

CHAPTER 5

Optimal cut-off values for high risk waist circumference in older adults based on related health outcomes

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Abstract

The study aim was to explore optimal cut-offs of waist circumference (WC) in older adults to assess health risks of obesity.

Prospective data from 4,996 measurements in 2,231 participants aged ≥ 70 y were collected at five subsequent triennial measurement cycles (1992/'93-2005/'06) of the population-based cohort study Longitudinal Aging Study Amsterdam (LASA). Cross-sectional associations of WC with pain, mobility limitations, incontinence, knee osteoarthritis, cardiovascular diseases, and diabetes were studied. Generalized estimating equations (GEE) models were fitted with restricted cubic spline functions in order to carefully study the shapes of the associations. Model fits for applying different cut-offs to categorize WC in the association with all outcomes were tested using the Quasi-likelihood under the Independence Criterion (QIC). Based on the curves, potential cut-offs of WC of approximately 109cm in men and 98cm in women were proposed.

Based on the model fit, cut-offs between 100cm and 106cm were equally applicable in men but should not be higher. In women, QIC confirmed an optimal cut-off of 99cm.

In older men, the analyses showed that cut-offs between 100cm and 106cm performed comparably and that higher cut-offs should be avoided. In older women, the data suggested an optimal WC cut-off of 99cm.

Introduction

In identifying the rapidly growing population of obese older adults, the applicability of currently used anthropometric indices and their cut-off values are subject to debate. Waist circumference is shown to be a strong predictor of chronic diseases and functional limitations in older adults (1-3). The cut-off values of waist circumference (88 cm in women and 102 cm in men) have been established in adult populations (4) and are adopted in the guidelines of the World Health Organization (WHO) for application in adults aged <70 years (5). Due to changes in stature and body composition with aging, concerns about misclassification of the health risks related to obesity in older persons when using waist circumference (cut-off values) have been described (6, 7).

The currently used cut-off values of waist circumference were designed in order to optimally classify people by high body mass index (BMI) and/or high waist-hip ratio in adult populations (4). Previous studies have suggested cut-off values of waist circumference for older adults by studying their relation to (cut-off values of) these or other anthropometric indices (7-11). Because there is no consensus on a threshold for high BMI or waist-hip ratio in older adults (12), it is more appropriate to directly relate waist circumference to negative health outcomes in order to identify the best threshold for high risk waist circumference in the population aged ≥ 70 years. In a previous study (11), we suggested the use of spline regression curves as the optimal method to study the relation of waist circumference with negative health outcomes in order to identify cut-off values for high risk waist circumference. In the identification of cut-off values of anthropometric measures in older adults, a broad range of health outcomes should be considered. While metabolic risk factors remain important in the study of obesity in old age, there is, and should be, a large emphasis on functional outcomes and quality of life in gerontological research. The independent associations of a large waist circumference with increased risk for diabetes (13), cardiovascular diseases (CVD)(14), mobility limitations (15-17), pain (18, 19), knee osteoarthritis (3) (OA), health related quality of life (20) and urinary incontinence (in women)(21) in older adults have all been previously established. However, in

order to identify cut-off values of waist circumference that optimally classify the risk for these adverse outcomes in a population aged 70 years and older, the shape of the associations between waist circumference and these outcomes needs to be carefully considered.

The aim of our study was to explore optimal cut-off values of waist circumference in older adults to assess health risks of obesity. The shapes of the associations with several important health outcomes in gerontological research were taken into account using advanced statistical methods.

