

Encouraging effects of a short-term, adapted Nordic diet intervention on skin microvascular function and skin oxygen tension in younger and older adults

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Published version

ROGERSON, David, MCNEILL, Scott, KONONEN, Heidi and KLONIZAKIS, Markos (2018). Encouraging effects of a short-term, adapted Nordic diet intervention on skin microvascular function and skin oxygen tension in younger and older adults. *Nutrition*, 49, 96-101.

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1 **Title: Encouraging effects of a short-term, adapted Nordic diet intervention on skin**
2 **microvascular function and skin oxygen tension in younger and older adults**

3

4 **Running Head: Adapted Nordic diet and microvascular function**

5

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14

15 **Authorship:** MK designed the study with the support of DR. SM and HK collected the data.
16 MK, SM and DR analysed and interpreted the data and wrote the manuscript. All authors
17 read and approved the final manuscript.

18

19 **Word Count:** 4876 words

20

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31

32 **Funding**

33 This study was funded by the University of Sheffield and Sheffield Hallam University.

34 Consumables supplied to the participants were provided by the Iceland Foods Charitable

35 Foundation. No funding body or organisation contributed to or influenced the design of the

36 study, or the collection, analysis and interpretation of data or and writing of the manuscript.

37

38

Highlights

- 39 • Effects of a 4-week adapted Nordic diet on microvascular function in younger and
40 older adults were assessed
- 41 • Laser Doppler Flowmetry measured cutaneous microvascular functioning
- 42 • Transcutaneous Oxygen monitoring measured skin oxygen tension
- 43 • Health markers were investigated concurrently
- 44 • Microvascular health, body-fat % and peak heart rate during exercise were improved
45 followed the diet.

46

Abstract

47 *Objective:* Microvascular benefits of regional diets are appearing in the literature however
48 little is known about Nordic-type diets. We investigated the effects of short-term adapted
49 Nordic diet on microvascular function in younger and older individuals at rest and during
50 activity.

51 *Research Method & Procedures:* Thirteen young [Mean: 28, SD: (5)] and fifteen older
52 participants [Mean: 68, SD: (6)] consumed a modified Nordic diet for four weeks. Laser
53 Doppler Flowmetry and Transcutaneous oxygen monitoring assessed cutaneous
54 microvascular function and oxygen tension pre and post-intervention; blood pressure, body
55 mass, body-fat%, ratings of perceived exertion and peak heart rate during activity were
56 examined concurrently.

57 *Results:* Axon-mediated vasodilation improved in older participants [1.17 (0.30) to 1.30
58 (0.30); $P < 0.05$]. Improvements in endothelium-dependent vasodilation were noted in young
59 [1.67 (0.50) to 2.03 (0.62); $P < 0.05$] and older participants [1.49 (0.37) to 1.63 (0.39); $P <$
60 0.05]. Reduced peak heart rate during activity was noted in older participants only [36.5(8.9)
61 to 35.3(8.5); $P < 0.05$] and reduced body-fat % in young participants only [young = 27.2
62 (8.3) to 25.2 (8.8); $P < 0.05$]. No other variables reached statistical significance however
63 trends were observed.

64 *Conclusions:* We observed statistically-significant improvements in microvascular function,
65 peak heart rate and body composition. Following an adapted Nordic diet might improve
66 microvascular health.

67

Keywords

68 Nordic Diet; Laser Doppler Flowmetry; Oxygen Tension

Introduction

70 Cardiovascular disease (CVD) is the number one cause of death worldwide with 17.5 million
71 deaths reported in 2012 (WHO, 2016). Risk factors for developing CVD include
72 inflammatory diseases such as type II diabetes and hypertension; aging, gender and lifestyle
73 factors such as smoking and poor nutrition (WHO 2016). Endothelial dysfunction, a
74 pathological condition characterised by impaired vasodilation and systemic inflammation
75 (Hadi et al. 2007), is a precursor of acute coronary syndromes, atherosclerosis and CVD
76 (Deanfield et al. 2007). Endothelial dysfunction however appears to be reversible and
77 endothelial health can be improved by modifying cardiovascular risk factors (Hadi et al.
78 2005). Emerging literature has therefore sought to investigate the effects of lifestyle
79 modifications as possible treatment strategies (Klonizakis et al. 2013) and dietary
80 intervention is one lifestyle modification that appears to be promising (Nordman et al. 2011).

