

1 Sagittal abdominal diameter and waist circumference are equally good as identifiers
2 of cardiometabolic risk

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12 *Short running head:* Measures of central obesity and metabolic syndrome markers

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22 *Abbreviations:* BMI, body mass index; CT, computed tomography; FFA, free fatty acids IDF,

23 International Diabetes Federation; IL, interleukin; MRI, magnetic resonance imaging; ROC,

24 Receiver Operating Characteristic; SAD, sagittal abdominal diameter; SAT, subcutaneous adipose

25 tissue; TNF, tumor necrosis factor; VAT, visceral adipose tissue, WC, waist circumference.

26 **Abstract**

27 **Background**

28 Body mass index (BMI) and waist circumference (WC) are commonly used markers of
29 cardiometabolic risk. However, sagittal abdominal diameter (SAD) has been proposed to be a better
30 marker of intra-abdominal obesity compared to WC and might better associate with metabolic
31 disturbances in high-risk populations. The objective of this study was to compare SAD, WC, and
32 BMI as determinants of an adverse metabolic phenotype.

33 **Method**

34 Anthropometric and metabolic measures of 1516 overweight or obese individuals with features of
35 the metabolic syndrome were included to examine differences between SAD, WC and BMI as
36 measures of an adverse metabolic phenotype. Multiple linear regression and logistic regression
37 models were used to investigate the association between SAD, WC, and BMI and markers of
38 metabolic syndrome, insulin resistance, blood lipids, and low grade inflammation.

39 **Results**

40 Both SAD and WC correlated with BMI, but as BMI increased, SAD proportionately estimated
41 higher abdominal adiposity compared to WC (slope = 0.0037 (0.0029; 0.0046), $p < 0.0001$). We did
42 not find major differences between SAD, WC and BMI in explained variance in models with the
43 different markers of metabolic risk. Furthermore, we did not find differences between SAD and WC
44 in the ability to identify individuals with metabolic syndrome according to the International
45 Diabetes Federation (IDF) cut-offs, but a few differences from BMI were indicated but mostly
46 before adjustments. Moreover, the differences between SAD and WC associations were not
47 modified by sex or degree of adiposity, but identification of individuals with a metabolic phenotype
48 was generally better in women.

49 **Conclusion**

50 These data indicate that SAD and WC are equally good indicators of an adverse metabolic
51 phenotype. Thus, from a public health perspective choice of anthropometric measure may depend
52 only on what is the most practical method in a given situation.

53 **Introduction**

54 Obesity is one of the most important risk factors for metabolic syndrome, cardiovascular disease
55 (CVD) and type 2-diabetes (T2D). Body mass index (BMI) is often used to evaluate overweight and
56 obesity, but BMI does not distinguish between lean and fat mass. Furthermore, BMI does not
57 provide information on fat distribution, and therefore does not specifically reflect central obesity
58 which is associated with an adverse metabolic phenotype and essential for the association between
59 obesity and lifestyle disease (1).

60 When assessing abdominal obesity it is important to distinguish between subcutaneous adipose
61 tissue (SAT) and visceral adipose tissue (VAT) as VAT is the most metabolically adverse type of
62 adipose tissue (1). Simple anthropometric indicators such as waist circumference (WC) and sagittal
63 abdominal diameter (SAD) are used to examine abdominal obesity, and have both been shown to be
64 better indicators measures of an adverse metabolic phenotype compared to BMI alone (2). WC is a
65 commonly used measure of abdominal obesity, but SAD has been proposed to be a better marker
66 for VAT and thus might better have improved predictive ability of metabolic disturbances (3,4).

67 SAD is measured as the height of the abdomen in a supine position, which increase with VAT
68 accumulation as VAT is contained within the abdominal cavity, while SAT in the supine position
69 will be distributed sideways, due to the force of gravity (5,6). Adjusting measures of WC and SAD
70 for height (as in BMI) have been shown to improve prediction of cardiometabolic risk and thus is
71 suggested to also improve the detection of adverse metabolic phenotypes (7).

72 Some studies have suggested that sex and degree of obesity might affect the predictive ability of
73 SAD and WC measurements differently (8,9). One study found that SAD compared to WC was a
74 stronger risk marker in women compared to men (8). This could be due to the sex specific fat
75 distribution as women have a higher ratio of SAT to VAT mass, which can lead to formation of a
76 so-called “abdominal apron” and make measurements of WC particularly tricky. Similarly,
77 difficulties might also make SAD a better measure than WC at higher levels of adiposity.

78 The overall aim of this study was to investigate whether SAD, WC and BMI associate differently
79 with metabolic syndrome and cardiometabolic risk, compromising markers of insulin resistance,
80 dyslipidemia, low grade inflammation and blood pressure. We hypothesized that SAD is stronger
81 associated with cardiometabolic health and a better measurement for identifying individuals with

82 metabolic syndrome markers above established cut-offs compared to WC and BMI. Furthermore,
83 we hypothesise that height-adjustment of SAD and WC improves the association with adverse
84 metabolic syndrome markers. Finally, we hypothesise that these associations depend on sex and that
85 a stronger association for SAD compared to WC is most pronounced at higher BMIs (>35 kg/m²).
86 These hypotheses were examined with data from several cohorts of primarily overweight and obese
87 individuals with an adverse metabolic phenotype.

88 **Methods**

89 *Study design*

90 This study included cross-sectional baseline data from six human intervention trials: 3G, OPUS,
91 DIOGENES, RIGHT, MyNewGut (MNG), and PROKA (10–15). The studies were registered at
92 <http://www.clinicaltrials.gov>; 3G (NCT01719913 and NCT01731366); SHOPUS (NCT01195610);
93 DIOGENES (NCT00390637); RIGHT (NCT02358122); MNG: (NCT02215343); PROKA
94 (NCT01561131) and approved by the Research Ethics Committees of the Capital Region of
95 Denmark in accordance with Helsinki Declaration 3G (H-2-2012-064 and H-2-2012-065);
96 SHOPUS (H-3-2010-058); RIGHT (H-1-2014-062); MNG (H-4-2014-052); and PROKA (H-2-
97 2011-145) or the local ethical committees in the respective countries (16).