Materials and methods

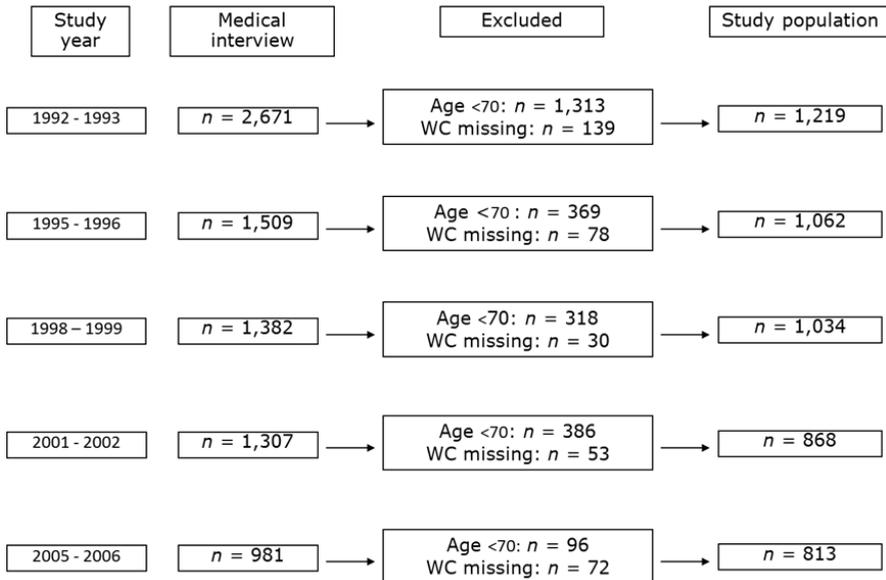
Study sample

Data for this study were collected within the Longitudinal Aging Study Amsterdam (LASA), a prospective study on predictors and consequences of changes in autonomy and well-being in the aging population in the Netherlands. A representative sample of older men and women (aged 55-85 years), stratified by age, sex, urbanicity and expected 5-year mortality, was drawn from the population registers of 11 municipalities (rural and urban) in three geographical areas of the Netherlands. Details on the sampling and data collection procedures have been described elsewhere (22, 23). In total, 3,107 subjects were enrolled in the baseline examination (1992/1993). Examinations were repeated every three years and consisted of a main interview followed by a medical interview, both administered in the participants' home. The examinations were conducted by specially trained and intensively supervised interviewers (main interview) and nurses (medical interview). Furthermore, a self-administered questionnaire was left at the participants' home after the main interview and collected during the medical interview. The study was approved by the Ethical Review Board of the VU University Medical Center and all participants gave informed consent.

The sample used in the present study comprised of participants who completed the medical examination of at least one of the five triennial measurement cycles between 1992/1993 and 2005/2006. Of each cycle, participants with complete data on waist circumference and who were 70 years or older at the time that the interview was conducted, were included. According to the WHO, the currently

used cut-off values are valid to use in persons aged younger than 70 years. Our aim was to develop cut-off values of WC for older adults above the age of 70 years in order to complement the WHO guidelines. Of the 2,232 individuals included in one or more measurement cycles, 866 participated in one measurement cycle only, 537 participated twice, 408 three times and 297 four times, 130 participants had complete data in all five measurement cycles. In total, 4,996 measurements were available. See the flow-chart for the number of participants at each cycle (Figure 1).

Figure 1. Flow chart of study sample, comprising of 2,231 participants of the Longitudinal Aging Study Amsterdam (LASA) and 4,996 measurements carried out between 1992/1993 - 2005/2006 in the Netherlands.



Measurements

In the current study, the independent variable used was measured waist circumference. The dependent variables studied were pain, self-reported mobility limitations, incontinence and the chronic conditions cardiovascular disease, knee osteoarthritis (OA) and diabetes. This broad range was considered to cover important issues for the health-related quality of life in old age. Health-related quality of life was considered being an overall summarizing outcome in a final step of analysis to test the validity of the potential cut-off values of waist circumference.

Waist circumference

Anthropometric measures were obtained by intensively trained nurses during the medical interview of each measurement cycle. Waist circumference (cm) was measured to the nearest 0,1 cm in standing position, midway between the lower rib and the iliac crest after a normal expiration.

Pain

During every measurement cycle, pain was assessed by a self-administered questionnaire. The pain scale used was based on a subscale of the Dutch version of the Nottingham Health Profile (24, 25). The six items included were the following: 'I am in pain when I am standing'; 'I find it painful to change position'; 'I am in pain when I am sitting'; 'I am in pain when I walk'; 'I have unbearable pain' and 'I am in constant pain'. Response categories were 'yes' and 'no'. The pain score (range 1-6) was used as a dichotomous variable with categories 'no pain' and 'any pain'.

Mobility limitations

Self-reported mobility limitations were assessed as part of the main interview in every measurement cycle, using the question; 'Can you walk up and down a staircase of 15 steps without resting?'. Response categories were 'Yes, without difficulty', 'Yes, with some difficulty', 'Yes, with much difficulty', 'Only with help' and 'No, I cannot'. Participants were considered to be limited in their mobility when they answered 'Yes, with much difficulty' or worse.

Incontinence

During the main interview of every measurement cycle, respondents were asked whether they (sometimes) lost urine unintentionally (yes/no).

Chronic diseases

The presence of chronic diseases was assessed by self-report at each measurement cycle. Participants were asked if they had knee OA and/or diabetes. The presence of CVD was assessed by asking respondents whether or not they had cardiac disease (including myocardial infarction), stroke and/or peripheral arterial diseases. If respondents reported to have one of these conditions they were coded to have CVD. It has previously been shown that the accuracy and reliability of the self-reported chronic disease in LASA is adequate (26).

Health related quality of life

Participants completed the Dutch version of the short form health survey (SF-12)(27) as part of the self-administered questionnaire during the third, fourth and fifth measurement cycles to assess general mental and physical health. The SF-12 health scores were dichotomized for the analyses. Participants in the lowest sex-specific quartiles were considered to have a low health related quality of life.