81 Dietary interventions, however, are difficult to sustain, and factors such as taste preferences,
82 culinary habits and social acceptability might contribute to poor long-term adherence
83 (Poulsen et al. 2015). Bere and Brug (2009) recommend that strategies tailored to regional
84 eating preferences might lead to better long-term success, and interestingly, data is beginning
85 to suggest that regional diets might offer health benefits. Indeed, evidence now suggests that
86 the Mediterranean diet can reduce CVD* risk (Nordmann et al. 2011), alleviate metabolic
87 syndrome (Kastorini et al. 2011), reduce blood pressure and enhance weight loss (Esposito et
88 al. 2011).

89 The Nordic diet is a regional diet that encourages the consumption of Nordic vegetables and
90 fruits as well as whole grains, fish, rapeseed oil and low-fat dairy products. Early data

* **Abbreviations:** CVD, Cardiovascular Disease; NND, New Nordic Diet; LDF, Laser Doppler Flowmetry; TcPO₂: Transcutaneous Oxygen monitoring; BMI, Body Mass Index; CVC, Cutaneous Vascular Conductance; RPE, Rating of Perceived Exertion; SD, Standard Deviation; NO, Nitric Oxide; MD, Mediterranean Diet; PUFA, Polyunsaturated Fatty Acids

91 suggests that this diet might lead to reduced inflammation (Kanerva et al. 2014a), improved
92 insulin metabolism (De Mello et al. 2011) and weight loss (Poulsen et al. 2015).
93 Cardiovascular-health benefits of the diet are also now beginning to appear in the literature:
94 Adamsson et al. (2011) demonstrated that a 10-week intervention led to lower cholesterol,
95 reduced blood pressure and decreased serum insulin in hypercholesterolaemic participants.
96 To date, however, microvascular health effects of Nordic diets have yet to be explored. The
97 integrity of the microcirculation to sustain blood flow, tissue oxygenation and nutrient
98 delivery affects susceptibility to disease, and appears to decline with age (Tew et al. 2010).
99 Identifying strategies that maintain or improve microvascular function are therefore important
100 for sustaining long-term health.

101 The aim of this study was to investigate the effects of a short-term, adapted Nordic diet
102 (AND), modified for British taste preferences, on the microvasculature, by assessing tissue
103 oxygenation and endothelial function. The circulatory system functions differently at rest
104 and during activity (Abraham et al. 2003) and age-related endothelial dysfunction,
105 characterised by diminished arterial vasodilation and reduced nitric oxide supply, has been
106 observed in older adults (Gates et al. 2009). We therefore compared the effects of the diet in
107 younger (18-35 years old) and older sedentary participants (55-75 years old) at rest and
108 during sub-maximal exercise. We hypothesised that the intervention would improve
109 microvascular health and endothelial function in both groups, with older participants
110 experiencing greater improvements.

111

Material and Methods

112 *Ethical Approval*

113 Ethical approval for this research was granted by the Sheffield Hallam University's Health
114 and Wellbeing Research Ethics Committee. This research was conducted in accordance with
115 the Declaration of Helsinki.

116 *Participants*

117 Sixteen young participants aged 18-35 years [M = 28(5)] and sixteen older participants aged
118 55-75 years [M = 64(6)] provided informed consent. Recruitment took place via posters,
119 word of mouth and through the emailing systems of Sheffield Hallam University and the
120 University of Sheffield. Participants' eligibility was assessed pre-intervention using physical
121 activity and nutrition questionnaires. The long International Physical Activity Questionnaire
122 (IPAQ) was used to assess physical activity; scores > 3000 MET minutes per week would
123 necessitate participants' exclusion due to non-sedentariness. A validated Nordic Diet Score
124 (NDS) questionnaire (Bjørnara et al. 2015) was used similarly, and participants scoring > 5
125 points would also need to be excluded. Exclusion criteria also included smoking, pregnancy
126 and chronic conditions that might affect safe participation.

