Effects of a palaeolithic diet on obstructive sleep apnoea occurring in females who are overweight after menopause—a randomised controlled trial

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BACKGROUND/OBJECTIVES: Obesity is the main risk factor for obstructive sleep apnoea, commonly occurring in females who are overweight after menopause. We aimed to study the effect of a palaeolithic diet on sleep apnoea in females with overweight after menopause from the population.

METHODS: Seventy healthy, non-smoking females with a mean age of 60 years and a mean BMI of 33 kg/m² were randomised to a palaeolithic diet or to a control low-fat diet according to Nordic Nutritional Recommendations, for 2 years. The apnoea-hypopnoea index was measured and daytime sleepiness was estimated during the intervention.

RESULTS: The mean apnoea-hypopnoea index at baseline was 11.6 (95% CI 8.6–14.5). The mean weight loss was 7.2 kg (95% CI 5.3–9.2 kg) in the palaeolithic diet group and 3.9 kg in the control group (95% CI 1.9–5.9 kg); p < 0.021 for the group difference. The reduction in weight corresponded to a reduction in the apnoea-hypopnoea index in the palaeolithic diet group (r = 0.38, p = 0.034) but not in the control group (r = 0.08, p = 0.69). The apnoea-hypopnoea index was reduced in the palaeolithic diet group when the weight was reduced by more than 8 kg. Daytime sleepiness according to the Epworth Sleepiness Scale score and the Karolinska Sleepiness Scale score was unaffected by dietary group allocation.

CONCLUSIONS: A substantial decrease in body weight of 8 kg was needed to achieve a reduction in sleep apnoea in this small trial of women who are overweight after menopause. The palaeolithic diet was more effective for weight reduction than a control low-fat diet and the reduction in sleep apnoea was related to the degree of weight decrement within this diet group.

TRIAL REGISTRATION: Clinicaltrials.gov: NCT00692536.

INTRODUCTION
Obstructive sleep apnoea is now estimated to affect almost a billion people worldwide [1] and up to 80% of women with obesity develop sleep apnoea [2]. Women after menopause run a particular risk of developing sleep apnoea. This may relate to fat mass redistribution, sex-hormone changes and age per se [3, 4]. Action to reduce weight in the population is needed to counteract poor health outcomes from obstructive sleep apnoea [5–13].

Obesity is an important risk factor for sleep apnoea and these patients are often recommended to reduce the severity of sleep apnoea by weight reduction. There are, however, mixed results regarding the resolution of sleep apnoea by dietary interventions or bariatric surgery [14–21]. The reason for this is unclear, but it may be due to the degree of weight reduction.

We and others have shown that a palaeolithic diet reduces body weight and improves metabolic factors [22–24]. The diet mimics our ancestors’ cuisine, with low carbohydrates and a high intake of monounsaturated fats and omega-3 fatty acids. To the best of our knowledge, no study has investigated the effect of a palaeolithic diet on sleep apnoea in people who are overweight from the population. This study aimed to investigate the effect of a palaeolithic diet on sleep apnoea in women who were overweight after menopause, compared with a low-fat control diet.

METHODS
This is a secondary analysis from a randomised controlled trial comparing a palaeolithic diet with a low-fat control diet according to the Nordic Nutritional Recommendations, conducted in Umeå, Sweden [24]. The eligible group comprised 210 females who responded to advertisements in two local newspapers. Seventy females fulfilled the inclusion criteria of being postmenopausal, non-smoking, body mass index >27 kg/m², healthy
Fig. 1 Flow chart of participants in the study. The inclusion of dropouts in the intention-to-treat analysis is noteworthy.

and free from medication, except for three women with well-controlled hypertension treated with an angiotensin-converting enzyme inhibitor. Investigations were recorded at baseline, after 6 months and after 2 years and included sleep apnoea recordings, subjective sleepiness scales, weight and height (Fig. 1). All the participants were invited to a follow-up, intention-to-treat analysis, regardless of whether they had continued the allocated diet. The participants were recruited from 4 September 2007 to 29 February 2008. Follow-up investigations were made from 4 October 2009 to 22 June 2010.

Ethical approval
The Regional Ethical Review Board at Umeå University approved the study protocols (no. 07-034 M), in accordance with the Helsinki Declaration, and all the patients gave their written informed consent.