Statistical analysis

In order to be able to use all data with adjustment for dependence of observations within persons, generalized estimating equations (GEE) were used to examine the cross-sectional associations between waist circumference and each of seven health outcomes (i.e. pain, mobility limitations, incontinence, knee OA, diabetes, CVD, and health-related quality of life). Optimal waist circumference cut-off values were determined using a three-step approach. First, restricted cubic spline regression functions with four knots were used in order to flexibly model the associations between waist circumference and all seven health outcomes, avoiding the need for an a priori assumption on the shape of the associations. Restricted cubic spline regression functions were chosen over unrestricted cubic splines in order to obtain more cautious estimates of the associations in the end regions of the distributions where data are sparse. In order to identify cut-off

values that optimally classify health risks for a heterogeneous population of older adults, univariate models were used (i.e. no adjustments for covariates were made). Three investigators (NH, MBS and MV) independently assessed the most appropriate potential cut-off value by visual inspection of the spline regression curves of six outcomes. The association of waist circumference with health-related quality of life was assessed at a later stage in order to validate our results by testing the applicability of the identified cut-off value to classify high risk for a general summarizing health outcome. A priori, there was consensus that an optimal cut-off value of waist circumference should be at the level of waist circumference from where on the risk for a particular health outcome starts to increase more rapidly. Because in linear associations a stable change in health risks occurs, this method was not applicable for linear associations. Using this method, three independent identifications of an optimal cut-off value of waist circumference for each particular health outcome were obtained and the mean was calculated for each considered health outcome. Then, an overall cut-off value for all health outcomes together was assessed by calculation of the mean, weighted by the prevalence of each of the outcomes in our study population. These potential waist circumference cut-off values were further investigated in the next step.

In a second and more objective step, a range of cut-off values for waist circumference surrounding the potential cut-off values were applied to dichotomize waist circumference. The fit of the GEE models of the associations with all of the outcomes was investigated. The cut-off value that provided the best fit would be the optimal waist circumference cut-off value to be proposed for older persons. The model fit was assessed using the Quasi-likelihood under the Independence Criterion (QIC)(28), a lower QIC value indicates a better model fit.

In the third and final step, the curve of the association of waist circumference with health-related quality of life was used to test the validity of the proposed cut-off value against an over-all and summarizing outcome measure. In literature, extensive evidence exists for a reverse relationship between (co-)morbidity and health-related quality of life (29, 30). The model fit was assessed according to the above described methods.

All analyses were performed separately for men and women in order to obtain potential sex-specific cut-off values of waist circumference. The descriptive analyses were performed using SPSS 17.0 (31). The GEE spline regression analyses were carried out using R 2.7.0 (32), for the assessment of the QIC values SAS 9.2 (33) was used.

Results

The men and women in the study population had a mean age of approximately 78 years during all five measurement cycles. The youngest participants were 70.0 years in every measurement cycle, the maximum age increased from 85.6 to 96.6 over the measurement cycles. The mean waist circumference in men ranged from 99.2 cm to 101.7 cm over the measurement cycles, while the mean waist circumference in women varied from 93.3 cm to 98.1 cm. The prevalence of the health outcomes studied are displayed in table 1 (Table 1).

In the first step of analyses, the spline regression curves showed an increased probability for all health outcomes with increasing waist circumference in both men and women (Figures 2-4). For outcomes CVD, diabetes, and knee OA there was a linear association with the waist circumference (Figure 2) and therefore, no potential cut-off value could be appointed by visual inspection. In contrast, the spline regression curves of pain, mobility limitations and incontinence showed a nonlinear association. Therefore, it was decided to use the curves of these three outcomes to propose the potential cut-off values in both men and women. In men, the curves of the association of waist circumference with pain and incontinence also showed increased probability in the lowest range of waist circumference (U-shaped association). The lowest probabilities for these outcomes were found at 94.5 cm and 106.0 cm, respectively. Based on visual inspection, the potential waist circumference cut-off values in men that seemed most appropriate in the associations with pain, mobility limitations and incontinence were 104 cm, 111 cm and 118 cm, respectively (Figure 3). In women, the potential cut-off values for each outcome were 102 cm, 94 cm and 95 cm for pain, mobility limitations and incontinence, respectively (Figure 4). After calculating the weighted mean of the potential cut-off values according to the

Table 1. Characteristics of the study sample: the Longitudinal Aging Study Amsterdam (LASA).