127 *Dietary Intervention*

128 Participants were advised to adhere to Public Health England's portion size guidelines (PHE
129 2016) but to follow the AND without restricting energy. During initial assessments,
130 participants were briefed about AND-compliant foods (Table 1), obtained individualised diet
131 plans, and provided with materials (recipes, etc.) and food items (root vegetables, cruciferous
132 vegetables, fish, rye bread and apples; enough for 2 weeks) to improve adherence and foster
133 behaviour change (Michie et al. 2011). Participants were also instructed to complete a 3-day
134 diet diary pre and post intervention (two assessments); data was inputted into software

135 (Nutritics, Dublin, Ireland) incorporating M^CCance and Widdowson's UK Composition of
 136 Food Database (2015) within its databank (Nutritics Ltd product version 1.7, Dublin Ireland),
 137 for dietary analysis. Kcals, Total Fat, Saturated Fat, Protein, Carbohydrates, Fibre and
 138 Omega 3 (Total *n*-3) were calculated, to measure dietary changes that might impact
 139 microvascular function (Calder et al. 2013). Follow-up consultations were conducted via
 140 telephone and email at weeks one and three to foster support, and a private social media
 141 group was created to engender social support similarly (Michie et al. 2011). Participants
 142 were advised to maintain activity as indicated by their pre-intervention IPAQ scores; no
 143 physical activity intervention was provided.

144 **Table 1** Nordic Foods

| Vegetables | Fruit | Fish/Meat | Grains | Other |
|-------------|---------------|-----------|-------------------|--------------|
| Cabbages | Blueberries | Game | Wholegrain breads | Dill |
| Cauliflower | Blackcurrants | Poultry | Rye | Parsley |
| Broccoli | Redcurrants | Cod | Oats | Chive |
| Kale | Gooseberries | Salmon | Barley | Legumes |
| Onions | Apples | Herring | | Rapeseed oil |
| Swede | Pears | Haddock | | |
| Carrots | Plums | Mackerel | | |
| Beetroot | | Halibut | | |
| Turnip | | | | |
| Potatoes | | | | |
| Parsnips | | | | |
| Mushrooms | | | | |

145

146 ***Protocol***

147 We used Laser Doppler Flowmetry (LDF) and Transcutaneous Oxygen Monitoring (TcP02)
 148 to assess microvascular function pre and post intervention, reflecting procedures described by

149 Wasilewski, Ubara and Klonizakis (2016). Laser Doppler Flowmetry was used to determine
150 cutaneous microvascular responsiveness to local heating (Tew et al. 2011); Transcutaneous
151 Oxygen Monitoring was used to assess tissue oxygen supply (Bajwa et al. 2014). To measure
152 LDF and TcPO₂ pre and post-intervention, we required participants to attend the laboratory
153 on two occasions, separated by a four-week intervention period, and instructed them to
154 abstain from caffeine prior to attending, to eliminate acute vasoconstriction (Umemura et al.
155 2006). Stature (cm) body mass (kg), body fat % and BMI (kg · m²) were measured
156 concurrently using a segmental body-composition analyser (InBody 720, Derwent
157 Healthcare; UK) and compared at both time points.

158 ***LDF Procedure***

159 Microvascular blood flow was measured as cutaneous red blood cell flux using a Laser
160 Doppler Flowmeter (Periflux system 5000, Perimed 122 AB, Järfälla; Sweden) and a 7-point
161 LDF probe (Probe 413, 123 Perimed AB), using procedures outline by Tew et al. (2010).
162 Participants were acclimated to a temperature-controlled room (ambient temperature set to 22
163 - 24 °C) before collecting data. Participants' forearms were cleansed prior to attaching the
164 LDF probe to the skin on the underside of the right arm, avoiding veins and hair, to
165 circumvent abnormal readings. Local thermal hyperaemia was induced using a heating disk
166 (Model 455, Perimed AB) connected to a heating unit (Model 5020, Perimed AB) and LDF
167 signals were recorded using PeriSoft software (PSW 9.0). Baseline blood-flow data were
168 recorded for five minutes with the local heating disc set to 30 °C. Temperature was then
169 increased (1° C · 10 s⁻¹) to 42 °C to induce rapid local heating, which was then maintained
170 for 30 minutes. After this, the probe temperature was increased to 44 °C for 10 minutes to
171 achieve maximal vasodilation. Resting blood pressure (mmHg) and heart rate (bpm) were
172 recorded at baseline and at every five minutes during data collection using a patient
173 monitoring device (Dinamap Dash 2500, GE Healthcare; USA). Thermal hyperaemic data

174 were recorded during the test and expressed as cutaneous vascular conductance (CVC) at four
175 regions (baseline, initial peak, plateau, and maximum regions) and presented as raw CVC and
176 CVC normalised to maximum (%CVCmax: [(CVC / maximum CVC) x 100]).