98 *Participants*

99 Individuals included in the present study, were primarily overweight or obese (98%) at risk of the
100 metabolic syndrome. We used the International Diabetes Federation (IDF) metabolic syndrome
101 definitions (17). For impaired fasting glucose we used both the 5.6 mmol/L IDF cut-off and a 6.1
102 mmol/L cut-off.

103 **Anthropometric, laboratory and analytical procedures**

104 Body weight, height, WC and SAD were measured by standard anthropometric procedures. SAD
105 was measured twice to the closest 0.1 cm using a Holtain-Kahn Abdominal Caliper (Holtain Ltd,
106 Crymch, United Kingdom) and we used the mean of the two measurements. The subjects were in
107 supine position when measured and were asked to bend their knees to a 45 degree angle and keep
108 their feet flat on the examination table. SAD was measured as the distance between the highest
109 point of the abdomen and the back as assessed by the distance between the two blades of the caliper

110 (by using a spirit level). The measurement was made at the end of a normal exhalation. WC was
111 measured between the bottom of the ribs and the top of the hipbone. WC was measured twice to the
112 nearest 0.5 cm using a non-elastic flexible measuring tape and the mean of the two measurements
113 was used. All cohorts used a similar standard operating procedure for the anthropometric
114 measurements.

115 Blood samples for all cohorts were drawn after overnight fasting. Standard clinical measurements of
116 plasma glucose, insulin, total-, LDL- and HDL cholesterol, triglycerides, C-reactive protein (CRP),
117 free fatty acids (FFA), and adiponectin were performed as well as measurements of serum
118 inflammatory markers interleukin (IL)-6 and tumor necrosis factor (TNF)- α (Supplemental methods
119 section). Blood pressure was measured using a digital blood pressure monitor (Supplemental
120 methods section).

121 **Statistical analysis**

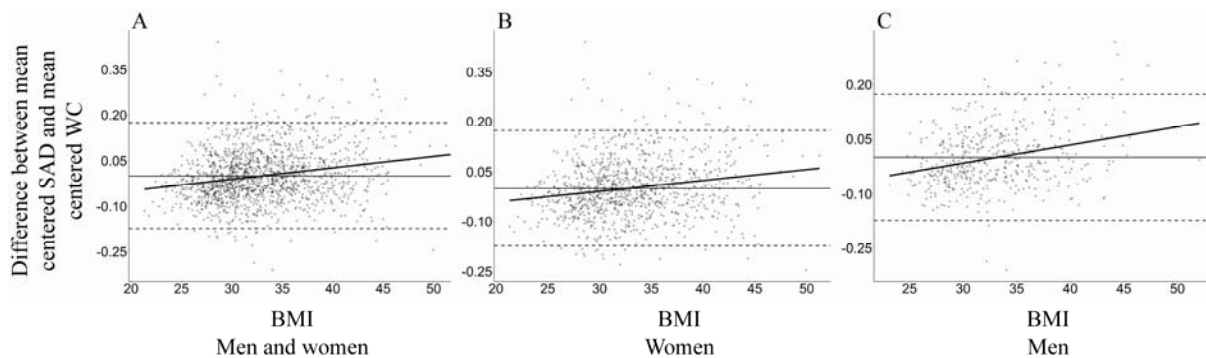
122 The statistical analyses were performed using R (v.3.5.1, R Core Team, Vienna, Austria) (18). Only
123 baseline data from the studies were used in the analyses. Pearson correlation was used for
124 evaluating the association between anthropometric measures. Simple linear regression of mean-
125 centered data was used to evaluate any bias between measurements of SAD and WC across the BMI
126 range, and reported as the slope. Multiple linear regression models were used to investigate the
127 association between SAD, WC, and BMI and markers of metabolic syndrome, insulin resistance,
128 blood lipids and measurements of low grade inflammation. Unadjusted analyses as well as analyses
129 adjusted for age, sex, smoking and study were conducted. Similar analyses were done for the SAD-
130 to-height and WC-to-height ratios. The ability of SAD, WC, and BMI to identify individuals with
131 metabolic syndrome markers above the IDF cut-offs was evaluated by means of area under the
132 receiver operating characteristics (ROC) curve using logistic regression models. Unadjusted
133 analyses as well as analyses adjusted for age, sex, smoking and study were conducted

134 **Results**

135 The six cohorts provided a total of 1516 individuals (485 men and 1031 women) (Table 1). The
136 participants had an average age of 42 years, and their BMI ranged from 21 to 52 kg/ m², WC ranged
137 from 64-155 cm and SAD ranged from 15-39 cm.

138 The three anthropometric measures were highly correlated ($r=0.82$ for SAD and WC; $r=0.74$ for
139 SAD and BMI; $r=0.76$ for WC and BMI). However, there was a systematic difference between the
140 correlations for SAD and WC over the range of BMI range of 21-52 kg/m². As BMI increased there
141 was a significant trend for SAD to measure proportionately higher abdominal adiposity compared to
142 WC. This was highly significant for men, women, and men and women combined (**Figure 1**).

143



144

145 **Figure 1 Difference between mean-centered sagittal abdominal diameter (SAD) and waist**
146 **circumference (WC) across the body-mass index (BMI) range of the participants** A) Men and
147 women combined slope = 0.0037 (0.0029; 0.0046), $p<0.0001$, $n=1516$. B). Women: slope = 0.0032
148 (0.0022; 0.0043), $p<0.0001$, $n=1031$. C). Men: slope = 0.0049 (0.0035; 0.0064), $p<0.0001$, $n=485$.