Year of assessment		1992-93	N	1995-96	N	1998-99	N	2001-02	N	2005-2006	N
% Male		52.2		51.9		45.6		45.0		42.7	
Age, mean (SD)	M	77.7 (4.2)		78.5 (5.1)		78.9 (5.7)		78.4 (6.0)		77.9 (5.8)	
	F	77.5 (4.4)		78.3 (5.3)		79.0 (5.8)		78.8 (6.0)		78.7 (6.0)	
Waist circumference, mean (SD)	M	100.3 (10.0)	636	99.2 (10.5)	511	100.2 (10.2)	472	101.6 (10.3)	391	101.7 (10.7)	347
	F	98.1 (11.8)	583	93.3 (11.5)	551	94.5 (11.5)	562	96.2 (11.6)	477	95.5 (11.9)	466
Pain (%)	M	30.1	498	28.0	450	33.6	435	30.2	371	34.0	203
	F	49.9	441	41.7	420	44.1	503	46.4	433	35.0	257
Mobility limitations (%)	M	9.1	635	12.3	506	16.3	466	11.8	389	11.2	347
	F	23.7	575	27.7	545	29.0	556	22.0	472	27.0	459
Osteoarthritis of the knee (%)	M	11.2	630	14.1	509	16.4	427	16.9	367	16.1	327
	F	29.9	559	37.2	541	38.3	493	39.1	442	39.2	429
Diabetes (%)	M	9.0	635	7.2	511	7.4	472	10.0	391	15.3	347
	F	11.4	580	9.6	550	11.4	562	9.3	474	14.8	466
Cardiovascular diseases (%)	M	38.7	635	44.8	511	48.5	472	47.6	391	49.0	347
	F	31.6	580	34.3	550	35.4	560	34.8	473	37.6	466
Incontinence (%)	M	11.3	635	17.6	511	17.8	472	19.7	391	18.4	347
	F	28.3	580	37.1	550	35.2	562	42.0	474	43.6	466

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Figure 2. Three spline regression curves of the associations of waist circumference with cardiovascular diseases, diabetes and knee osteoarthritis in men (top) and women (bottom), participants of the Longitudinal Aging Study Amsterdam (LASA) (1992/1993 - 2005/2006 in the Netherlands).

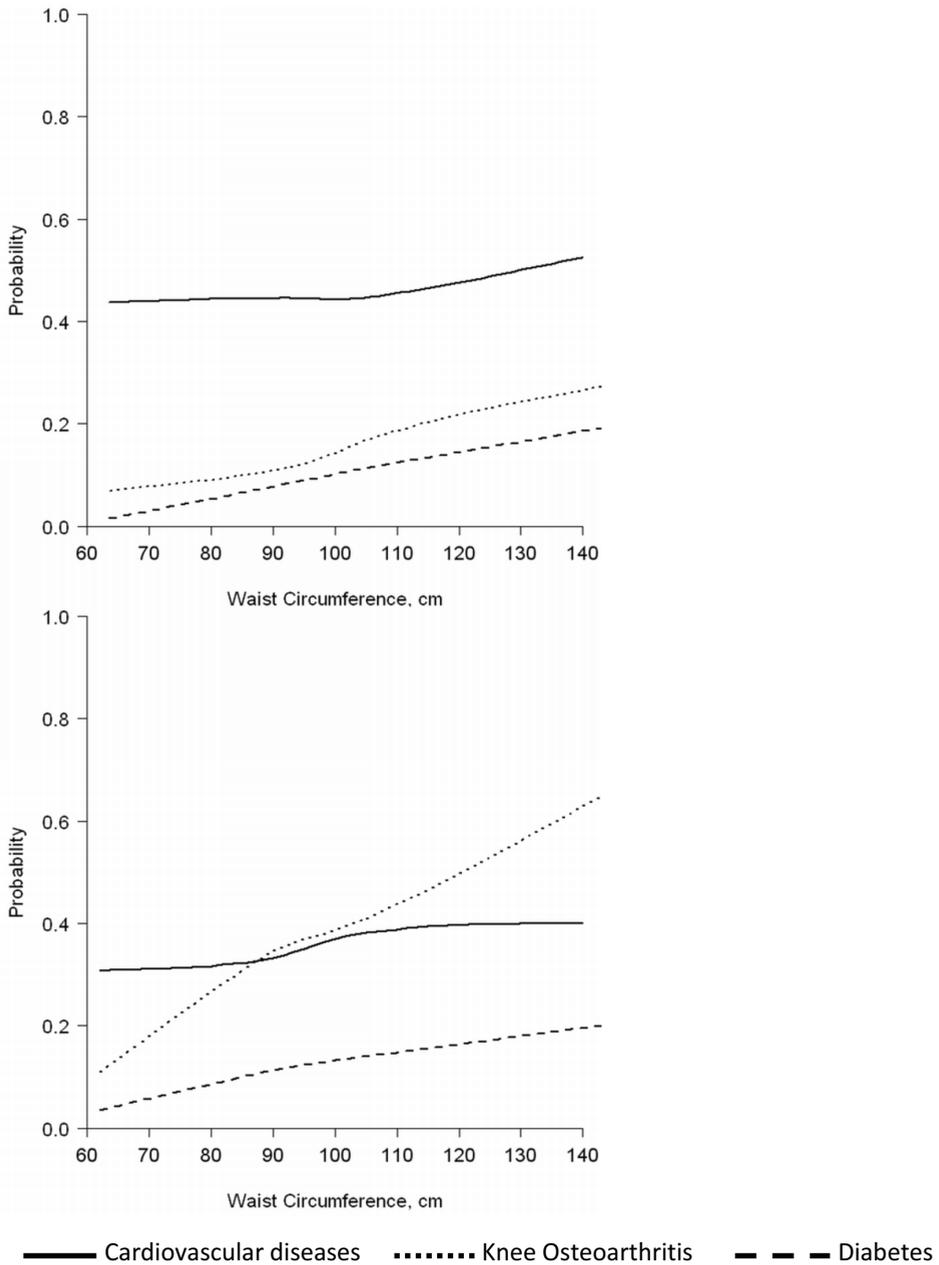
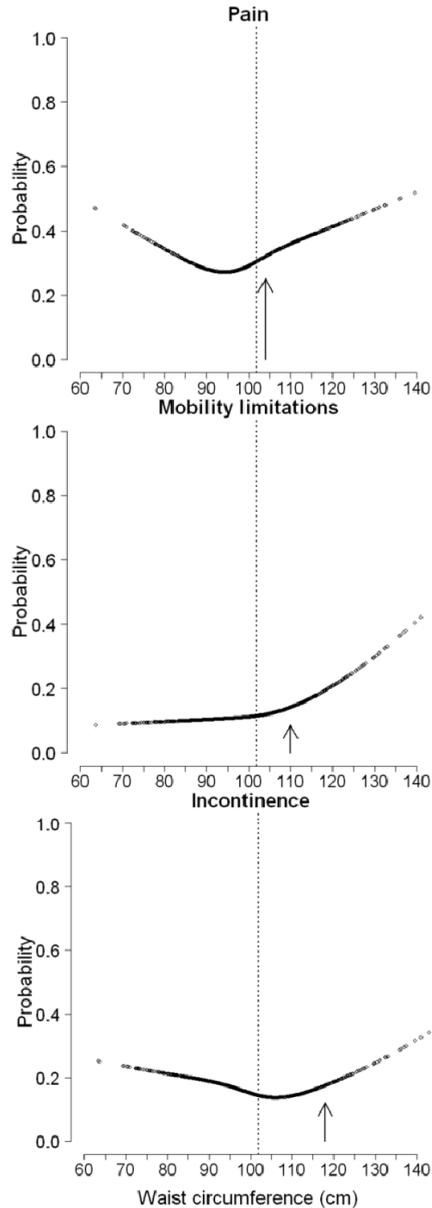


