CHAPTER 7

General discussion

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In this Chapter, the main findings of the studies included in this thesis will be discussed. The results and the methods used will be put into context of scientific literature. Finally, directions for future practice and research will be addressed.

Main findings

Overweight history and physical function

A cumulative effect of overweight over the life course on functional limitations at young old age was described in Chapter 2. We found that being overweight, as assessed by BMI, since young adult age (25 years) increased the odds for the (development of) functional limitations at young old age (55-65 years). As compared to older adults who were never overweight, persons who were overweight since age 25 years or 40 years had an approximately twofold higher risk, after adjustment for socioeconomic and lifestyle factors, chronic diseases and grip strength. Older adults who were only currently overweight had a 30% increased risk for functional limitations as compared to their peers who were never overweight. A longer overweight history at age 55-65 years also increased the risk for a deterioration of self-reported functioning during three years of follow-up. Both cross-sectionally and prospectively, these associations were strongly attenuated after adjusting for current BMI. The mean current BMI was higher with longer overweight history, so this could be an important reason for the higher risk for functional limitations. However, one does not get high BMI in old age without either a high BMI at young adult age or a large increase of BMI over the adult life course. The different roles of these two factors are difficult to disentangle.

Obesity and pain

In Chapter 3, we showed that pain is highly prevalent among older adults and that overweight in older adults is strongly associated that both the prevalence and the incidence of pain. The associations with both BMI and waist circumference were assessed and found to be equally strong. A two- to threefold higher risk for the development of pain during 6 years of follow-up in the highest quartiles of BMI and waist as compared to the lowest quartiles was found. One of the leading causes of pain in older adults is osteoarthritis, which is also strongly associated with obesity itself. Adjustment for self-reported osteoarthritis, however, attenuated the associations in both men and women, but they remained statistically significant.

Development of new standards for overweight in old age

In Chapter 4 through 6 we described the process of developing new standards for the assessment of overweight in older adults. We decided to explore the usability of known and accepted anthropometric measures to assess health risks. Waist circumference was considered to have the highest potential to be able to correctly categorize health risks in older adults if optimal cut-off values would be defined. In the literature, the waist circumference has been described to be a strong predictor of both chronic diseases and functional limitations in older adults.

In search of the optimal method to study the applicability of cut-off values for waist circumference in Chapter 4, we started off by studying the linear association of waist circumference with BMI in a representative population of Dutch older adults aged ≥70 years. Translating the widely used BMI cut-off values to cut-off values for waist circumference, the waist circumference cut-off values needed to be shifted upwards in both older men and women as compared to the cut-off values according to the WHO. Comparing both sets of cut-off values, we found stronger associations between our newly identified categories of waist circumference and mobility limitations. Furthermore, when applying the newly identified cut-off values, the area under the Receiver Operating Characteristics curve (ROC) increased and the quality of the regression models improved based on the Akaike's Information Criterion (AIC) measure for model fit. On the purpose of assessing the applicability of the cut-off values in stratifying health risks, spline regression curves were drawn to carefully visualize the shape of the dose-response relationship between waist circumference and mobility limitations. The visual inspection of the spline regression curves confirmed the appropriateness of an upward shift of the cut-off values of waist circumference in older men and women as compared to the WHO cut-off values.

In Chapter 5, we continued by to assess the dose-response relationships between waist circumference and several additional important health outcomes in older adults. The shapes of the associations with cardiovascular diseases (CVD), diabetes and knee osteoarthritis were almost linear and no thresholds could be detected. By visually inspecting the non-linear curves of the associations between waist circumference and pain, mobility limitations and urinary incontinence, appropriate cut-off values were proposed. A cut-off value of 109 cm was selected in men and a cut-off value of 98 cm was selected in women. The quality of the models when applying several cut-off values was assessed using proper statistical techniques. The results of these analyses in women closely matched the proposed cut-off values based on the visual inspection of the spline regression curves; a shift of one centimeter to 99 cm further improved the performance of the models. In men, cut-off values between 100 cm and 106 cm were shown to perform comparably well, but applying higher cut-off values deteriorated the models. Therefore, cut-off values of 106 cm in men and 99 cm in women were proposed.

In Chapter 6 we aimed to assess the validity of the proposed cut-off values for waist circumference, when applied in data of other cohort studies. The associations of waist circumference with the same health outcomes studied in Chapter 5 were assessed in four different cohort studies of older men and women from four different countries. Shifting the cut-off values upwards from the WHO cut-off value of 88 cm to 99 cm in women consistently improved the classification of health problems with 5-10% in association with the majority of health outcomes in all cohorts. In men, no significant improvements or deteriorations of the classification of health risks were found. It can be concluded that in men aged 70 years and older, there is no need for a shift upwards of the waist cut-off value, as compared to the cut-off used in adult populations. A shift of the waist circumference cut-off value from 88 cm to 99 cm in women aged 70 years and older seemed to be a valuable improvement of the classification of health risks.

Anthropometric indicators and cut-offs

Optimal anthropometric indicator for assessing health risks in older adults

We aimed to develop a standard for the assessment of overweight in older adults that would be feasible to implement in both a clinical and a public health context. BMI and waist circumference are by far the anthropometric indicators most often used, but some others have been described in literature, such as waist-to-hip ratio, abdominal sagittal diameter and waist-to-height ratio. Because BMI and waist circumference are already widely known and widely used, we wanted to assess the possibility of correctly classifying health risks related to overweight in older adults using these indicators.