177 *Transcutaneous Oxygen Measurement*

178 The sub-maximal exercise test (Table 2) was performed after the LDF procedure using a
179 cycle ergometer (824E, Monark AB; Sweden). Heart Rate (HR) (Sports Tester, Polar;
180 Finland) and Ratings of Perceived Exertion (RPE; CR10 scale, Borg, 1998) were recorded at
181 each minute and blood pressure (mmHg) was recorded one minute into every two-minute rest
182 period using participants' contralateral arm, using the patient monitoring device (Dinamap
183 Dash 2500, GE Healthcare; USA). Oxygen tension was measured using a calibrated TINA
184 TCM400 tcpO₂ device (Radiometer; DK) during the test. A temperature probe, set to 44.5 °C
185 to achieve maximal skin vasodilatation, was attached to the skin of the participants' sub-
186 scapular area using a fixation ring, which was attached to participants' back approximately 10
187 mm below the left scapula, avoiding bone, and using contact solution. The solution was
188 allowed to heat, causing skin dilatation. Dilatation of the skin-blood capillaries increases
189 blood flow, causing a diffusion of oxygen through the skin into the sensor, which then
190 measures TcPO₂. After this, TcPO₂ measurements were temperature corrected to 37 °C by
191 the TINA device. For the purposes of this study, TcPO₂ was defined as the raw oxygen
192 perfusion values obtained directly from the TINA recordings (Table 3).

193

194 **Table 2** Submaximal Exercise Protocol

| Interval : Time (mins) | Resistance (kg) | Speed (RPM: revolutions per minute | Power output (Watts) |
|------------------------|-----------------|---------------------------------------|----------------------|
| Interval 1 : 5 mins | 1kg | 80 RPM | 80W |
| Rest : 2 mins | - | - | |
| Interval 2: 5 mins | 1.2kg | 80 RPM | 96W |
| Rest : 2 mins | - | - | |
| Interval 3: 5 mins | 1.4kg | 80 RPM | 112W |
| Rest : 2 mins | - | - | |
| Interval 4: 5 mins | 1.6kg | 80 RPM | 128W |

195

196 **Table 3** TcPO2 Variables

| TcPO2 Quantity | Definition |
|-------------------|-----------------------------------------------------------------------|
| Baseline | The arithmetic mean of maximum TcPO2 at rest |
| TcPO2max | The greatest TcPO2 value each minute of exercise or rest. |
| Δ TcPO2max | The maximum change from baseline value e.g. TcPO2max – baseline. |
| Δ TcPO2 | Average sum of change in Transcutaneous oxygen tension from baseline. |

197

198 **Statistical Analysis**

199 Independent t-tests were performed on baseline physical characteristic and dietary analysis
 200 data. A two-by-two mixed design Analysis of Variance (ANOVA) compared the effects of
 201 the AND intervention on blood pressure (systolic and diastolic), body-mass, body-fat %, peak
 202 heart rate, RPE, Δ TcPO2, Δ TcPO2max, CVC, %CVCmax and diet data (NDS, Kcals, Total
 203 Fat, Saturated Fat, Carbohydrates, Protein, Fibre and Omega 3) in the older and younger
 204 participants using SPSS (SPSS Inc., Chicago Illinois, version 23 for Windows). The alpha
 205 level was set at $P = 0.05$. To accomplish normality or homogeneity of variance, Δ TcPO2,
 206 Body Fat %, Peak Heart Rate and dietary data (NDS, Kcals, Omega 3) were log transformed

207 prior to inferential analyses, after checking for and ensuring underlying assumptions.

208 Independent and dependent-samples t-tests followed up significant interactions. Data are

209 presented as mean \pm SD.

210

211

Results212 ***Participants***

213 Thirteen young (18 - 35 years) and fifteen older (55 – 75 years) participants completed the
 214 study from the sixteen young and sixteen older participants originally recruited, equating to
 215 an 82 % and 94 % completion rate. Participants' characteristics are presented in Table 4.