Figure 3. Spline regression curves of the three non-linear associations in men (participants of the Longitudinal Aging Study Amsterdam (LASA), (1992/1993 - 2005/2006) in the Netherlands) between waist circumference and pain (top), mobility limitations (middle) and incontinence (bottom) respectively. The arrows indicate the potential cut-off value based on visual inspection of each unique association, while the dashed lines indicate the currently used cut-off value (102 cm).



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Figure 4. Spline regression curves of the three non-linear associations in women (participants of the Longitudinal Aging Study Amsterdam (LASA), (1992/1993 - 2005/2006) in the Netherlands) between waist circumference and pain (top), mobility limitations (middle) and incontinence (bottom) respectively. The arrows indicate the potential cut-off value based on visual inspection of each unique association, while the dashed lines indicate the currently used cut-off value (88 cm).

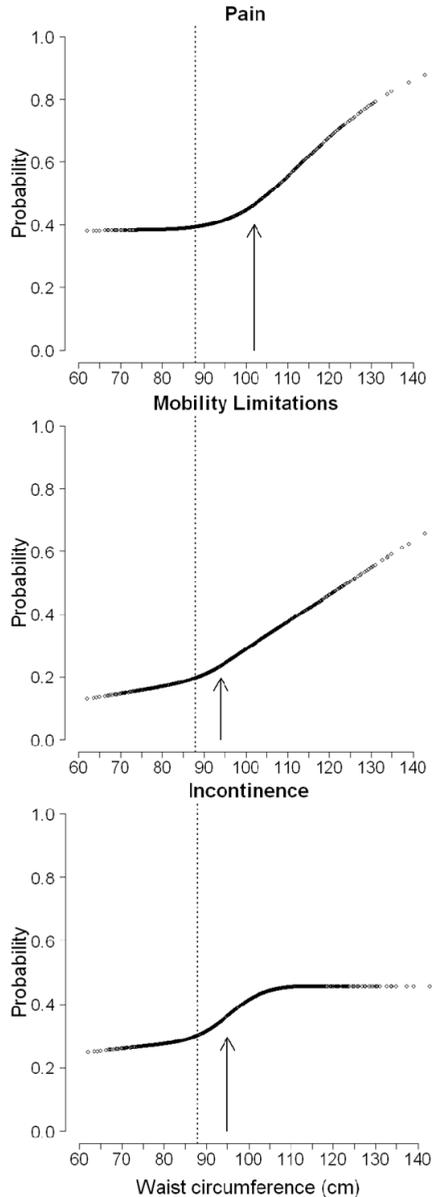


Table 2. Cut-off values of waist circumference based on visual inspection of the spline regression curves of the associations of waist circumference with pain, mobility limitations and incontinence as assessed by investigators I, II, and III. The mean of the three observed cut-off values for each outcome was weighted by the prevalence of the outcomes to calculate the potential cut-off values.