149

150 *Associations between anthropometric measures and cardiometabolic health*

151 BMI, WC and SAD were associated with all markers of an adverse metabolic phenotype (Table 2).
152 There were little difference between the measures in terms of R^2 values between SAD and WC,
153 indicating that they explained the variation in cardiometabolic measures equally well (Table 2).
154 Furthermore, there were no differences between the variance explained by SAD-to-height ratio and
155 WC-to-height ratio (Supplemental table 1) and the variation explained by these measures did not
156 from those of SAD and WC alone.

157

158 *The ability of anthropometric measurements to identify individuals with metabolic syndrome*
159 *markers above the IDF cut-offs*

160 We found that BMI, WC and SAD were overall fair in their ability to identify individuals with
161 metabolic syndrome markers above the IDF cut-offs after adjustments for age, sex, smoking and
162 study and there was no differences between BMI, WC and SAD in their ability to identify these
163 individuals (Table 3). However, in the unadjusted analysis WC and SAD performed slightly better
164 than BMI in identifying individuals with metabolic syndrome markers above the IDF cut-offs for
165 glucose >6.1 mmol/L, triglycerides, systolic and diastolic blood pressure, compared to BMI (Table
166 3). Using WC-to-height ratio and SAD-to-height ratio for identification of individuals with
167 metabolic syndrome markers above the IDF cut-offs did not show any differences between the two
168 (Supplementary table 2) or between these and SAD and WC alone.

169

170 *Differences between sexes and between BMI categories*

171 Contrary to the differences observed between the three anthropometric measures in the unadjusted
172 models in men and women combined, there were no differences between BMI, WC and SAD in
173 men or women alone (Supplementary table 3). However, we observed sex differences in the
174 measures ability of the measures to identify individuals with metabolic syndrome markers above the
175 IDF cut-offs. The prediction was generally better in women than in men especially for glucose >6.1
176 mmol/L, HDL and sBP in the unadjusted models and the prediction for sBP was still better for both
177 SAD and BMI after adjustment (Supplementary table 3).

178 As for the models for the entire population, WC and SAD had a better ability to identify individuals
179 with glucose >6.1 mmol/L, TAG, sBP, and dBP above the IDF cut-offs than BMI, but only in the
180 unadjusted models and only in those with a BMI <35 kg/m² (Supplementary table 4). For
181 individuals with a BMI >35 kg/m² a differences was only observed for glucose >5.6 mmol/L, where
182 BMI and WC showed better associations than SAD. We found no differences in the associations at
183 high and low BMI except for TAG, which had a higher AUROC at lower BMI even after
184 adjustment. Similar tendencies were observed in the unadjusted models for all metabolic syndrome
185 markers except HDL-cholesterol (Supplementary table 4).

186 **Discussion**

187 In the present study, we found distinct differences between SAD and WC over the BMI range,
188 which may indicate differences in adipose distribution across BMI categories. However, we did not
189 find that any of the anthropometric measures were superior in the association with cardiometabolic
190 health markers or in identifying people/subjects? with metabolic syndrome markers above the IDF
191 cut-offs. Moreover, we did not find that one anthropometric measurement were superior depending
192 on sex or BMI category. Finally, adjusting SAD and WC for height did not improve the
193 identification ability of the anthropometric measures.

194 Earlier studies comparing SAD and WC show conflicting results and only examine a few risk
195 markers at a time whereas our study measures multiple cardiometabolic risk markers giving a more
196 complete metabolic overview. Similar to other studies our study show no difference between SAD
197 and WC as markers of cardiometabolic health (19,20). One study in 826 elderly Dutch men and
198 women report differences in correlations with markers of insulin resistance, dyslipidemia, and blood
199 pressure between SAD or WC both above and below the age of 65 years of age but no consistently
200 with respect to which was the better (19). However, other studies have shown that SAD is a
201 superior anthropometric measure compared to WC and BMI (2,21,22) although some studies only
202 show a minor benefit of SAD compared to WC (2,22). One study showed that SAD was a better
203 predictor of insulin resistance compared to WC in high-risk group of 59 moderately obese men (21),
204 whereas a study including 885 men and women only found that SAD was marginally better
205 correlated with total and LDL-cholesterol, blood pressure and serum glucose and insulin (22). The
206 latter is in line with results from a study with 4032 participants which showed small improvements
207 in identifying elevated cardiometabolic risk in men with SAD compared to WC, but no difference
208 women (2)

209 For hard endpoints such as CVD, SAD has been shown to be a better predictor than WC (4,9). One
210 study showed that SAD >25 cm was the only anthropometric measurement associated with major
211 CVD events in patients with T2D (4). Similarly, a different study showed that SAD was the only
212 measure that significantly predicted CVD in men, but not in women (9). This study also showed
213 that SAD could predict CVD after adjustments for traditional biomarkers such as total- and HDL
214 cholesterol and systolic blood pressure. This indicates that SAD might have predictive ability

215 beyond established biomarkers of CVD. In the present study we tried to address this by including
216 additional biomarkers linked to abdominal obesity, CVD and T2D including inflammatory
217 cytokines. However, we did not find that SAD and WC were differentially associated with
218 inflammatory markers.

219 The proposed mechanism behind the association of abdominal obesity and an adverse
220 cardiometabolic profile is that increased adipose tissue mass and adipocyte size, leads to
221 amplification in pro-inflammatory response of adipose tissue and raise FFA release into circulation
222 (23,24). The increase of FFA and pro-inflammatory cytokines in circulation may increase the fat
223 accumulation in skeletal muscle and liver which may lead to insulin resistance and related
224 cardiometabolic abnormalities (23,24). Especially VAT is associated with increased cytokine
225 production and FFA release into circulation. In the present study, we included inflammatory
226 cytokines in order to elucidate whether SAD was really, a better predictor of adverse metabolic
227 cytokine production associated with increased VAT. We did not find that SAD and WC were
228 differentially associated with inflammatory markers and thus cannot shed any light on whether this
229 could explain the before mentioned superior predictive ability of SAD on top of established risk
230 markers.