Randomisation and masking
The included females were put in order according to their body mass index and randomised in blocks of four with an equal probability of being randomised to the palaeolithic diet \( n = 35 \) or to the low-fat control diet \( n = 35 \). The randomisation sequence was created by a statistician, using statistical software (IBM SPSS v. 19, Chicago, IL). All study personnel except the dieters were blinded to dietary allocation.

Outcome measurements
The primary outcome of the trial was a change in fat mass over a period of 2 years [24]. Secondary outcomes included the apnoea-hypopnoea index and daytime sleepiness.

Procedures

Dietary intervention. The palaeolithic diet was based on lean meat, fish, eggs, vegetables, fruits, berries and nuts. Additional fat sources were avocado, rapeseed oil and olive oil. Dairy products, cereals, added salt, refined fats and sugar were excluded. The diet aimed at 30% of energy intake from protein, 40% of energy intake from fat, with a recommended high intake of mono- and polyunsaturated fatty acids, and 30% of energy intake from carbohydrates [25]. The control diet according to the official Nordic Nutritional Recommendations was based on low-fat and high-fibre products, aiming at a daily intake of 15% energy intake from protein, 25–30% energy intake from fat and 55–60% energy intake from carbohydrates [25].

One dietician per dietary group held 12 group sessions. Four cooking classes and four follow-up sessions were held during the first 6 months, followed by group meetings at 6, 12, 18 and 24 months. Participants were recommended to eat the advised food at three main meals and two snacks a day. Food intake was ad libitum for both diets, meaning that women could eat as much as they liked, without restriction. Recipes, written instructions and suggestions of food for breakfast, lunch and dinner were given during the 12 group sessions. The group sessions consisted of information on how to prepare and cook meals and dishes in the intervention diet. The sessions also included information about dietary effects on health, body weight and how to maintain behavioural changes. The group session on behavioural change was devoted to a discussion of different aspects of motivation, including group discussions of benefits and difficulties changing diet. Adherence to the diet intervention was monitored using self-reported 4-day food records at study start, monthly during the first 6 months and at 9, 12, 18 and 24 months. Participants were instructed to estimate the amount of food eaten from coloured food-portion photographs and household measuring utensils. Adherence to the different diets was assessed using the Dietist XP nutritional analysis package (version 3.0, Kost och Näringsdata AB, Bromma, Sweden), which converted the food intake to estimates of energy intake and nutrients. Adherence to protein intake was measured by nitrogen excretion in urine at baseline and after 6 and 24 months [24]. Body weight was measured at baseline and after 6, 12, 18 and 24 months.

Sleep apnoea recordings
The apnoea-hypopnoea index was measured with overnight sleep apnoea recordings (Embletta X10, Natus Medical Inc., CA, USA). It included continuous recordings of airflow using a nasal flow pressure sensor, thoracic and abdominal respiratory effort (XactTrace respiratory effort belts), finger pulse oximetry (Nonin Oximeter XPOD) and a body position sensor.

An obstructive apnoea was defined as a drop in airflow of at least 90% of the pre-event baseline for at least 10 s with continuing abdominal and thoracic movements, according to the American Academy of Sleep Medicine [26]. An obstructive hypopnoea was defined as a 50% reduction
The sample size needed was estimated at 30 females in each arm to detect a significant difference in fat mass (\(p < 0.05\)) with a power of 80% [24]. In a post-hoc analysis, it was estimated that 65 patients in each group would be needed to detect a mean (SD) apnoea-hypopnoea index difference of 5 [10] units with a power of 80% and a significance level of 5%.

Baseline characteristics were presented as means and 95% confidence intervals. The differences between baseline and outcome were analysed with Student’s \(t\) test when comparing the diet groups. Model evaluations were carried out with residual analysis. The Mann–Whitney U-test was used when analysing differences in the apnoea-hypopnoea index due to outlier problems. All the tests were two sided. Pearson’s correlation coefficient was used to measure the linear correlation between the change in weight and body mass index and the change in apnoea-hypopnoea index. All the analyses were performed on an intention-to-treat basis. They included patients with low adherence to the diet intervention and all the patients were analysed with respect to randomisation. Patients who dropped out were also invited to a follow-up. A complete case analysis was performed, and missing data were assumed to be missing at random. A significance level of 0.05 was used. SPSS Statistics for Windows, Version 26.0, Armonk, NY: IBM Corp was used for statistical analysis.