216 **Table 4** Participants' Characteristics Pre and Post Intervention

| | Group A (Young) | | Group B (Old) | |
|-------------------------------|----------------------------|----------------|--------------------------|----------------|
| | Visit 1 | Visit 2 | Visit 1 | Visit 2 |
| Gender | 5 male, 8 female | | 7 male, 8 female | |
| Age (years) | 28 (5) [†] | | 64 (6) [†] | |
| Resting BP (systolic) | 129 (10) [†] | 123 (9) | 150 (14) [†] | 148 (19) |
| Resting BP (diastolic) | 78 (15) | 72 (8) | 81(12) | 79 (16) |
| Stature (cm) | 171 (6.0) | | 168 (6.6) | |
| Body Mass (kg) | 69.1 (22.1) | 67.4 (22.1) | 81.6(16.8) | 80.6 (16.7) |
| BMI (kg·m²) | 24.3 (7.9) | 23.6 (7.9) | 30.5 (5.4) | 29.7 (5.4) |
| Body Fat (%) | 27.2 (8.3) | 25.2 (8.8)* | 36.5(8.9) | 35.3(8.5) |

217 [†]P = <0.05 between groups (at baseline),

218 *P = <0.05 between visits (within groups)

219

220 ***Dietary Analysis***

221 Baseline Kcals [young = 1615.2 (645.6), old = 2595.2 (567.3); *P* = 0.14], Total Fat [young =
 222 61.2 g (22.6), old = 122.0 g (56.4); *P* = 0.03], Saturated Fat [young = 22.0 g (7.3), old = 38.5
 223 g(13.8); *P* = 0.027] and Fibre [young = 15.4 g (4.9), old = 27.7 g (4.3); *P* = 0.001] were lower
 224 in the younger participants (Table 6). Post intervention, only Kcals [young = 1353.0 (274.3),
 225 old = 2042.7 (676.0); *P* = 0.29] and Total Fat [young = 45.5 g (11.6), old = 87.7 g (36.5); *P* =
 226 0.022] differed between groups. Between visits, NDS [young = 2.5 (0.8) to (5.7 (1.4); *P* =

227 0.01, old = 2.3 (1.2) to 5.2 (0.8); $P = 0.02$] increased in both groups similarly. Fibre intake
 228 increased in the younger group (15.4 g (4.9) to 24.3 g (3.0); $P = 0.05$). No other dietary data
 229 reached statistical significance (Table 5).

230 **Table 5** Raw Dietary Data Pre and Post Intervention

| | Young | | Old | |
|----------------------|------------------|----------------|------------------|----------------|
| | Pre-NND | Post- NND | Pre-NND | Post-NND |
| NND Score | 2.5 (0.8) | 5.7 (1.4) * | 2.3 (1.2) | 5.2 (0.8) * |
| Kcals | 1615.2 (645.6) † | 1353.0 (274.3) | 2595.2 (567.3) † | 2042.7 (676.0) |
| Total Fat | 61.2 (22.6) † | 45.5 (11.6) | 122.0 (56.4) † | 87.7 (36.5) |
| Saturated Fat | 22.0 (7.3) † | 13.9 (7.3) | 38.5 (13.8) † | 22.9 (10.8) |
| CHO | 194.8 (99.2) | 163.8 (54.8) | 237.3 (63.1) | 207.3 (102.5) |
| Protein | 80.7 (26.1) | 81.2 (13.3) | 101.3 (30.5) | 92.3 (28.9) |
| Fibre | 15.4 (4.9) † | 24.3 (3.0) * | 27.7 (4.3) † | 25.1 (6.3) |
| Omega 3 | 0.5 (0.5) | 0.5 (0.3) | 3.4 (5.0) | 2.4 (3.3) |

231 † $P < 0.05$ between groups (at baseline)

232 * $P < 0.05$ between visits (within groups)

233

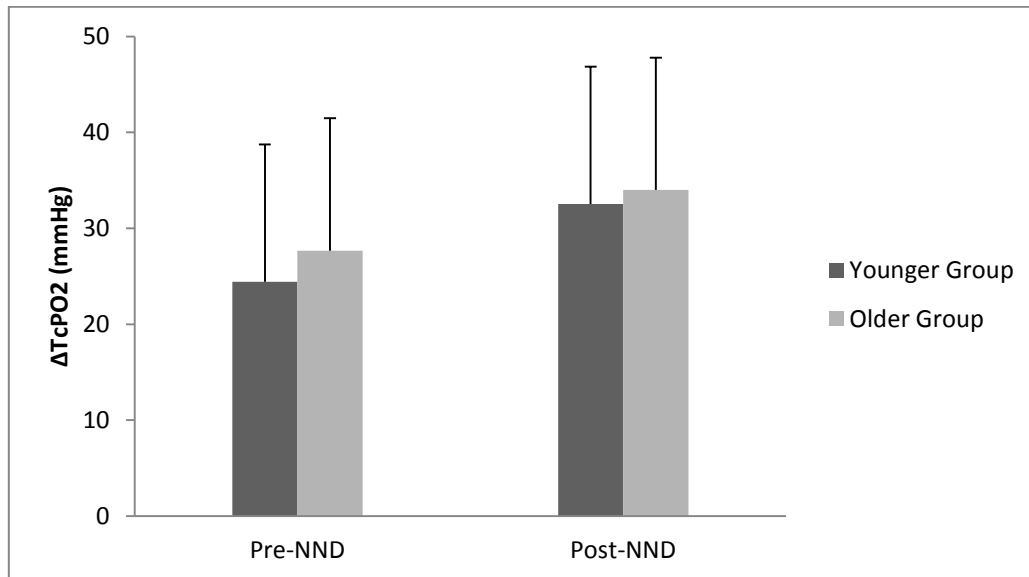
234 ***BMI, Body Mass, Body Fat and Blood Pressure***