231 The discrepancies in results between studies might also be because of age, ethnicity, sex, phenotype
232 or methodological differences. One of the methodological differences that might lead to
233 discrepancies in the results is the choice measurement sites and the optimal point of measuring SAD
234 is still debated (3). We used the highest point of the abdomen, which differ from the protocol
235 described in the US National Health and Nutrition Examination Survey (NHANES). This might
236 result in lower correlation with cardiometabolic measures (3,25,26) and could prevent us from
237 observing differences between SAD and WC. However, if minor differences in measurement point
238 can affect the associations drastically, its clinical utility may be limited. Furthermore, it has been
239 argued that assessment of WC requires less tools and is more practical compared to SAD, which
240 might limit the use of SAD as a clinical screening tool. However, similarly to others(2) we find that
241 difference is negligible. SAD has also shown to have a high intraclass correlation in both lean and
242 obese individuals, while the intraclass correlation was lower in obese compared to lean individuals
243 when measuring WC (27). This could indicate that SAD is more reliable when measuring
244 individuals of different weight categories and that SAD is better than WC in individuals with high

245 amounts of abdominal fat, especially SAT. SAD may therefore be more reliable when measuring
246 individuals of different weight categories with low variation and might also be less sensitive to the
247 investigator performing the measurement compared to WC.

248 One limitation of the present study is the cross-sectional design using biomarkers which is a weaker
249 design compared to studies with a prospective design and hard endpoints such as T2D, CVD and
250 mortality. Such studies are highly warranted. Furthermore, the present study used individuals,
251 which were primarily overweight and obese (98%), whereas other studies that used both normal
252 weight and overweight individuals (7,8). This limits our generalizability to normal weight
253 populations. However, our study used a clinically relevant population group, which are at risk of
254 developing T2D and CVD, and thus a clear relevance for establishing a highly predictable
255 anthropometric measure. The current study has measured many different cardiometabolic outcomes
256 including markers of insulin resistance, dyslipidemia, low grade inflammation and blood pressure.
257 As previous studies have not included all these markers, this study provides a good view of overall
258 cardiometabolic health. Furthermore, the sample size in the present study is appropriate to examine
259 the research questions posed.

260 **Conclusions**

261 In conclusion, the data from 6 cohorts of high-risk individuals showed that neither SAD, WC nor
262 BMI seems to be superior as an indicator of an adverse metabolic phenotype or in their ability to
263 identify individuals with metabolic syndrome markers above the IDF cut-offs regardless of sex and
264 BMI category. Thus choosing the most practical anthropometric measure might be the best solution
265 from a public health perspective.

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268 conduction of the studies.

269 **Author contributions**

270 MVL, MK, AA, TML, CR and GM were involved in conception and design of the study. MVL,
271 LK, SV, SKK, OP, LL, TML, WS, AA and MK were involved in the collection of data and
272 biological samples. CR, GM and MVL did the statistical analysis. MVL and GM drafted the

273 manuscript. All authors were involved in the interpretation of the data and all authors read, revised
274 and approved the final manuscript.

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278 **References**

- 279 1. O'Neill S, O'Driscoll L. Metabolic syndrome: A closer look at the growing epidemic and its
280 associated pathologies. *Obes Rev.* 2015;16:1–12.
- 281 2. Risérus U, de Faire U, Berglund L, Hellénius M-L. Sagittal Abdominal Diameter as a
282 Screening Tool in Clinical Research: Cutoffs for Cardiometabolic Risk. *J Obes.*
283 2010;2010:1–7.
- 284 3. Kahn HS. Sagittal abdominal diameter predicts cardiovascular events. *Nutrition, Metabolism
285 and Cardiovascular Diseases.* 2017. p. 1031–2.
- 286 4. Rådholm K, Tengblad A, Dahlén E, Länne T, Engvall J, Nystrom FH, Östgren CJ. The
287 impact of using sagittal abdominal diameter to predict major cardiovascular events in
288 European patients with type 2 diabetes. *Nutr Metab Cardiovasc Dis.* 2017;27:418–22.
- 289 5. Sampaio LR, Simões EJ, Assis AMO, Ramos LR. Validity and reliability of the sagittal
290 abdominal diameter as a predictor of visceral abdominal fat. *Arq Bras Endocrinol Metabol.*
291 2007;51:980–6.
- 292 6. Pimentel GD, Moreto F, Takahashi MM, Portero-McLellan KC, Burini RC. Sagittal
293 abdominal diameter, but not waist circumference is strongly associated with glycemia,
294 triacylglycerols and HDL-C levels in overweight adults. *Nutr Hosp.* 2011;26:1125–9.
- 295 7. Kahn HS, Cheng YJ. Comparison of adiposity indicators associated with fasting-state
296 insulinemia, triglyceridemia, and related risk biomarkers in a nationally representative, adult
297 population. *Diabetes Res Clin Pract.* 2018;136:7–15.
- 298 8. Kahn HS, Gu Q, Bullard KMK, Freedman DS, Ahluwalia N, Ogden CL. Population
299 distribution of the sagittal abdominal diameter (SAD) from a representative sample of US
300 adults: Comparison of SAD, waist circumference and body mass index for identifying
301 dysglycemia. *PLoS One.* 2014;9:e108707.
- 302 9. Carlsson AC, Riserus U, Ärnlov J, Borné Y, Leander K, Gigante B, Hellénius M-L, Bottai
303 M, de Faire U. Prediction of cardiovascular disease by abdominal obesity measures is
304 dependent on body weight and sex – Results from two community based cohort studies. *Nutr*