**RESULTS**

The mean apnoea-hypopnoea index at baseline was 11.6 (95% CI 8.6–14.5, range 0.3–73.8) among the 70 included females and 70% had an apnoea-hypopnoea index of 5 or more. No woman had central sleep apnoea. Two women with previously diagnosed sleep apnoea were treated with continuous positive airway pressure (CPAP), one in each dietary group, and they were investigated after three nights without treatment. The baseline characteristics did not differ between the diet groups (Table 1). Four females in the palaeolithic group and nine females in the control group quit further participation during the study period. Thirty-two females randomised to the palaeolithic diet and 30 females in the control group were invited to follow-up after 2 years. The intention-to-treat analysis included five females who had stopped following the dietary recommendations during the study period, four in the palaeolithic group and one in the control group (Fig. 1).

In the palaeolithic diet group, body weight decreased by a mean of 7.2 (95% CI 5.3–9.2) kg, \(p < 0.001\), from baseline to follow-up after 2 years, and the corresponding weight reduction was 3.9 kg (95% CI 1.9–5.9 kg) in the control group. The between-group difference in weight was 3.4 (95% CI 0.5–6.2) kg, \(p = 0.021\). There was no between-group difference in the apnoea-hypopnoea index at 2 years (Table 2). The effect on outcome remained in a sub-

### Table 1. Baseline characteristics.

| All women \(n = 70\) | Palaeolithic diet group \(n = 35\) | Control low-fat diet group \(n = 35\) | \(p\) value |
|---------------------|----------------------------------|-----------------------------------|-----------|
| Age, years          | 60 (95% CI 58–61) (range 49–71)  | 60 (95% CI 58–61) (range 52–69)  | 60 (95% CI 58–62) (range 49–71) | 0.637    |
| Weight, kg          | 86.7 (95% CI 84.2–89.2) (range 67.0–114.3) | 87.0 (95% CI 83.6–90.5) (range 67.0–114.3) | 86.8 (95% CI 82.6–90.1) (range 71.7–108.9) | 0.940    |
| Body mass index, kg/m² | 32.5 (95% CI 31.7–33.3) (range 27.3–44.6) | 32.7 (95% CI 31.5–33.9) (range 27.3–44.6) | 32.5 (95% CI 31.4–33.7) (range 28.3–40.0) | 0.803    |
| Apnoea-hypopnoea index | 11.6 (95% CI 8.6–14.5) (range 0.3–73.8) | 11.1 (95% CI 8.0–14.1) (range 0.9–32.3) | 11.9 (95% CI 7.5–16.5) (range 0.3–73.8) | 0.774    |

The data are presented as the means, 95% confidence intervals and range.

**Daytime sleepiness scales.** Subjective sleepiness over a longer period was measured using the Epworth Sleepiness Scale, with a summary of answers from 0 to 8 on 8 questions on sleepiness during the daytime, leading to a summary score of 0–24 [27]. The Karolinska Sleepiness Scale that assesses immediate sleepiness on a scale from 1 to 9 was measured at awakening in the morning, at 3 pm and at 10 pm [28].

