (IGT) implies an increased risk for CVD and for type 2 diabetes mellitus. In fact, some consider IGT as the strongest measurable risk factor for future type 2 diabetes. However, not all individuals with IGT seem to develop diabetes and the conversion rate varies considerably between different ethnic populations. The thrifty genotype syndrome, originally described by Neel, has been suggested as a possible explanation for this phenomenon (41). In the Västerbotten Intervention Programme in north Sweden, a strong association was found between obesity and IGT. As shown in Figure 5.3, BMI was divided into seven subgroups from underweight (<20 kg/m²) to severe obesity (≥35 kg/m²). The relative frequency of IGT among obese subjects (BMI ≥ 30 kg/m²) was four times that of subjects with normal body weight (BMI 20–24.9 kg/m²). Subjects with overweight (BMI 25–29.9 kg/m²) had a frequency of IGT twice that of subjects with normal weight. However, com-
paring absolute numbers of individuals with IGT in the different body weight classes, as indicated by the bars in the figure, did show that the majority of individuals with IGT were found among those with a modestly increased body weight (45%) or with a normal body weight (27%). Only 25% of the subjects with IGT were classified as obese (42). In the study, the impact of selecting certain age groups to be screened was examined by calculating the numbers-needed-to-screen to find one individual with abnormal glucose tolerance. It was shown that three to six times as many 40-year-old men and women were needed to be screened when compared to 60-year-old subjects, after adjustments were made for body weight and heredity for diabetes.

Although the relative risk of having IGT increased with increased body weight and with reported heredity for diabetes, the study also clearly demonstrated that the majority of IGT subjects were non-obese and had no heredity for diabetes. The implication of this in screening programmes aimed at preventing type 2 diabetes must be that the screening procedure for IGT should not be targeted solely towards obesity, at least, if we assume that IGT is the predominant risk variable for progression to diabetes. On the other hand, if the screening was to target only 60-year-old individuals with overweight, it ought to be effective from a cost–benefit point of view, even if the chosen subgroup represents only a small portion of IGT in the population. Another way of reasoning could be that our screening strategy should be adjusted to our ability in preventing diabetes by lifestyle and/or pharmacological interventions. Logically, then, it feels as though there is more to offer to obese subjects.

CONCLUSIONS

The prevention of type 2 diabetes by combating obesity and counteracting a sedentary lifestyle is one of the most important health issues of today, and based on projections of future development the issue will be even more important tomorrow. There is much to indicate that our preventive efforts must be based on a population strategy, engaging different sectors of the society. Having health-promoting legislation and agreements with the food industry go hand in hand with health professionals’ ambition to change people’s attitudes and lifestyles. However, at the same time, not least for ethical reasons, there must be a concentration of resources within the health care system to treat as effectively as possible those identified to be at highest risk of suffering serious health consequences by their choice of lifestyle (high-risk strategy).

Looking at the association between obesity and type 2 diabetes, many indications suggest that a high-risk strategy may be worthwhile, not only from an individual standpoint, but also from a population perspective. The role of screening programmes is to identify and treat these high-risk individuals. The question from a cost-effective point of view, when screening for obesity, is not how to find these high-risk individuals, whether by using mass screening, opportunistic screening or screening by educating people to seek advice and support from the health care system when BMI or waist circumference is above a certain level. The costs for the detection of obesity in screening programmes will be within reasonable limits, irrespective of screening methods used. A potential danger is that many high-risk individuals from low socioeconomic groups will abandon the screening activities. We must remember that the central issue, with respect to obesity, is to find an acceptable treatment open to all defined as high-risk individuals. In other words to allocate enough resources for the treatment programme.

Selective rather than mass screening programmes have been advocated and exemplified in the second part of this chapter. These screening proposals may be regarded as the first line of screening programmes for obesity, especially in view of the present level of resources for prevention within most health care systems.
REFERENCES