- 305 Metab Cardiovasc Dis. 2014;24:891–9.
- 306 10. Ibrugger S. Two Randomized Cross-Over Trials Assessing the Impact of Dietary Gluten or
307 Wholegrain on the Gut Microbiome and Host Metabolic Health. *J Clin Trials*. 2014;04.
- 308 11. Larsen TM, Dalskov S-M, van Baak M, Jebb SA, Papadaki A, Pfeiffer AFH, Martinez JA,
309 Handjieva-Darlenska T, Kunešová M, Pihlsgård M, et al. Diets with high or low protein
310 content and glycemic index for weight-loss maintenance. *N Engl J Med*. 2010;363:2102–13.
- 311 12. Suhr J, Vuholm S, Iversen KN, Landberg R, Kristensen M. Wholegrain rye, but not
312 wholegrain wheat, lowers body weight and fat mass compared with refined wheat: A 6-week
313 randomized study. *Eur J Clin Nutr*. 2017;71:959–67.
- 314 13. Poulsen SK, Due A, Jordy AB, Kiens B, Stark KD, Stender S, Holst C, Astrup A, Larsen
315 TM. Health effect of the new nordic diet in adults with increased waist circumference: A 6-
316 mo randomized controlled trial. *Am J Clin Nutr*. Oxford University Press; 2014;99:35–45.
- 317 14. Kjølbæk L, Sørensen LB, Søndertoft NB, Rasmussen CK, Lorenzen JK, Serena A, Astrup A,
318 Larsen LH. Protein supplements after weight loss do not improve weight maintenance
319 compared with recommended dietary protein intake despite beneficial effects on appetite
320 sensation and energy expenditure: A randomized, controlled, double-blinded trial. *Am J Clin*
321 *Nutr*. 2017;106:684–97.
- 322 15. Kjølbæk L, Benítez-Páez A, Gómez del Pulgar EM, Brahe LK, Liebisch G, Matysik S,
323 Rampelli S, Vermeiren J, Brigidi P, Larsen LH, et al. Arabinoxylan oligosaccharides and
324 polyunsaturated fatty acid effects on gut microbiota and metabolic markers in overweight
325 individuals with signs of metabolic syndrome: A randomized cross-over trial. *Clin Nutr*.
326 Churchill Livingstone; 2019;
- 327 16. Larsen TM, Dalskov S, van Baak M, Jebb S, Kafatos A, Pfeiffer A, Martinez JA, Handjieva-
328 Darlenska T, Kunesova M, Holst C, et al. The Diet, Obesity and Genes (Diogenes) Dietary
329 Study in eight European countries - a comprehensive design for long-term intervention. *Obes*
330 *Rev*. 2010;11:76–91.
- 331 17. Alberti KGMM, Zimmet P, Shaw J. Metabolic syndrome - A new world-wide definition. A

- 332 consensus statement from the International Diabetes Federation. *Diabetic Medicine*. 2006. p.
333 469–80.
- 334 18. R Development Core Team (2018), R: A Language and Environment for Statistical
335 Computing, version 3.5.1, Foundation for Statistical Computing: Vienna, Austria; Available
336 online: <https://www.R-project.org>.
- 337 19. Mukuddem-Petersen J, Snijder MB, van Dam RM, Dekker JM, Bouter LM, Stehouwer CDA,
338 Heine RJ, Nijpels G, Seidell JC. Sagittal abdominal diameter: no advantage compared with
339 other anthropometric measures as a correlate of components of the metabolic syndrome in
340 elderly from the Hoorn Study. *Am J Clin Nutr*. 2006;84:995–1002.
- 341 20. Pouliot MC, Després JP, Lemieux S, Moorjani S, Bouchard C, Tremblay A, Nadeau A,
342 Lupien PJ. Waist circumference and abdominal sagittal diameter: Best simple anthropometric
343 indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in
344 men and women. *Am J Cardiol*. 1994;73:460–8.
- 345 21. Riserus U, Arnlov J, Brismar K, Zethelius B, Berglund L, Vessby B. Sagittal abdominal
346 diameter is a strong anthropometric marker of insulin resistance and hyperproinsulinemia in
347 obese men. *Diabetes Care*. 2004;27:2041–6.
- 348 22. Ohrvall M, Berglund L, Vessby B. Sagittal abdominal diameter compared with other
349 anthropometric measurements in relation to cardiovascular risk. *Int J Obes*. 2000;24:497–
350 501.
- 351 23. Schenk S, Saberi M, Olefsky JM. Insulin sensitivity: modulation by nutrients and
352 inflammation. *J Clin Invest*. 2008;118:2992–3002.
- 353 24. Lionetti L, Mollica MP, Lombardi A, Cavaliere G, Gifuni G, Barletta A. From chronic
354 overnutrition to insulin resistance: The role of fat-storing capacity and inflammation. *Nutr*
355 *Metab Cardiovasc Dis*. 2009;19:146–52.
- 356 25. Anunciação PC, Ribeiro RCL, Pereira MQ, Comunian M. Different measurements of waist
357 circumference and sagittal abdominal diameter and their relationship with cardiometabolic
358 risk factors in elderly men. *J Hum Nutr Diet*. 2014;27:162–7.