Waist circumference and BMI are strongly correlated with each other and waist circumference has been shown to be strongly correlated with both total and visceral fat (1, 2). Waist circumference was considered to have some advantages over BMI. First, waist circumference has been shown to be a stronger predictor of obesity-related health consequences in older adults as compared to BMI (3-5). Furthermore, the age-related body height loss, caused by shrinkage of the spine, causes BMI to be prone to overestimation in an aging population (6, 7). An increase of the BMI in old age can be the result of weight gain, but also of a loss of body height. Waist circumference has been shown to be fairly independent of body height and adjusting waist circumference for body height seems to be unnecessary (8). Because gains of fat mass are potentially accompanied by age-related losses of lean mass, BMI might not increase with increasing adiposity (9, 10). With aging, fat is progressively stored in the abdominal cavity and increasing adiposity is expected to lead to an increased waist circumference in older adults (9). The age-related fat redistribution causes the waist circumference to be higher in older adults at a given BMI (9). Finally, the assessment of waist circumference can be performed taking a single measure using an inexpensive measuring tape. BMI requires two measurements using two more expensive instruments. Furthermore, a calculation has to be made before the measured values can be interpreted, which is prone to error (11).

Objectives for the use of anthropometric indicators

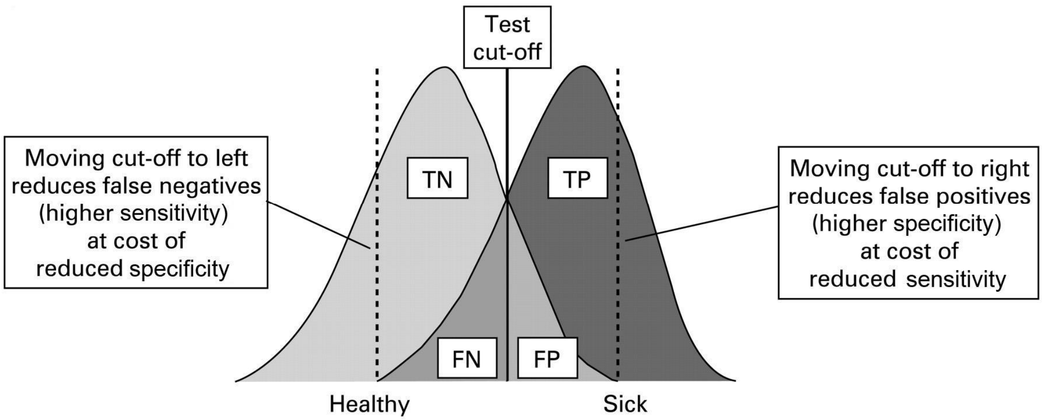
The WHO has listed several objectives for the use of anthropometric indices in their technical report in 1995 (12). First, it was stated that indicators can be used to identify individuals and populations at risk for health complications and that for this purpose, the indicator should reflect past or present risk or predict future risk. Secondly, they are useful for the selection of individuals or populations eligible for an intervention and for the evaluation of the effects of an intervention. For the sake of the selection of individuals, the indicator should predict the benefit to be derived from an intervention, while for the application to the evaluation of interventions an indicator should be able to reflect the response to the intervention. Furthermore, research purposes of anthropometric indicators were also mentioned in the WHO report, but not elaborated on. Anthropometric indicators are widely used in epidemiological research to model the health consequences of obesity. The use of standardized measures and cut-off values allows a comparison of study results. Finally, the uses of anthropometric indicators to reflect normality in a population or to exclude individuals from, for example, high risk treatment or employment were briefly described.

Implications of the newly proposed cut-off value

The different objectives for the use of anthropometric indicators might require different quality standards. For example, for some objectives the specificity might be more important than the sensitivity and visa versa. However, using different standards of anthropometric indices on different occasions is prone to result in confusion by the public and health professionals. In this paragraph, the implications of the newly proposed cut-off value in women will be evaluated in the light of various possible applications.

Our study of the dose-response relationships between waist circumference and obesity-related health problems resulted in the proposal of an upwards shift of the cut-off value for high risk waist circumference in older women. Using a higher cut-off value of a sole predictor will lead to an increased specificity and, consequently, a decreased sensitivity (Figure 1). The sensitivity of a test is the proportion of people having a certain condition that is recognized as being at risk for having this condition by that test. Using a higher cut-off value, less people will be identified as being at risk and thus the sensitivity is decreased. The specificity, on the other hand, represents the proportion of people recognized by the test as being at risk that actually has the condition of interest. In our case, by shifting the cut-off value upwards, less people were considered to be overweight while they were not at risk for health problems, so the specificity went up. In our cross-validation study, the number of older women rightfully classified as being at high-risk for health complications increased with 5-10% by the new cut-off values according to the Net Reclassification Improvement (NRI), which weights sensitivity and specificity equally.

Figure 1. Illustration of the changes of the sensitivity-specificity trade-off by shifting the cut-off value of a sole predictor of a diagnostic test.