### Table 2. Longitudinal analysis of outcome variables at 2 years in women with overweight after menopause.

| Palaeolithic diet \(n = 32\) | Control diet \(n = 30\) | Between-group difference | \(p\) value |
|-----------------------------|------------------------|--------------------------|-----------|
| Weight, kg                  | 86.2 (82.7–89.8)       | 79.0 (74.9–83.1)         | 85.3 (81.7–89.0) | 81.4 (77.1–85.6) | -3.4 (−6.2−0.5) | 0.021    |
| AHI events/h                | 11.8 (7.5–16.0)       | 12.3 (7.1–17.5)          | 12.7 (8.3–17.1) | 13.9 (8.6–19.3) | -0.6 (−5.4–4.2) | 0.807    |
| ODI, events/h               | 15.0 (10.3–19.6)      | 14.8 (9.5–20.0)          | 18.8 (14.1–23.5) | 19.1 (13.8–24.4) | -0.5 (−5.7–4.7) | 0.845    |
| Nocturnal hypoxia, SaO₂ < 90%, minutes | 4.7 (1.3–8.2) | 6.4 (2.9–15.6)          | 7.0 (3.5–10.5) | 14.9 (5.5–24.3) | -6.2 (−17.7–5.3) | 0.285    |
| Sleep time,minutes          | 437 (420–454)          | 411 (388–435)            | 436 (418–454) | 439 (414–463) | -28.8 (−63.8–6.2) | 0.105    |
| ESS                         | 6.5 (5.3–7.8)         | 6.2 (4.9–7.6)            | 8.0 (6.7–9.3) | 8.2 (6.8–9.6) | -0.4 (−1.8–1.0) | 0.562    |
| KSS on awakening            | 4.6 (3.8–5.5)         | 4.8 (4.0–5.6)            | 5.5 (4.6–6.4) | 5.2 (4.4–6.0) | 0.5 (−0.5–1.6) | 0.295    |
| KSS at 3 pm                 | 4.0 (3.5–4.6)         | 3.9 (3.2–4.6)            | 4.7 (4.2–5.3) | 4.4 (3.7–5.0) | 0.1 (−0.9–1.1) | 0.848    |
| KSS at 10 pm                | 6.9 (6.2–7.5)         | 6.5 (5.9–7.8)            | 6.5 (5.9–7.1) | 6.5 (5.9–7.1) | -0.4 (−1.4–0.6) | 0.418    |
| Supine sleep, %             | 27 (19–36)            | 29 (20–38)               | 32 (23–40) | 33 (22–43) | -0.5 (−9.9–10.9) | 0.924    |

The data are presented as means and 95% confidence intervals.

\(AHI\) apnoea-hypopnoea index, \(ESS\) Epworth Sleepiness Scale, \(KSS\) Karolinska Sleepiness Scale.

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**SPRINGER NATURE**
The reduction in weight corresponded to a reduction in the apnoea-hypopnoea index (AHI) in the palaeolithic diet group ($r = 0.38, p = 0.034$) but not in the control low-fat diet group ($r = 0.08, p = 0.69$). A decrease in the apnoea-hypopnoea index was mainly present in individuals with a weight reduction of more than 8 kg in the palaeolithic diet group.

The reduction in weight was associated with a reduction in the apnoea-hypopnoea index. This was linked to high adherence to the palaeolithic diet for 2 years, with a substantial weight reduction in women who were overweight after menopause, compared with a low-fat diet. A reduction in sleep apnoea occurred in women with a pronounced weight loss >8 kg, regardless of the diet group. This supports the finding that, the more weight that is lost, the greater the reduction in the apnoea-hypopnoea index, found in previous trials [14–16, 18].

Despite significant weight reductions, there was no significant change in the mean apnoea-hypopnoea index in either diet group after 2 years. The fact that the women were 2 years older at follow-up could explain the lack of effect on the apnoea-hypopnoea index. It is known that sleep apnoea worsens with age, especially in women in the menopausal transition [2, 29]. This further underlines the importance of weight reduction in women in relation to menopause.

The weight reduction was more pronounced in the palaeolithic group and 40% of them had a weight reduction of over 8 kg vs. 20% in the control group. We found a significant, albeit weak, dose-response relationship between weight loss and improvements in the apnoea-hypopnoea index in the palaeolithic diet group. One potential mechanism may be that palaeolithic diets, compared with low-fat diets, in previous randomised controlled trials have shown greater improvements in components of the