	I	II	III	Mean	Prevalence (%)	Potential cut-off value
Men						
Pain	108	101	102	104	30.8	
Mobility limitations	110	112.5	110	111	12.0	
Incontinence	117	115	122	118	16.4	
						109
Women						
Pain	98	105	103	102	44.2	
Mobility limitations	94	95	94	94	25.9	
Incontinence	95	94	94,5	95	36.8	
						98

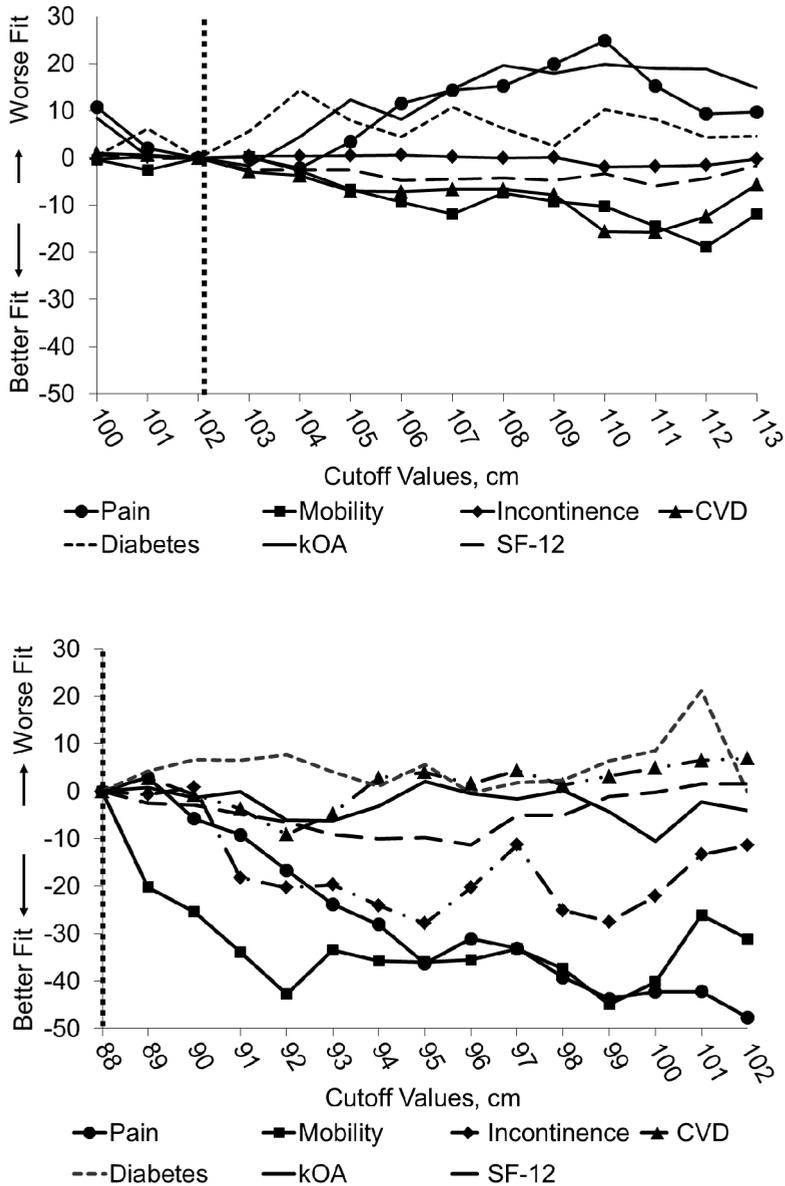
prevalence of each respective outcome, the potential cut-off values were 109 cm in men and 98 cm in women (Table 2).

In step two, the fit of the models of all associations in men remained fairly stable when applying cut-off values of waist circumference between 100 and 106 cm (Figure 5, top). As compared to the currently used cut-off value of 102 cm, the models for CVD and mobility limitations slightly improved, while the models for pain and knee OA deteriorated. With the application of cut-off values higher than 106 and 108 cm, the improvement of the models stagnated, while the deterioration for other outcomes progressed. At higher cut-off values the improvements of the models for CVD and mobility limitations was clearly exceeded by the deterioration of the models for pain and knee OA. So based on the QIC the cut-off values of waist circumference in men, cut-off values in the

range of 100 to 106 cm are equally applicable and cut-off values higher than 106 cm should not be applied. In women, the models for mobility limitations, pain and incontinence improved when applying higher cut-off values than the currently used 88 cm. A break in the trend of progressive improvement of the model fit for mobility limitations and incontinence was evident when cut-off values higher than 99 cm were applied, also the fit of the model for diabetes then clearly deteriorated (Figure 5, bottom). Therefore, 99 cm seemed the most appropriate cut-off value in women based on the fit of the models.