TN = True negatives, TP = True positives, FN = False negatives, FP = False positives

Because of the high prevalence of a large WC among older adults, an improved specificity is desirable in terms of the allocation of financial means (12). By a high specificity, the percentage classified as high risk that actually has health problems is high. Only few persons will be unnecessarily referred to, and treated by a doctor. Specificity is especially important if an intervention is associated with health risks (12). Interventions targeting a large waist circumference obviously involve weight loss. Weight loss interventions in older adults have been reported to be beneficial for cardiovascular and metabolic health and for function, but to also have adverse health effects in some subjects (13). Accompanying losses of muscle mass have been described to be prevented by exercise (14). The reported inability to prevent losses of bone mass (15) increases the importance of selecting individuals for weight loss interventions with high specificity. Targeting persons at high risk encourages benefits of weight loss to be frankly appraised. Furthermore, an anthropometric indicator with a cut-off value that is too low (or too high) might cause a low relative risk for negative health outcomes of persons who are above the cut-off as compared with persons below, and as a consequence, the relative risk will not be considered high enough to take action. So, accurate cut-off values will prevent underestimation of health risks in epidemiological research which may lead to unawareness of the importance of maintaining a healthy weight throughout old age.

The decreased sensitivity of the new cut-off values also has its drawbacks when the criteria are applied for some specific aims. A highly sensitive measure is important when the objective is to raise awareness among the population; people will feel addressed by a public health message even though their individual health risk might not be shockingly elevated. When an intervention is suitable and affordable for virtually everybody and has no adverse side effects, a cut-off value can be chosen at 100% sensitivity to be able to treat all those at risk (12). Adopting a healthy lifestyle for example is suitable and safe for virtually everybody. When less people feel addressed by public health messages because they are below a cut-off value that is shifted upwards, it might decrease their willingness to adopt a health lifestyle.

Published methods for defining cut-offs

Molarius and Seidell (16) summarized the criteria used in literature for the selection of classification systems of anthropometric indicators in 1998. The first of the described criteria, is the use of percentiles of population distributions and standard deviations of the mean. A drawback of this approach is the assumption that the population distribution of an anthropometric indicator is desirable and that a certain percentage of the population has values that are undesirable. Further disadvantages are that, by the use of this method, population-specific cut-off values are defined and that cut-off values will change over time. A second method often used is substitute one anthropometric indicator with another by a comparison of the two. This method was applied when the original waist circumference cut-off values were established based on those of BMI by Lean et al (17). The cut-off values constructed by this method are highly dependent on the validity of the comparative anthropometric indicator and its cut-off values.

Finally, two methods were described by Molarius and Seidell relying on the (relative or the absolute) health risk associated with the anthropometric indicator under study. One is the evaluation of the Receiver Operating Characteristics (ROC) curve to asses the sensitivity, specificity and/or the positive and negative predictive values. The ROC method has been applied many times over recent years, especially in studies aiming for ethnic-specific cut-off values of waist circumference and other anthropometric indicators. However, in a recent paper (18) the authors concluded that methods relying solely on maximizing sensitivity and specificity to determine cut-off values might oversimplify the complexity of the matter. By assessing the relationship between the population mean waist circumference and the reported optimal cut-off values of waist circumference in published papers, it has been shown that the variation in cut-off values proposed by these studies was mainly driven by the mean level of waist circumference in the populations studied. The second method described by Molarius and Seidell to define cut-off values relying on health risks associated with the anthropometric indicator, is studying the absolute risks for health problems of interest. They stated that defining a cut-off value based on the visual inspection of the shape of an association showing a gradual increase of risk is rather arbitrary. They argue that an important drawback is the difficulty of well defining the criteria on which the establishment of a cut-off value was based. Nevertheless, this method was suggested as a promising direction of future research by Wang et al (18).

Methods used for defining cut-offs in this thesis

In the studies described in this thesis we applied different methods complementing each other in terms of reliability of the results and to compensate for the drawbacks of each individual method. First, we used the association between waist circumference and BMI basing new waist circumference cut-off values on the existing BMI cut-off values. In literature, as a result of the redistribution of fat, higher waist circumferences relative to BMI in older as compared to younger adults have been described (9). As expected, higher cut-off values were suggested by the results of this analysis, but we also recognized that the results were highly dependent on the validity of BMI and its cut-off values which is questionable in older adults (19).

We proceeded using a sensitivity/specificity-based method to test the performance of our newly defined cut-off values in association with mobility limitations. The area under the ROC curves was higher when the higher cut-off values were applied, pointing out that the sensitivity-specificity trade-off was improved. However, the cut-off values under comparison were established using a method with some serious drawbacks (the association between BMI and waist). In a next step we drew spline regression curves in which the dose-response relationship showed that the risks for mobility limitations were not yet increased at the level of the WHO cut-off values of waist circumference in both men and women. However, as Molarius and Seidell already stated (16), it was difficult to define one optimal cut-off value based on the gradual increase of the risk. When taking into account several additional important health outcomes, we felt that we might be able to define a general cut-off value at which the risk was increased for all outcomes. By using the dose-response relationships with six different, important health outcomes we aimed to adequately define new cut-off values of waist circumference in older adults. We aimed to lower the arbitrariness that was suggested to be involved in identifying cut-off values this way, by obtaining three independent assessments of the potential optimal cut-off value. Than, model fit analyses were performed to objectively determine the potential improvement by shifting the cut-off values upwards.

To establish whether or not the higher, new cut-off values were highly dependent of the data used, the cut-off values were cross-validated using different cohort data. The new cut-off values were tested for a positive sensitivity specificity trade-off (as compared to the WHO cut-off values) using the Net Reclassification Improvement (NRI), in four cohorts of older adults from four different countries. Results consistently confirmed that an upwards shift of the cut-off value in women improved the classification of health problems. In men, consistent results of the different study cohorts showed that the classification of health complications would not be improved by an upwards shift of the cut-off value for waist circumference.