- 359 26. de Almeida Paula HA, de Cássia Lanes Ribeiro R, de Lima Rosado LEFP, Abranches M V.,
360 do Carmo Castro Franceschini S. Relationship between waist circumference and supine
361 abdominal height measured at different anatomical sites and cardiometabolic risk factors in
362 older women. *J Hum Nutr Diet.* 2012;25:563–8.
- 363 27. Nordhamn K, Sodergren E, Olsson E, Karlstrom B, Vessby B, Berglund L. Reliability of
364 anthropometric measurements in overweight and lean subjects: consequences for correlations
365 between anthropometric and other variables. *Int J Obes.* 2000;24:652–7.
- 366
- 367

Table 1 Characteristics of the participants at baseline (n = 1516)

Variables	n	3G	n	SHOPUS	n	DIOGENES	n	RIGHT	n	MNG	n	PROKA	n	Across studies
Age (years)	117	48.70 ± 11.25 ^a	181	42.10 ± 13.08 ^b	902	41.14 ± 6.26 ^{b,c}	73	50.85 ± 9.26 ^c	29	43.97 ± 11.53 ^{a,b}	214	40.03 ± 10.68 ^b	1516	42.20 ± 9.17
Men % (M/F)	117	39.3 (46/71) ^a	181	31.0 (53/128) ^a	902	33.4 (301/601) ^{a,b}	73	43.8 (32/41) ^b	29	28.0 (8/21) ^a	214	39.5 (45/169) ^a	1516	32.0 (485/1031)
Weight (kg)	117	85.9 ± 13.0 ^a	181	89.9 ± 17.1 ^a	902	99.6 ± 17.4 ^b	73	83.5 ± 9.1 ^a	29	88.0 ± 13.7 ^a	214	96.6 ± 13.6 ^b	1516	96.0 ± 17.0
Sagittal abdominal diameter (cm)	117	22.9 ± 2.9 ^{c,d}	181	23.0 ± 3.2 ^c	902	25.2 ± 3.8 ^a	73	21.5 ± 2.1 ^d	29	22.0 ± 2.5 ^{c,d}	214	24.0 ± 2.5 ^b	1516	24.4 ± 3.6
Waist circumference (cm)	117	100.0 ± 9.0 ^{b,c}	181	100.1 ± 12.4 ^{b,c}	902	107.5 ± 13.0 ^a	73	96.0 ± 8.0 ^c	29	96.5 ± 8.8 ^c	214	103.2 ± 10.6 ^b	1516	104.70 ± 12.6
Body-mass index (kg/m ²)	117	28.7 ± 3.5 ^a	181	30.3 ± 4.9 ^c	902	34.5 ± 4.8 ^b	73	27.8 ± 1.9 ^a	29	30.1 ± 3.1 ^{a,c}	214	33.2 ± 3.3 ^d	1516	33.0 ± 5.0
Smoking, % (no/yes)	117	7 (109/8) ^a	181	22 (136/39) ^b	851	28 (616/235) ^b	73	0 (73/0) ^b	29	0 (29/0) ^a	214	0 (214/0) ^c	1459	19 (1177/282)
Fasting insulin (pmol/L)	114	65.0 ± 32.1 ^a	181	75.4 ± 45.3	799	83.4 ± 72.1 ^b	73	74.2 ± 39.4	28	43.6 ± 30.3 ^a	210	74.6 ± 44.5	1405	78.3 ± 61.2
Fasting glucose (mmol/L)	117	5.7 ± 0.6 ^c	181	5.3 ± 0.5 ^b	817	5.0 ± 0.7 ^a	73	5.9 ± 0.6 ^c	28	5.5 ± 0.4 ^b	210	5.7 ± 0.7 ^c	1426	5.3 ± 0.7
2-h glucose (mmol/L)		-	181	5.6 ± 1.4 ^a	794	6.7 ± 2.2 ^b		-		-		-	975	6.5 ± 2.1
HOMA-IR	114	2.4 ± 1.3 ^{b,c}	181	2.5 ± 1.6 ^c	798	3.2 ± 2.9 ^a	73	2.8 ± 1.6 ^{a,c}	28	1.0 ± 0.7 ^b	210	1.9 ± 1.4 ^{b,c}	1404	2.8 ± 2.4
Matsuda index		-	180	5.7 ± 3.0 ^a	783	5.3 ± 3.3 ^b		-		-		-	963	5.4 ± 3.2
TNF- α (pg/mL)	117	1.8 ± 2.2 ^a	181	1.2 ± 2.2 ^b		-		-		-		-	298	1.4 ± 2.2
IL-6 (pg/mL)	116	1.7 ± 1.6 ^a	180	1.3 ± 0.9 ^b		-	73	2.1 ± 1.6 ^c		-		-	369	1.6 ± 1.3
CRP (mg/L)	117	1.5 ± 1.8 ^a	181	2.6 ± 2.3 ^c	744	3.3 ± 2.3 ^d	72	1.8 ± 1.6 ^{a,c}	26	2.0 ± 2.0 ^{a,c}		-	1113	2.9 ± 2.3
Adiponectin (μ g/mL)		-		-	832	9.1 ± 4.3		-		-		-	832	9.1 ± 4.3
Total cholesterol (mmol/L)	117	5.3 ± 1.0 ^c	180	4.6 ± 0.9 ^b	832	4.9 ± 1.0 ^a	73	5.2 ± 0.9 ^{a,c}	28	5.0 ± 0.9	210	5.3 ± 0.9 ^c	1440	5.0 ± 1.0
HDL cholesterol (mmol/L)	117	1.3 ± 0.3 ^b	180	1.2 ± 0.3 ^a	834	1.2 ± 0.3 ^a	73	1.4 ± 0.3 ^b	28	1.4 ± 0.4 ^b	210	1.4 ± 0.4 ^b	1442	1.2 ± 0.3
LDL cholesterol (mmol/L)	117	3.1 ± 0.7	180	3.0 ± 0.8	828	3.1 ± 0.9	73	3.3 ± 0.8	28	3.1 ± 0.9	210	3.2 ± 0.8	1430	3.1 ± 0.8
Triglycerides (mmol/L)	117	1.3 ± 0.6 ^{b,c}	180	1.2 ± 0.6 ^b	822	1.4 ± 0.7 ^c	73	1.2 ± 0.6 ^b	28	2.8 ± 1.1 ^a	210	1.4 ± 0.8 ^c	1430	1.4 ± 0.7
FFA (mmol/L)	117	0.48 ± 0.16 ^a	159	-	735	0.65 ± 0.32 ^b		-		-	211	0.46 ± 0.16 ^c	1063	0.6 ± 0.3
Systolic blood pressure (mmHg)	117	129 ± 13 ^a	181	122 ± 14 ^b	885	125 ± 15 ^{a,b}	73	129 ± 17 ^a	29	120 ± 15 ^{b,c}	214	118 ± 11 ^c	1499	124.0 ± 14.5
Diastolic blood pressure (mmHg)	117	81 ± 9 ^a	181	81 ± 10 ^a	885	77 ± 11 ^b	73	85 ± 12 ^a	29	78 ± 10 ^{b,c}	214	76 ± 9 ^c	1499	78.3 ± 10.8