235 No differences in BMI or Body Mass were observed in either group at any time and no
 236 between-groups differences were noted for body fat % pre or post intervention. Only
 237 younger participants experienced reductions in body fat % between visits [27.2 (8.3) to 25.2
 238 (8.8); $P = 0.028$] (Table 4). Baseline systolic blood pressure appeared to be lower in the
 239 younger participants [129 (10) vs. 150 (14); $P = 0.01$] however the AND had no effect on
 240 systolic blood pressure in either group (Table 4). Further, there were no changes in diastolic
 241 blood pressure in either group at any time (Table 4).

242 **Oxygen Tension**

243 There were no differences between the groups or changes to any of the TcPO2 variables
244 measured despite Δ TcPO2 appearing to increase post intervention ($P = 0.26$) (Figure 1).

245 **Figure 1** Δ TcPO2 Pre and Post Intervention



246

247

248 **Cutaneous Vascular Conductance**

249 **Baseline**

250 **Raw CVC**

251 The younger group experienced no changes to raw CVC however the older group
252 experienced an improvement during the 2nd assessment [0.35 (0.14) to 0.42 (0.16); $P = 0.02$]
253 (Table 5). Baseline between-groups differences observed for Raw CVC were not present
254 post-intervention (Table 6).

255 **%CVC MAX**

256 There were no differences between the groups or changes to %CVC MAX in either group at
257 any time (Table 6).

258

259 **Initial Peak**

260 **Raw CVC**

261 Post-intervention, older participants exhibited lower Raw CVC [1.71 (0.53) vs 1.30 (0.30); P
262 = 0.01] at the initial peak compared to the young participants despite experiencing an
263 increase from baseline [1.17 (0.30) to 1.30 (0.30); $P = 0.01$] (Table 6). Pre-intervention
264 between-groups differences were not apparent post-intervention.

265 **%CVCmax**

266 No changes in % CVCmax were observed in either group at any time (Table 6).

267 **Plateau**

268 **Raw CVC**

269 Both groups experienced improvements in raw CVC at visit 2 (Table 5). No between-groups
270 differences were noted at the pre intervention stage for Raw CVC; however, between-groups
271 differences became apparent at the post-intervention period (young = 2.03 (0.62), old = 1.63
272 (0.39); $P = 0.03$) (Table 6).

273 **%CVCmax**

274 Improvements to %CVCmax were experienced in the younger participants only [78.8 (12.0)
275 to 85.0 (10.7); $P = 0.03$]. Similar to Raw CVC, no between-groups differences were noted at
276 the pre-intervention stage but were noted at the post-intervention period [young = 85.0 (10.7),
277 old = 77.7 (7.3); $P = 0.03$] (Table 6).

278

279 **Table 6** Cutaneous Vascular Conductance Pre and Post Intervention

| | Group A (younger group) | | Group B (older group) | |
|-----------------------------|--------------------------|--------------------------|---------------------------|-------------|
| | Raw CVC | % CVC MAX | Raw CVC | % CVC MAX |
| Baseline | | | | |
| Visit 1 (pre-intervention) | 0.33 (0.12) [†] | 12.7 (5.2) | 0.35 (0.14) [†] | 13.9 (4.3) |
| Visit 2 (post-intervention) | 0.39 (0.11) | 15.0 (8.2) | 0.42 (0.16) [*] | 11.0 (7.7) |
| Initial Peak | | | | |
| Visit 1 (pre-intervention) | 1.55 (0.47) | 72.7 (10.4) | 1.17 (0.30) | 63.0 (16.1) |
| Visit 2 (post-intervention) | 1.71 (0.53) [†] | 76.0 (13.6) | 1.30 (0.30) ^{†*} | 71.9 (10.4) |
| Plateau | | | | |
| Visit 1 (pre-intervention) | 1.67 (0.50) [†] | 78.8 (12.0) [†] | 1.49 (0.37) [†] | 71.7 (12.1) |
| Visit 2 (post-intervention) | 2.03 (0.62) [*] | 85.0 (10.7) [*] | 1.63 (0.39) [*] | 77.7 (7.3) |