Methodological considerations

Representativeness and attrition in longitudinal studies of aging

In the studies included in this thesis, data from longitudinal population-based studies have been used. Using this type of observational studies, the natural course of the development of health and functional problems in a real-life setting can be studied over time which encourages the generalizibility of the results. However, some important limitations should also be discussed. Longitudinal observational studies, particularly those conducted in older adults, suffer from missing data and attrition. Because health and functional problems are more prevalent in old age, data collection can be hampered and selective survival is likely to occur. Mortality accounts for by far the largest part of the drop-out in the described study samples, while a considerably smaller part is caused by participants refusing or becoming too frail to participate. Mortality does not necessarily influence the representativeness of the sample because in the general older population a high mortality rate is typical as well (20). Still, the drop-out caused by death can bias estimations of relationships between variables under study. The attrition and its effects in the LASA cohort have been previously studied (21, 22). Attrition was found to be dependent on several population characteristics, but how the attrition might influence the relationship between predictors and outcomes studied in the current thesis remains unknown. Because obesity increases the risk for mortality and frailty (23), obese persons might be underrepresented in the oldest age groups. Also, many of the outcomes under study might have negatively influenced participation rates. The obese participants who are still in the study, might represent the ones less susceptible for the consequences of overweight on their health and physical function. Therefore, the associations in this thesis could be underestimated.

Longitudinal versus cross-sectional analyses

An advantage of longitudinal as compared to cross-sectional analyses is that conclusions can be drawn on the order in which determinant and outcome occur. Even after accurate adjustments for confounding, knowing the order of occurrence does not necessarily imply a causal relationship. There might be unmeasured or unknown (underlying) factors influencing both the determinant and the outcome.

In order to establish the sequence in which determinants and outcomes occur, longitudinal analyses are necessary. In Chapter 3, we performed cross-sectional as well as longitudinal associations. These analyses showed that the development of pain was preceded by having a high BMI or waist circumference, but that having pain did not increase the risk for subsequent weight gain. However, performing analyses longitudinally not always represents the strength of the associations under study. When studying the incidence of, for instance, mobility limitations or chronic diseases, participants with prevalent conditions at baseline need to be excluded from analyses. Besides from the consequences from these exclusion criteria in terms of statistical power, the selectiveness of the sample needs to be taken into account. Obese older persons (≥70y) without the excluded condition might represent a rather selective group of people relatively insusceptible for the negative consequences of obesity for their health. In Chapter 2, a longitudinal association between weight history and an increase of functional limitations was found, while no association with the incidence of functional limitations was found. Both the phenomenon of selectivity and/or the decreased statistical power might have played a role.

Although longitudinal data were available for the studies described in Chapter 4 and 5, data were analyzed cross-sectionally. When performing preliminary longitudinal analyses on the dose-response relationship between waist circumference and several health outcomes by means of spline regression curves, we found no associations. The analyses resulted in flat lines of the spline regression curves which is probably caused by the selectiveness of the sample (due to exclusion of subjects having prevalent conditions at baseline), as described above. Because the associations between waist circumference and the selected important health outcomes have all been established in previous research, we felt confident that studying the cross-sectional associations would answer our study questions focusing on the determinant, being waist circumference.

Multivariate versus univariate analyses

With adjustment for confounding factors in the analyses, the influence of waist circumference on health outcomes would be assessed, given that all factors adjusted for are stable. In order to assess the power to predict health problems solely by someone's waist circumference, univariate analyses were performed in the studies described in Chapter 4 through 6. This way, we aimed to identify cut-off values that optimally classify health risks for a heterogeneous population of older adults. The independent associations of a large waist circumference with the outcomes under study all have been previously established in older adults (24-33). In practice, (extensively) adjusted analyses would resemble the screening for health risks based on several risk factors like, for instance, socio-demographic factors (e.g. age, education), cardiovascular risk factors (e.g. blood pressure, cholesterol) and/or medical history. Because our aim was to establish an easy assessable measure to screen for elevated overweight-related health risks, the decision was made to conduct unadjusted analyses.

Measurement of waist circumference

Different protocols for the measurement of waist circumference are being used and there is currently no consensus on the optimal site or protocol. According to the WHO guidelines, measures should be taken at the midpoint between the superior border of the iliac crest and the lowest rib (34). Other guidelines recommend the measures to be taken directly above the surperior border of the iliac crest, at maximal or minimal waist or at the umbilicus. In LASA, waist circumference was measured midway between the superior border of the iliac crest and the lowest rib in standing position after a normal expiration (in accordance with the WHO guidelines). The measurement of waist circumference has been performed differently in the different cohort studies used in Chapter 6. In the InCHIANTI study the protocol was similar to the LASA protocol. The largest abdominal circumference between the superior border of the iliac crest and the lowest rib was measured in the Health ABC study and in the AGES-Reykjavik study. All measures were taken at the end of a normal expiration with the participant in standing position using a flexible plastic tape measure.

Several studies have been performed to determine whether the magnitude of waist circumference differs across measurement sites (35, 36). The reproducibility, both intra- and interobserver, of the measures taken by the different protocols was equally high. The variability of the measurement was found to be substantial, particularly in women (for example 8.6 cm difference between the minimal waist and the umbilicus (35)). As a consequence, prevalence rates of abdominal obesity when using waist circumference dichotomously, differed dramatically between the minimal waist (30.7%) and the umbilicus (55.2%) in women (35). These differences might hamper comparisons of prevalence data between studies using different measurement protocols.