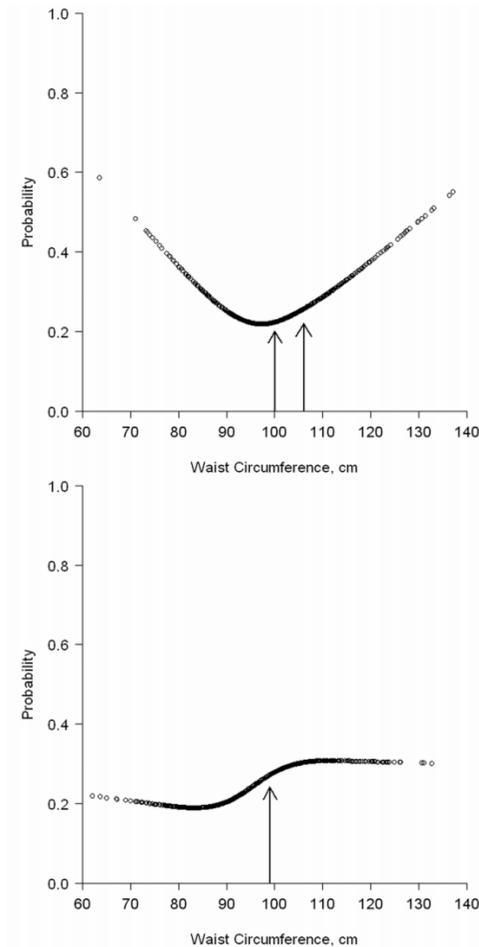
In a final step, it was tested whether the proposed cut-off values were valid in the association between waist circumference and health-related quality of life, an over-all summarizing outcome measure. Spline regression curves (Figure 6) and the model fit (Figure 5) were assessed of this association. In men, a U-shaped association was found. The lowest probability for a low health-related quality of life was found at a waist circumference of 97.2 cm. Based on the spline regression curve, 106 cm seemed a more appropriate cut-off value of waist circumference than 100 cm, because the risk was only marginally increased at a waist circumference of 100 cm. The QIC measure for model fit remained stable when applying the range of cut-off values in the association with health-related quality of life in men. In women, the proposed cut-off value of 99 cm was appropriate in the association with health-related quality of life both in terms of the shape of the association (Figure 6) and the model fit (Figure 4), and was more optimal compared to the currently used cut-off value.

Figure 5. Model fit of the application of a range of potential cut-off values (displayed on the x-axes) assessed by the Quasi-likelihood under the Independence Criterion (QIC) relative to the fit of the model when the currently used cut-off values are applied (dashed lines) in men (top) and women (bottom) participants of the Longitudinal Aging Study Amsterdam (LASA), (1992/1993 - 2005/2006) in the Netherlands).



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Figure 6. Spline regression curves of the association between waist circumference and health-related quality of life in men (top) and women (bottom). The arrows indicate the proposed cut-off values of waist circumference in men (between 100 cm and 106 cm) and women (99 cm) (participants of the Longitudinal Aging Study Amsterdam (LASA), (1992/1993 - 2005/2006) in the Netherlands).



Discussion

Based on this large-scale study relating waist circumference to relevant health outcomes in older persons, we propose higher cut-off values for large waist circumference in older adults as compared to the cut-off values according to current guidelines for adults (102 cm in men and 88 cm in women). In both men and women, the shapes of the associations between waist circumference and pain, mobility limitations and incontinence suggested higher cut-off values of waist circumference. Model fit analyses when applying of a range of cut-off values to the association of waist circumference with seven health outcomes in men, showed a stable fit when applying cut-off values in the range of 100 to 106 cm, but indicated that higher cut-off values than 106 cm should be avoided. In women, the model fit analyses confirmed the results based on the shapes of the associations and a cut-off of 99 cm was shown to optimally indicate a high-risk waist.

Although the WHO guidelines clearly state that the cut-off values of waist circumference are applicable to adults up to the age of 70 years, often these cut-off values are used to classify a large waist circumference in older adults. Our study confirms that applying the cut-off values to persons aged over 70 years leads to misclassification of health risks. Previous studies have considered the feasibility of the currently used cut-off values of waist circumference in older adults based on their relation to other obesity measures with inconsistent results. Two studies proposed lower cut-off values for older adults than those adopted in current guidelines, based on the amount of visceral fat and the ability to predict a high BMI (7, 8). In contrast, three studies (9-11) proposed cut-off values higher than the current ones based on the association between waist circumference and BMI in older adults. These previous studies all focused on how waist circumference cut-off values relate to other anthropometric indices and their cut-off values. Changes of body composition and body fat distribution occur with aging (34, 35). At a given waist circumference, the BMI of an older adult is lower, while the amount of visceral fat and the waist-hip ratio is higher as compared to (younger) adults. No consensus is reached in scientific literature on optimal cut-off values of anthropometric indices like BMI and waist-hip ratio in older adults (36). In the

search for the optimal cut-off value for waist circumference to estimate obesity related health risks in older adults, the association of waist circumference with health outcomes is much more relevant since this approach avoids the use of other obesity measures that may have limited validity in older persons or for which no generally accepted cut-off values exist.