Data shown as mean ± SD. ^{a,b,c} Values with different superscripts letters indicate statistically significant differences between studies, assessed by analysis of variance or chi-square tests, p < .05. Abbreviations: CRP, C-reactive protein; FFA, Free fatty acids; HOMA-IR, Homeostatic model assessment for insulin resistance; IL-6, Interleukin 6, TNF- α , Tumor necrosis factor α .

Table 2 Associations between SAD, WC, BMI and markers of cardiometabolic health

	n	SAD (cm)			WC (cm)			BMI (kg/m ²)		
		Slope (CI)	p-value	R ²	Slope (CI)	p-value	R ²	Slope (CI)	p-value	R ²
Fasting insulin (pmol/L)										
Unadjusted	1405	14.6 (12.7, 16.5)	<0.001	0.139	16.8 (14.9, 18.7)	<0.001	0.180	15.0 (11.1, 14.9)	<0.001	0.110
Adjusted	1354	14.7 (12.5, 16.9)	<0.001	0.173	17.7 (15.5, 19.9)	<0.001	0.213	14.8 (12.6, 17.0)	<0.001	0.173
Fasting glucose (mmol/L)										
Unadjusted	1426	0.04 (0.007, 0.1)	0.019	0.004	0.1 (0.1, 0.1)	<0.001	0.014	-0.02 (-0.1, 0.01)	0.180	0.001
Adjusted	1376	0.09 (0.06, 0.1)	<0.001	0.252	0.1 (0.1, 0.2)	<0.001	0.263	0.1 (0.1, 0.1)	<0.001	0.256
2-h glucose (mmol/L)										
Unadjusted	975	0.3 (0.2, 0.4)	<0.001	0.023	0.2 (0.1, 0.3)	<0.001	0.016	0.3 (0.2, 0.4)	<0.001	0.026
Adjusted	925	0.3 (0.2, 0.4)	<0.001	0.083	0.2 (0.1, 0.4)	<0.001	0.077	0.2 (0.1, 0.4)	<0.001	0.077
HOMA-IR										
Unadjusted	1404	0.6 (0.5, 0.7)	<0.001	0.151	0.7 (0.6, 0.8)	<0.001	0.198	0.5 (0.4, 0.6)	<0.001	0.110
Adjusted	1353	0.5 (0.5, 0.6)	<0.001	0.247	0.7 (0.6, 0.7)	<0.001	0.285	0.6 (0.5, 0.6)	<0.001	0.248
Matsuda index										
Unadjusted	963	-0.9 (1.1, -0.8)	<0.001	0.121	-1.1 (-1.3, -1.0)	<0.001	0.181	-0.8 (-0.9, -0.6)	<0.001	0.081
Adjusted	913	-0.8 (-1.01, -0.7)	<0.001	0.140	-1.1 (-1.3, -0.9)	<0.001	0.191	-0.8 (-1.0, -0.6)	<0.001	0.137
TNF-α (pg/mL)										
Unadjusted	298	0.1 (0.001, 0.2)	0.047	0.013	0.1 (0.001, 0.2)	0.048	0.013	0.1 (-0.02, 0.1)	0.123	0.008
Adjusted	292	0.1 (-0.002, 0.2)	0.043	0.221	0.1 (-0.002, 0.2)	0.056	0.220	0.1 (0.04, 0.2)	0.003	0.233
IL-6 (pg/mL)										
Unadjusted	369	0.2 (0.1, 0.3)	<0.001	0.048	0.2 (0.1, 0.3)	<0.001	0.036	0.2 (0.1, 0.3)	<0.001	0.054
Adjusted	364	0.3 (0.2, 0.4)	<0.001	0.237	0.3 (0.2, 0.4)	<0.001	0.217	0.3 (0.2, 0.4)	<0.001	0.247
CRP (mg/L)										
Unadjusted	1087	0.8 (0.7, 1.0) ^a	<0.001	0.093	0.8 (0.6, 0.9) ^a	<0.001	0.126	1.3 (1.1, 1.4) ^b	<0.001	0.178
Adjusted	1039	0.8 (0.6, 1.0)	<0.001	0.191	0.9 (0.7, 1.0)	<0.001	0.205	0.9 (0.8, 1.1)	<0.001	0.221
Adiponectin (μg/mL)										
Unadjusted	832	-0.7 (-0.9, -0.4) ^a	<0.001	0.027	-0.9 (-1.1, -0.6) ^a	0.001	0.043	-0.3 (-0.6, 0.1) ^b	0.098	0.003
Adjusted	787	-0.3(-0.6, -0.1)	0.017	0.092	-0.5 (-0.8, -0.2)	0.001	0.099	-0.2 (-0.5, 0.1)	0.142	0.072
Total cholesterol (mmol/L)										
Unadjusted	1440	0.1 (0.04, 0.1)	<0.001	0.009	0.1 (-0.003, 0.1)	0.066	0.002	0.03 (-0.03, 0.1)	0.323	0.001
Adjusted	1389	0.1 (0.04, 0.2)	<0.001	0.097	0.04 (-0.02, 0.1)	0.127	0.090	0.04 (-0.01, 0.1)	0.139	0.091
HDL cholesterol (mmol/L)										
Unadjusted	1442	-0.09 (-0.1, -0.1)	<0.001	0.066	-0.1 (-0.1, -0.1)	<0.001	0.111	-0.1 (-0.1, -0.04)	<0.001	0.030
Adjusted	1391	-0.04 (-0.1, -0.03)	<0.001	0.216	-0.1 (-0.1, -0.1)	<0.001	0.237	-0.1 (-0.1, -0.03)	<0.001	0.221
LDL cholesterol (mmol/L)										