Also, it has been studied whether the protocol influences associations between waist circumference and health outcomes. Ross et al. (37) concluded that the waist circumference measurement protocol has no substantial influence on the associations between waist circumference and mortality and morbidity. The WHO cut-off values for waist circumference were established using the WHO measurements protocol (17). The same protocol was used for the establishment of the new cut-off value in our studies (Chapter 5). It is possible that the proposed cut-off value would have been slightly different when another measurement protocol was used. However, as reported in Chapter 6, our new cut-off value of waist circumference in older women was found to better classify health risks as compared to the WHO cut-off value independently of the measurement protocol used.

Outcome measures

In our studies, we looked at the consequences of obesity in old age by assessing the associations with a range of important health outcomes in old age. In deciding on the outcomes of interest, great emphasis was put on quality of life-related aspects, apart from studying the cardiovascular and metabolic consequences of (abdominal) obesity. The direct association between obesity and quality of life has been previously described, as has the indirect association trough comorbidities (38). The large impact of mobility and functional limitations (39), osteoarthritis (40), pain (41) and urinary incontinence (42) on quality of life in old age has been previously established. Also, the ability to perform activities of daily living and to move around and to be healthy and independent were among the facets of quality of life which were shown to be particularly important to 7,401 older adults from 22 countries (43). Functional capacity, osteoarthritis, (back) pain, diabetes, and depression were all suggested to be of great importance for the quality of life of older adults by other studies (44, 45). Although various important health outcomes in older adults were studied in the assessment of new cut-off values, many have not been studied. Outcomes such as health care use, independence and nursing home admission are good examples of other important outcomes to study in association with overweight in older adults. The applicability to categorize risk for (these) other health outcomes by the new cut-off value needs to be studied in future research.

Weight management in old age

The emphasis given to the dose-response relationships in our studies shows that priority was given to the identification of individuals at risk as the aim of the newly developed cut-off value. Nonetheless, the use of the new cut-off value might also be suitable for other purposes like for example selecting individuals to participate in interventions and evaluating the effects of such interventions. Now that the association between waist circumference and important health outcomes is established, the question whether or not these health problems can be reversed by weight loss at old age is very relevant.

Monitoring weight loss by waist circumference

Based on our studies, no conclusions can be drawn on the applicability of the cut-off values of waist circumference to evaluate the effects of (weight loss) interventions in older adults. To our knowledge, only one weight loss intervention study in older adults has evaluated the effects of an intervention on waist circumference (46). In a small sample of men and women with a mean age of 70 years with a BMI of ≥30 kg/m^2, a mean decrease of waist circumference of 10 cm was reported after 26 weeks of lifestyle intervention. The applicability of waist circumference to reflect the response to a weight loss intervention in older adults however, needs to be further addressed in future research.

Benefits of voluntary weight loss in older adults

Weight loss treatment in older adults is still a controversial topic with limited scientific knowledge. The paucity of conducted trials increases in older age groups. Several reviews on weight loss trials in older adults have been conducted in recent years (13, 47-49), and one of these studies also performed a meta-analysis (13). In this meta-analysis, nine randomized controlled trials among persons with a mean age of ≥60 years and a follow-up of over one year were included. Only one of the included studies was performed in participants with a mean age of over 70 years (15). All interventions were based on weight loss through lifestyle modifications, most interventions contained both caloric restriction as well as a physical activity program. A drawback of this approach is the inability to separate effects of weight loss and an increased physical activity level. However, the studies that included both a diet only and/or a physical activity only as well as a combined intervention group, positive effects on weight and/or health and function outcomes were largest in the combined groups. All four reviews (13, 47-49) conclude that weight loss interventions in older adults should contain physical exercise programs additional to restrictive diets.

The meta-analysis showed that a modest but significant reduction in body weight of 3.0 kg was achieved after 12 months by the different weight loss interventions. Based on the meta-analysis, the only health parameter other than weight loss on which conclusions could be drawn was total cholesterol, which was not significantly lowered. Data on other health outcomes were all insufficiently measured but individual studies reported positive results. Based on these data, positive effects of weight loss interventions in older adults on physical function, quality of life, osteoarthritis and cardiovascular and metabolic risk factors seem plausible. The lack of high quality long term interventions was emphasized in all reviews. Addressing outcomes that are directly relevant to older people like physical function, pain, urinary incontinence and quality of life is of great importance.

Adverse effects of voluntary weight loss in older adults

Apart from the lack of convincing evidence, other issues enhance the controversy on weight loss treatment in older adults. Concerns are raised about the loss of muscle strength and muscle mass (14), bone mass (15, 50, 51) and an increased risk for mortality accompanying intentional weight loss (52, 53). Losses of lean mass are suggested to be proportional to the amount of weight loss as compared to studies performed in younger adults. However, older adults already experience age-related losses of lean mass and the risk for becoming frail might rise with intentional weight loss (54, 55).

It has been described that intentional weight loss achieved by a combined intervention on diet and exercise might prevent the adverse effects on muscle strength (10). Although it has been found to be difficult to prevent any loss of muscle mass during a weight loss intervention, muscle strength can be maintained by adding exercise to the weight loss program (14, 56, 57). Muscle strength is found to be higher among obese older adults, which is thought to be an effect the greater strength needed to bear their own weight (58). Relative to their body weight however, obese older persons are reported to have a lower strength as compared to their lean peers (32, 58). The effects of simultaneously having a high body weight and low muscle strength, which is called dynapenic/sarcopenic obesity, have been reported to be more detrimental than would be expected by adding the separate effects of obesity and muscle weakness (59). The prevention of dynapenia and/or dynapenic obesity is important to take into account in developing a weight loss intervention in older adults.