An age-related redistribution of fat mass takes place in both older men and women. In women, an accelerated shift to a more central fat distribution takes place after menopause (37-40), while men already have a more centrally located fat distribution during adulthood as compared to women. This more pronounced redistribution of fat in women is a possible explanation for the finding that the cut-off value for high-risk WC needs to be shifted upwards in women but not in men.

To our knowledge, no previous study assessed cut-off values of waist circumference by considering the (shape of the) dose-response relationship between waist circumference and a wide range of health outcomes. In a previous study we assessed the shape of the association between waist circumference and mobility limitations as part of an examination of several methods to explore cut-off values (11). In the current study we applied the most optimal method, spline regression curves, to study a wide range of health outcomes that are very relevant to the quality of life in older adults.

The spline regression curves for the outcomes CVD, diabetes and knee OA in the current study showed gradual linear increase of health risk. Therefore, in these curves a clear threshold for a high risk waist circumference was absent. In men, the curves of the associations of waist circumference with some of the health outcomes also showed increased probability in the lowest range of waist circumference (U-shaped associations). To test the robustness of the shape of the associations against confounding by the increased risk for several outcomes at the lowest end of the range waist circumference values, additional analyses were performed excluding participants with a low waist circumference (≤ 85 cm in men and ≤ 75 cm in women). The shapes of the remaining range of waist circumference in association with the health outcomes remained virtually the same (results not shown). The lowest probabilities for these negative outcomes (and thus the optimal waist circumference) were found very close to or even above the

currently used waist circumference cut-off value (102 cm) for a high risk waist circumference in adults. In women, an increased probability for a negative health outcome was not, or only marginally, found on the level of the currently used cut-off value (88 cm), with an exception for the association of waist circumference with knee OA. These results support that the currently used cut-off values are not applicable in older adults. When taking multiple, important health outcomes into account, it is unlikely that a single cut-off value would be optimal for all health outcomes. However, for optimal clinical use and feasibility in daily practice, a single cut-off value for high-risk waist in older persons is to be preferred.

As compared to the model fit when applying the currently used cut-off value of 102 cm, the fit of the GEE models in men did not improve when applying a range of cut-off values surrounding 102 cm. In women, the fit of the models for pain, mobility limitations and incontinence improved as we expected based on the shapes of the associations. Possibly, the fit of the models in men did not improve because the explained variance of the outcomes by waist circumference is smaller than in women, and the QIC might not be a measure sensitive enough to detect an improvement of the model by shifting the waist circumference cut-off value.

Although data of five subsequent measurement cycles of the LASA study covering 12 years of follow-up were available and used, a limitation of the current study is its cross-sectional design. Therefore, a reversed causation can not be completely ruled out. However, performing longitudinal analyses was not possible. If associations of waist circumference with the incidence of negative health outcomes were to be considered, excluding all respondents with prevalent health problems at baseline would have made the sample size too small resulting in curves estimated with less precision. By using the longitudinal data in a cross-sectional manner in GEE models, all available data were used very efficiently, which led to an increased power and more accurate estimates of the shapes of the associations. A further limitation of the current study was the use of self-reported data on health outcomes, possible sub-clinical problems might have been missed by this assessment method.

By optimally differentiating low-risk from high-risk groups using more accurate cut-off values will prevent underestimate of the consequences of a large WC. The importance of maintaining a healthy weight throughout old age might be

misjudged when health risks are underestimated in epidemiological research. Also, when the cut-off values used to select the target group for intervention better specify those in need of intervention, the effects of an intervention can be rated at its true value. The feasibility and the efficacy of weight loss programmes in older adults are still subject of discussion in scientific literature (41, 42). Adverse health effects of weight loss on muscle mass and even more so, on bone mineral density have been described (43-45). Using the newly defined higher cut-off values will lead to an increased specificity but also, inseparably, a decreased sensitivity. An improved specificity is desirable in terms of the prevention of accelerated bone loss associated with weight loss and the allocation of financial means, especially because of the high prevalence of a large WC among older adults.

Our study of the shapes of the associations of waist circumference with multiple important health outcomes indicated that cut-off values of waist circumference should be shifted upwards in older adults. When assessing the quality of the models, shifting the cut-off values upwards did not improve the model fit in men. Cut-off values between 100 cm and 106 cm were shown to perform comparably, but higher cut-off values should be avoided. In women, the data suggested an optimal cut-off value of 99 cm to be optimal considering both the shape of the associations with important health outcomes and in terms of model fit. In future research, these proposed cut-off values should be validated in other, large (inter-) national samples before the final cut-off values can be established and applied in clinical practice.

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