Unadjusted	1436	0.1 (0.1, 0.2)	<0.001	0.018	0.09 (0.1, 0.1)	<0.001	0.012	0.06 (0.01, 0.1)	0.014	0.004
Adjusted	1386	0.1 (0.1, 0.1)	<0.001	0.064	0.07 (0.02, 0.1)	0.003	0.058	0.06 (0.01, 0.1)	0.015	0.058
Triglycerides (mmol/L)										
Unadjusted	1430	0.2 (0.1, 0.2)	<0.001	0.072	0.1 (0.2, 0.2)	<0.001	0.061	0.1 (0.1, 0.1)	<0.001	0.024
Adjusted	1380	0.1 (0.1, 0.2)	<0.001	0.185	0.1 (0.1, 0.1)	<0.001	0.173	0.1 (0.1, 0.1)	<0.001	0.166
FFA (mmol/L)										
Unadjusted	1063	0.03 (0.02, 0.04)	<0.001	0.018	0.01 (0.00, 0.03)	0.058	0.003	0.5 (0.04, 0.07)	<0.001	0.048
Adjusted	1022	0.04 (0.02, 0.05)	<0.001	0.203	0.04 (0.02, 0.05)	<0.001	0.189	0.04 (0.02, 0.05)	<0.001	0.199
Systolic blood pressure (mmHg)										
Unadjusted	1499	3.8 (3.1, 4.5) ^a	<0.001	0.072	3.9 (3.2, 4.6) ^a	<0.001	0.073	1.9 (1.3, 2.6) ^b	<0.001	0.017
Adjusted	1445	2.9 (2.2, 3.6)	<0.001	0.209	2.5 (1.7, 3.2)	<0.001	0.199	2.6 (1.9, 3.4)	<0.001	0.203
Diastolic blood pressure (mmHg)										
Unadjusted	1499	2.8 (2.8, 3.3) ^a	<0.001	0.068	2.1 (1.6, 2.6) ^a	<0.001	0.038	0.9 (0.4, 1.4) ^b	<0.001	0.007
Adjusted	1445	3.5 (2.9, 4.0)	<0.001	0.188	2.4 (1.8, 3.0)	<0.001	0.142	2.3 (1.8, 2.9)	<0.001	0.143

Data shown as estimated slope and confidence interval (CI) from multiple linear regression models. The adjusted models included age, gender, smoking and study.^{a,b} Values with different superscripts letters indicate statistically significant differences between studies assessed by chi-squared test, $p < 0.05$. Abbreviations: CRP, C-reactive protein; FFA, Free fatty acids; HOMA-IR, Homeostatic model assessment for insulin resistance; IL-6, Interleukin 6; SAD, sagittal abdominal diameter; TNF- α , Tumor necrosis factor alpha; WC, waist circumference.

Table 3 SAD, WC, and BMI as identifiers of individuals with metabolic syndrome markers above the IDF cut-offs measured as area under the receiver operating characteristics curve (AUROC) (n=1516).

	SAD (cm)	WC (cm)	BMI (kg/m²)
Glucose (>5.6 mmol/L)			
Unadjusted	0.53 (0.50, 0.57)	0.56 (0.52, 0.59)	0.53 (0.50, 0.56)
Adjusted	0.79 (0.77, 0.82)	0.80 (0.77, 0.83)	0.80 (0.77, 0.82)
Glucose (>6.1 mmol/L)			
Unadjusted	0.60 (0.55, 0.64) ^{a,b}	0.61 (0.57, 0.65) ^a	0.52 (0.47, 0.56) ^b
Adjusted	0.78 (0.74, 0.82)	0.78 (0.75, 0.82)	0.78 (0.74, 0.82)
Triglycerides (>1.7 mmol/L)			
Unadjusted	0.63 (0.60, 0.67) ^a	0.62 (0.58, 0.65) ^{a,b}	0.56 (0.52, 0.59) ^b
Adjusted	0.72 (0.69, 0.76)	0.71 (0.68, 0.74)	0.71 (0.67, 0.74)
HDL cholesterol (< 1.03 (men) or <1.29 (women) mmol/L)			
Unadjusted	0.59 (0.56, 0.62)	0.60 (0.57, 0.63)	0.58 (0.55, 0.61)
Adjusted	0.65 (0.62, 0.68)	0.66 (0.63, 0.69)	0.64 (0.61, 0.67)
Systolic blood pressure (> 130 mmHg)			
Unadjusted	0.63 (0.60, 0.66) ^a	0.62 (0.59, 0.65) ^a	0.55 (0.52, 0.58) ^b
Adjusted	0.74 (0.72, 0.77)	0.73 (0.71, 0.76)	0.73 (0.71, 0.76)
Diastolic blood pressure (>85 mmHg)			
Unadjusted	0.62 (0.59, 0.65) ^a	0.59 (0.56, 0.62) ^{a,b}	0.53 (0.50, 0.57) ^b
Adjusted	0.72 (0.69, 0.76)	0.70 (0.67, 0.73)	0.70 (0.67, 0.73)

Data shown as estimated AUROC and 95% confidence interval using logistic regression models. The adjusted models included age, gender, smoking and study. Values with different superscripts letters indicate statistically significant differences between anthropometric measurements assessed by overlapping confidence intervals.

Difference between mean
centered SAD and mean
centered WC