It has been suggested that the loss of bone mass during weight loss therapy among older adults can not be prevented (15). Both resistance and endurance training, the prescription of high doses of calcium and vitamin D as well as antiresorptive therapy have been suggested to have a potential protective effect against the loss of bone mass during weight loss intervention (56). Because obesity is associated with an increased bone mineral density, the clinical implications of the bone loss accompanied with weight loss remain unclear.

Based on data from observational studies, it has been suggested that the risk for mortality increases with both intentional as well as unintentional weight loss (60, 61). However, questions have been raised whether the self-report of weight loss intention is accurate. To our knowledge, Shea and colleagues (62) were the first to report on the effects of a weight loss intervention on mortality. They concluded that weight loss, either dietary only or by dietary weight loss and exercise, yielded no additional risk for all-cause mortality during an average of 8 years of follow-up as compared to the non-weight loss groups.

Prevention of weight gain in life course perspective

The prevention of weight gain is of course the best measure to remain healthy. Because weight loss therapy in older adults is still controversial, the prevention of weight gain is also desirable for safety reasons. Furthermore, the adverse effect of excess weight during (early) adult life on several health conditions in old age has been described in literature (63). Apart from the association between overweight history and physical function, as has been extensively described in Chapter 2 of this thesis, the associations between, for instance, overweight history and diabetes (64), quality of life (65) and walking limitations (66) have been reported. These results suggest that losing weight during late life might be too late to counteract the detrimental effects of overweight and that prevention of overweight throughout the lifespan is a far better option to promote healthy aging. Targeting health promotion strategies for overweight prevention to older adults has been argued to be potentially more efficient and cost-effective as compared to targeting children and adolescents (67, 68). Main reasons for this hypothesis are the increasing absolute and population attributable risk for disease associated with obesity with increasing age and the shortened time to onset of disease in older adults (68).

The currently defined WHO overweight and obesity classification systems based on waist circumference and BMI provide cut-off values for two different action levels. Persons within the overweight range of BMI (25-30 kg/m^2) or a waist circumference above the lower cut-off value (action level I) are suggested to be in need of weight maintenance and should be advised not to gain any (more) weight. Only persons within the obesity range of BMI (≥30 kg/m^2) or with a waist circumference above the upper cut-off value (action level II) were stated to be in need of weight loss treatment. In the current thesis, a single cut-off value for older women was proposed based on increased health risks. To our knowledge, no research has been conducted on the value of an extra cut-off value to indicate the rising risk in order to persuade people to take action to avoid gaining more weight. Possibly, application of a warning sign could raise awareness and prevent people to gain more weight and reach the upper cut-off value.

Conclusions

The growing population of overweight older adults, driven by demographic changes and the ongoing obesity epidemic, will increasingly suffer from important health problems. Future studies should point out whether or not the improved cut-off value of 99 cm in women, sufficiently predicts future health risks and is able to select older women in need for weight management interventions. Although waist circumference is suggested to be a good starting point, other individual health problems should be taken into account when prescribing weight management treatment in older adults.

This thesis added to the knowledge of health problems related to overweight in old age and to the understanding of the levels of overweight that deteriorate health in old age. Research aimed to find feasible and successful ways to prevent and to treat overweight in older adults, should be given high priority.

References

1. Harris TB, Visser M, Everhart J, et al. Waist Circumference and Sagittal Diameter Reflect Total Body Fat Better Than Visceral Fat in Older Men and Women: The Health, Aging and Body Composition Study. *Ann NY Acad Sci.* 2000;904(1):462-473.
2. Goodman-Gruen D, Barrett-Connor E. Sex differences in measures of body fat and body distribution in the elderly. *Am J Epidemiol.* 1996;143(9):898-906.
3. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr.* 2004;79(3):379-384.
4. Bigaard J, Tjonneland A, Thomsen BL, et al. Waist circumference, BMI, smoking, and mortality in middle-aged men and women. *Obes Res.* 2003;11(7):895-903.
5. Visscher TL, Seidell JC, Molarius A, et al. A comparison of body mass index, waist-hip ratio and waist circumference as predictors of all-cause mortality among the elderly: the Rotterdam study. *Int J Obes Relat Metab Disord.* 2001;25(11):1730-1735.
6. Visser M, Deeg DJH. The effect of age-related height loss on the BMI classification of older men and women. *International Journal of Body Composition Research.* 2007;5(1):35-40.
7. Nishiwaki Y, Michikawa T, Eto N, et al. Body mass index misclassification due to kyphotic posture in Japanese community-dwelling adults aged 65 years and older. *J Gerontol A Biol Sci Med Sci.* 2011;66(3):326-331.
8. Han TS, Lean ME, Seidell JC. Waist circumference remains useful predictor of coronary heart disease. *Bmj.* 1996;312(7040):1227-1228.
9. Stevens J, Katz EG, Huxley RR. Associations between gender, age and waist circumference. *Eur J Clin Nutr.* 2010;64(1):6-15.
10. Stevens J, Knapp RG, Keil JE, et al. Changes in body weight and girths in black and white adults studied over a 25 year interval. *Int J Obes.* 1991;15(12):803-808.
11. Cook Z, Kirk S, Lawrenson S, et al. Use of BMI in the assessment of undernutrition in older subjects: reflecting on practice. *Proc Nutr Soc.* 2005;64(3):313-317.
12. World Health Ogranisation (WHO) Expert Committee. *Physical status: the use and interpretation of anthropometry*. Technical Report Series. Geneva: WHO, 1995.
13. Witham MD, Avenell A. Interventions to achieve long-term weight loss in obese older people: a systematic review and meta-analysis. *Age Ageing.* 2010;39(2): 176-184.
14. Wang X, Miller GD, Messier SP, et al. Knee strength maintained despite loss of lean body mass during weight loss in older obese adults with knee osteoarthritis. *J Gerontol A Biol Sci Med Sci.* 2007;62(8):866-871.