280 [†]P = <0.05 between groups

281 ^{*}P<0.05 between visits (within groups)

282

283 ***Peak Heart Rate and RPE***

284 A reduction in peak heart rate was observed in the older group only [149.5 (7.9) to 146.1
 285 (6.5); P = 0.01]. No differences between the groups or changes in RPE were noted.

286

288 Our study is the first to investigate the effects of a short-term, adapted Nordic diet
289 intervention on endothelial function and tissue oxygenation in adults at rest and during mild-
290 to-moderate exercise. These results highlight the short-term effects of the diet with respect to
291 a number of parameters which define CVD risk and day-to-day function in older and younger
292 individuals. Further, our findings support previous work elucidating the effects of sedentary
293 aging on cutaneous microvascular function: Similar to Tew et al. (2010), our older
294 participants demonstrated lower pre-intervention raw CVC during the initial peak and plateau
295 stages, suggesting age-related vasodilation impairment in response to local skin heating. The
296 mechanisms underpinning the weakened initial peak observed in older adults are not fully
297 understood however evidence suggests that local sensory nerve dysfunction, diminished
298 noradrenergic sympathetic nerve stimulation and reduced NO synthesis might attenuate the
299 rapid skin hyperaemic response in older individuals (James et al. 2006)—reduced
300 endothelial-mediated NO synthesis is thought to explain the diminished plateau. Age-related
301 microvascular impairment is associated with coronary events (James et al. 2006). Strategies
302 to improve microvascular function are clinically important therefore.

303 Tew et al. (2010) identified that maintaining aerobic fitness into advanced age might be one
304 such strategy, while findings elsewhere (Klonizakis et al. 2013, Klonizakis et al. 2016)
305 suggest that diet and exercise might also provide long-term benefits. Our data supports this
306 suggestion, and highlights encouraging benefits of a short-term dietary modification. Older
307 participants experienced improvements in raw CVC at baseline, initial peak and plateau
308 stages, suggesting that the AND led to improvements in axon-mediated vasodilation (during
309 the initial peak) and endothelial-mediated NO synthesis (during the plateau). Decreasing
310 axon-mediated vasodilation indicates microcirculatory dysfunction (Nouri et al, 2012) and
311 increased risk of cardiovascular events (Hadi et al. 2007). Our data therefore provide a

312 preliminary indication that diet might be a mechanism to attenuate this dysfunction in an
313 aging population. Younger participants experienced improvements in a number of CVC
314 parameters similarly, the magnitude of which appeared to be greater than the older
315 individuals. While drawing comparisons with other studies is erroneous given the novelty
316 and specificity of dietary-intervention research, our data reflects those observed elsewhere:
317 Klonizakis et al. (2013, 2014) and Alkhatib and Klonizakis (2014) revealed that the MD,
318 when coupled with exercise, led to greater improvements in endothelium-dependent
319 vasodilation than an exercise-only condition in older sedentary individuals (55 ± 4 years).
320 Collectively, data is beginning to suggest that wholefood; nutrient-dense diets might promote
321 endothelial health by also increasing NO synthesis, given adequate consumption of nitrate-
322 rich foods (Sobko et al. 2010). Indeed, age-related NO decline is also associated with CVD
323 risk (James et al. 2006); augmenting endothelial-dependent NO production via dietary
324 modification might mitigate such risk however.

325 The role of dietary fat in microvascular health is multifaceted: High-fat meals appear to
326 promote endothelial dysfunction (Esposito et al. 2007) and a high-saturated-fat diet might
327 impair endothelial vasodilation (Keogh et al. 2005). However, *n*-3 Polyunsaturated Fatty
328 Acids (PUFA) might *improve* endothelial health (Calder et al. 2013). While our participants
329 reduced saturated and total fat (trends only) intakes, neither group increased *n*-3 PUFA
330 concomitantly. This was despite the AND encouraging fish consumption. Data indicates that
331 *n*-3 PUFA might activate NO synthesis and reduce oxidative stress and inflammation (Zanetti
332 et al. 2015). It is possible therefore that substituting a proportion of saturated and total fat in
333 the diet for *n*-3 PUFAs might have led to superior changes to a number of microvascular
334 parameters we assessed. Future research might need to ensure greater fish consumption for
335 these to be realised however.