15. Villareal DT, Shah K, Banks MR, et al. Effect of weight loss and exercise therapy on bone metabolism and mass in obese older adults: a one-year randomized controlled trial. *J Clin Endocrinol Metab.* 2008;93(6):2181-2187.
16. Molarius A, Seidell JC. Selection of anthropometric indicators for classification of abdominal fatness--a critical review. *Int J Obes Relat Metab Disord.* 1998;22(8): 719-727.
17. Lean ME, Han TS, Morrison CE. Waist circumference as a measure for indicating need for weight management. *BMJ.* 1995;311(6998):158-161.
18. Wang Z, Ma J, Si D. Optimal cut-off values and population means of waist circumference in different populations. *Nutr Res Rev.* 2010;23(2):191-199.
19. Zamboni M, Mazzali G, Zoico E, et al. Health consequences of obesity in the elderly: a review of four unresolved questions. *Int J Obes (Lond).* 2005;29(9): 1011-1029.
20. Brilleman SL, Pachana NA, Dobson AJ. The impact of attrition on the representativeness of cohort studies of older people. *BMC Med Res Methodol.* 2010;10:71.
21. Deeg DJ, van Tilburg T, Smit JH, et al. Attrition in the Longitudinal Aging Study Amsterdam. The effect of differential inclusion in side studies. *J Clin Epidemiol.* 2002;55(4):319-328.
22. Huisman M, Poppelaars J, van der Horst M, et al. Cohort Profile: The Longitudinal Aging Study Amsterdam. *Int J Epidemiol.* 2011;40(4):868-876.
23. Hubbard RE, Lang IA, Llewellyn DJ, et al. Frailty, body mass index, and abdominal obesity in older people. *J Gerontol A Biol Sci Med Sci.* 2010;65(4):377-381.
24. Folsom AR, Kushi LH, Anderson KE, et al. Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. *Arch Intern Med.* 2000;160(14):2117-2128.
25. Dey DK, Lissner L. Obesity in 70-year-old subjects as a risk factor for 15-year coronary heart disease incidence. *Obes Res.* 2003;11(7):817-827.
26. LaCroix AZ, Guralnik JM, Berkman LF, et al. Maintaining mobility in late life. II. Smoking, alcohol consumption, physical activity, and body mass index. *Am J Epidemiol.* 1993;137(8):858-869.
27. Launer LJ, Harris T, Rumpel C, et al. Body mass index, weight change, and risk of mobility disability in middle-aged and older women. The epidemiologic follow-up study of NHANES I. *JAMA.* 1994;271(14):1093-1098.
28. Visser M, Langlois J, Guralnik JM, et al. High body fatness, but not low fat-free mass, predicts disability in older men and women: the Cardiovascular Health Study. *Am J Clin Nutr.* 1998;68(3):584-590.

29. Adamson J, Ebrahim S, Dieppe P, et al. Prevalence and risk factors for joint pain among men and women in the West of Scotland Twenty-07 study. *Ann Rheum Dis.* 2006;65(4):520-524.
30. Heim N, Snijder MB, Deeg DJ, et al. Obesity in older adults is associated with an increased prevalence and incidence of pain. *Obesity (Silver Spring).* 2008;16(11): 2510-2517.
31. Janssen I, Mark AE. Separate and combined influence of body mass index and waist circumference on arthritis and knee osteoarthritis. *Int J Obes (Lond).* 2006;30(8):1223-1228.
32. Villareal DT, Banks M, Siener C, et al. Physical frailty and body composition in obese elderly men and women. *Obes Res.* 2004;12(6):913-920.
33. Krause MP, Albert SM, Elsangedy HM, et al. Urinary incontinence and waist circumference in older women. *Age Ageing.* 2010;39(1):69-73.
34. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults--The Evidence Report. National Institutes of Health. *Obes Res.* 1998;6 Suppl 2:51S-209S.
35. Mason C, Katzmarzyk PT. Variability in waist circumference measurements according to anatomic measurement site. *Obesity (Silver Spring).* 2009;17(9): 1789-1795.
36. Matsushita Y, Tomita K, Yokoyama T, et al. Relations between waist circumference at four sites and metabolic risk factors. *Obesity (Silver Spring).* 2010;18(12):2374-2378.
37. Ross R, Berentzen T, Bradshaw AJ, et al. Does the relationship between waist circumference, morbidity and mortality depend on measurement protocol for waist circumference? *Obes Rev.* 2008;9(4):312-325.
38. Heo M, Allison DB, Faith MS, et al. Obesity and Quality of Life: Mediating Effects of Pain and Comorbidities. *Obesity Res.* 2003;11(2):209-216.
39. Groessl EJ, Kaplan RM, Rejeski WJ, et al. Health-related quality of life in older adults at risk for disability. *Am J Prev Med.* 2007;33(3):214-218.
40. Salaffi F, Carotti M, Stancati A, et al. Health-related quality of life in older adults with symptomatic hip and knee osteoarthritis: a comparison with matched healthy controls. *Aging Clin Exp Res.* 2005;17(4):255-263.
41. Reyes-Gibby CC, Aday L, Cleeland C. Impact of pain on self-rated health in the community-dwelling older adults. *Pain.* 2002;95(1-2):75-82.

42. Temml C, Haidinger G, Schmidbauer J, et al. Urinary incontinence in both sexes: prevalence rates and impact on quality of life and sexual life. *Neurourol Urodyn.* 2000;19(3):259-271.
43. Molzahn A, Skevington SM, Kalfoss M, et al. The importance of facets of quality of life to older adults: an international investigation. *Qual Life Res.* 2010;19(2):293-298.
44. Kempen GI, Ormel J, Brilman EI, et al. Adaptive responses among Dutch elderly: the impact of eight chronic medical conditions on health-related quality of life. *Am J Public Health.* 1997;87(1):38-44.
45. Orfila F, Ferrer M, Lamarca R, et al. Gender differences in health-related quality of life among the elderly: the role of objective functional capacity and chronic conditions. *Soc Sci Med.* 2006;63(9):2367-2380.
46. Villareal DT, Miller BV, 3rd, Banks M, et al. Effect of lifestyle intervention on metabolic coronary heart disease risk factors in obese older adults. *Am J Clin Nutr.* 2006;84(6):1317-1323.
47. Bales CW, Buhr G. Is obesity bad for older persons? A systematic review of the pros and cons of weight reduction in later life. *J Am Med Dir Assoc.* 2008;9(5):302-312.
48. Han TS, Tajar A, Lean ME. Obesity and weight management in the elderly. *Br Med Bull.* 2011;97(1):169-196.
49. McTigue KM, Hess R, Ziouras J. Obesity in Older Adults: A Systematic Review of the Evidence for Diagnosis and Treatment. *Obesity (Silver Spring).* 2006;14(9):1485-1497.
50. Chao D, Espeland MA, Farmer D, et al. Effect of voluntary weight loss on bone mineral density in older overweight women. *J Am Geriatr Soc.* 2000;48(7):753-759.
51. Ricci TA, Heymsfield SB, Pierson RN, Jr., et al. Moderate energy restriction increases bone resorption in obese postmenopausal women. *Am J Clin Nutr.* 2001;73(2):347-352.
52. Newman AB, Yanez D, Harris T, et al. Weight change in old age and its association with mortality. *J Am Geriatr Soc.* 2001;49(10):1309-1318.
53. Yaari S, Goldbourt U. Voluntary and involuntary weight loss: associations with long term mortality in 9,228 middle-aged and elderly men. *Am J Epidemiol.* 1998;148(6):546-555.
54. Newman AB, Lee JS, Visser M, et al. Weight change and the conservation of lean mass in old age: the Health, Aging and Body Composition Study. *Am J Clin Nutr.* 2005;82(4):872-878.

55. Lee JS, Visser M, Tylavsky FA, et al. Weight loss and regain and effects on body composition: the Health, Aging, and Body Composition Study. *J Gerontol A Biol Sci Med Sci.* 2010;65(1):78-83.
56. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. *N Engl J Med.* 2011;364(13):1218-1229.
57. Frimel TN, Sinacore DR, Villareal DT. Exercise attenuates the weight-loss-induced reduction in muscle mass in frail obese older adults. *Med Sci Sports Exerc.* 2008;40(7):1213-1219.
58. Hulens M, Vansant G, Lysens R, et al. Study of differences in peripheral muscle strength of lean versus obese women: an allometric approach. *Int J Obes Relat Metab Disord.* 2001;25(5):676-681.
59. Stenholm S, Harris TB, Rantanen T, et al. Sarcopenic obesity: definition, cause and consequences. *Curr Opin Clin Nutr Metab Care.* 2008;11(6):693-700.
60. French SA, Folsom AR, Jeffery RW, et al. Prospective study of intentionality of weight loss and mortality in older women: the Iowa Women's Health Study. *Am J Epidemiol.* 1999;149(6):504-514.
61. Sorensen TI, Rissanen A, Korkeila M, et al. Intention to lose weight, weight changes, and 18-y mortality in overweight individuals without co-morbidities. *PLoS Med.* 2005;2(6):e171.
62. Shea MK, Houston DK, Nicklas BJ, et al. The effect of randomization to weight loss on total mortality in older overweight and obese adults: the ADAPT Study. *J Gerontol A Biol Sci Med Sci.* 2010;65(5):519-525.
63. Houston DK, Stevens J, Cai J, et al. Role of weight history on functional limitations and disability in late adulthood: the ARIC study. *Obes Res.* 2005;13(10):1793-1802.
64. Wannamethee SG, Shaper AG. Weight change and duration of overweight and obesity in the incidence of type 2 diabetes. *Diabetes Care.* 1999;22(8):1266-1272.
65. Daviglus ML, Liu K, Yan LL, et al. Body Mass Index in Middle Age and Health-Related Quality of Life in Older Age: The Chicago Heart Association Detection Project in Industry Study. *Arch Intern Med.* 2003;163(20):2448-2455.
66. Stenholm S, Rantanen T, Alanen E, et al. Obesity History as a Predictor of Walking Limitation at Old Age. *Obesity (Silver Spring).* 2007;15(4):929-938.
67. van Baak MA, Visscher TL. Public health success in recent decades may be in danger if lifestyles of the elderly are neglected. *Am J Clin Nutr.* 2006;84(6):1257-1258.
68. Seidell JC, Nooyens AJ, Visscher TL. Cost-effective measures to prevent obesity: epidemiological basis and appropriate target groups. *Proc Nutr Soc.* 2005;64(1):1-5.