336 We adopted an incremental, sub-maximal exercise test such that tissue oxygenation could be
337 assessed at rest and during activity. Reduced oxygen perfusion is associated with aging:
338 Free-radical mediated endothelium-dependent NO degradation has been demonstrated in
339 older adults, leading to arterial narrowing, increased blood pressure and cardiac
340 complications (Gates et al. 2009). We observed no effects of the AND on any TcPO₂
341 parameters, contrasting data suggesting that short-term green tea consumption might lead to
342 improved tissue perfusion (Wasilewski et al. 2016). This was surprising considering that the
343 AND is a flavonoid-rich diet and that the flavonoids found in green tea explain its efficacy
344 (Wasilewska et al. 2016). While not measured specifically, insufficient consumption of
345 flavonoid-rich foods (e.g. berries, apples, and parsley) might explain our findings. Future
346 studies should ensure sufficient consumption of these foods for improvements in TcPO₂ to be
347 possible as part of an AND intervention.

348 We observed statistically-significant reductions in body-fat % in younger participants and
349 improved peak heart rate in older participants, adding to existing data revealing health
350 benefits of Nordic-type diets (Kanerva et al. 2014b). The reductions in body fat we observed
351 (young = -2%) corresponded with a weight-loss trend (young = -2.5%). While the AND
352 might have led to this weight loss, we cannot rule out that participating in a dietary
353 intervention might have prompted some participants to lose weight intentionally, and that this
354 weight loss might explain some of the improvements we noted. Nevertheless, owing to such
355 changes being observed, and that Nordic eating appears to be associated with low obesity
356 prevalence (Kanerva et al. 2013), and weight loss elsewhere (Poulsen et al. 2015), future
357 research should investigate the potential of a Nordic diet for weight-management purposes
358 specifically.

359 The efficacy of the AND to elicit improvements in microvascular function appeared to
360 greatest in younger participants, contrasting our original hypothesis. This might be due to

361 younger participants experiencing larger changes to habitual eating patterns via compliance
362 to the AND: while pre-to-post intervention NDS differed for both groups, a higher mean
363 change was observed in younger participants. It is also possible that younger individuals
364 might be more responsive to the AND: lifestyle (diet, physical activity) *and* biological factors
365 (hormonal changes, etc.) are known to lead to endothelial dysfunction with age; older
366 participants might have experienced dampened responsiveness due to such age-related
367 factors. However, complex interventions (diet and physical activity) have been shown to lead
368 to important, long-lasting improvements in microvascular function in older individuals
369 (Klonizakis et al. 2014). Future research might need to account for older participants'
370 responsiveness to diet-only intervention; complex interventions might be needed for greater
371 changes to be realised.

372 Limitations of this research include the lack of objective measures to determine compliance
373 to the AND, and the absence of control groups. Compliance measurements could be explored
374 in future studies; the lack of control group might make inferences about the efficacy of the
375 AND to elicit functional change to the endothelium difficult without a comparator. However,
376 baseline measurements were used here for such comparisons, and it was felt that control
377 groups were unnecessary owing to previous data highlighting the efficacy of dietary
378 intervention to stimulate microvascular change in young and old groups (Wasilewski et al.
379 2016). The short study duration, which might also be considered a limitation by some, was
380 intentional, with the view to explore the minimum duration after which medium-term effects
381 can be identifiable across populations. Our results have provided such indications, and so
382 further studies with a longer-duration might now be explored. Finally, an additional limitation
383 here is the lack of objective exercise-behaviour monitoring employed outside of testing. Such
384 monitoring should be implemented in future investigations.

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Conclusion

This study supports current evidence highlighting health benefits of regional diets. Our participants, who were sedentary, observed improvements in body composition and microvascular function by integrating Nordic foods into their diet for a 4-week period. There is now a need to investigate effects of Nordic-type diets over longer intervention periods, particularly among older individuals (55+ years), who appeared to be less responsive to the intervention. Age-related endothelial dysfunction might be a preliminary indicator of CVD events; strategies to attenuate age-related microvascular deterioration therefore require further investigation.

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