**Table 3.** Longitudinal analysis of outcome variables at 2 years in women with apnoea-hypopnoea index >5 at baseline.

|                          | Palaeolithic diet | Control diet | Between-group difference | p value |
|--------------------------|------------------|--------------|--------------------------|---------|
|                          | n = 25           | n = 24       |                         |         |
| Weight, kg               |                  |              |                         |         |
| Baseline                 | 86.8 (82.7–91.0) | 80.0 (75.2–84.7) | -4.0 (–7.2—0.82) | 0.015   |
| Two years                | 87.3 (82.9–91.6) | 84.1 (79.5–89.4) |                         |         |
| AHI, events/h            |                  |              |                         |         |
| Baseline                 | 15.0 (10.0–20.0) | 16.5 (11.3–21.7) | -1.6 (–8.1–4.9) | 0.622   |
| Two years                | 23.3 (17.7–28.8) | 24.3 (18.0–30.6) |                         |         |
| ODI, events/h            |                  |              |                         |         |
| Baseline                 | 17.4 (12.1–22.7) | 17.1 (11.1–23.1) | -1.3 (–8.1–5.5) | 0.696   |
| Two years                | 23.1 (17.7–30.8) | 21.4 (16.5–26.9) |                         |         |
| Nocturnal hypoxia, SaO2 < 90%, minutes | 5.8 (1.7–10.0) | 7.8 (–3.6–19.3) | -8.3 (–23.1–6.5) | 0.263   |
| Sleep time, hours        |                  |              |                         |         |
| Baseline                 | 443 (422–464)    | 435 (412–457) | -26.8 (–69.1–15.6) | 0.209   |
| Two years                | 410 (380–440)    | 428 (397–459) |                         |         |
| ESS                      |                  |              |                         |         |
| Baseline                 | 6.2 (4.8–7.6)    | 8.8 (7.2–10.2) | -0.4 (–2.2–1.5) | 0.710   |
| Two years                | 6.0 (4.4–7.6)    | 8.9 (7.1–10.6) |                         |         |
| KSS on awakening         |                  |              |                         |         |
| Baseline                 | 4.9 (3.9–5.8)    | 5.8 (4.9–6.7) | -0.5 (–0.7–0.18) | 0.395   |
| Two years                | 5.1 (4.1–6.0)    | 5.4 (4.5–6.3) |                         |         |
| KSS at 3 pm              |                  |              |                         |         |
| Baseline                 | 4.2 (3.5–4.9)    | 4.7 (4.1–5.4) | -0.4 (–1.6–0.8) | 0.522   |
| Two years                | 3.9 (3.2–4.6)    | 4.8 (4.1–5.6) |                         |         |
| KSS at 10 pm             |                  |              |                         |         |
| Baseline                 | 6.7 (5.9–7.5)    | 6.5 (5.7–7.3) | -0.5 (–1.8–0.7) | 0.371   |
| Two years                | 6.5 (5.8–7.2)    | 6.9 (6.1–7.6) |                         |         |
| Supine sleep, %          |                  |              |                         |         |
| Baseline                 | 29.6 (20.8–38.5) | 32.9 (22.6–43.2) | -0.5 (–12.6–12.7) | 0.930   |
| Two years                | 32.9 (22.6–43.2) | 30.0 (19.2–40.8) |                         |         |

The data are presented as means and 95% confidence intervals.

AHI apnoea-hypopnoea index, ESS Epworth Sleepiness Scale, KSS Karolinska Sleepiness Scale.

**Fig. 2** The association between weight loss in kg and change in the apnoea-hypopnoea index (AHI) in the two dietary groups. A reduction in weight corresponded to a reduction in the apnoea-hypopnoea index in the palaeolithic diet group ($r = 0.38, p = 0.034$) but not in the control low-fat diet group ($r = 0.08, p = 0.69$). A decrease in the apnoea-hypopnoea index was mainly present in individuals with a weight reduction of more than 8 kg in the palaeolithic diet group.

**DISCUSSION**

Here, we show that the reduction in weight in the palaeolithic diet group correlated with a reduction in the apnoea-hypopnoea index. This was linked to high adherence to the palaeolithic diet for 2 years, with a substantial weight reduction in women who were overweight after menopause, compared with a low-fat diet. A reduction in sleep apnoea occurred in women with a pronounced weight loss >8 kg, regardless of the diet group. This supports the finding that, the more weight that is lost, the greater the reduction in the apnoea-hypopnoea index, found in previous trials [14–16, 18].

Despite significant weight reductions, there was no significant change in the mean apnoea-hypopnoea index in either diet group after 2 years. The fact that the women were 2 years older at follow-up could explain the lack of effect on the apnoea-hypopnoea index. It is known that sleep apnoea worsens with age, especially in women in the menopausal transition [2, 29]. This further underlines the importance of weight reduction in women in relation to menopause.

The weight reduction was more pronounced in the palaeolithic group and 40% of them had a weight reduction of over 8 kg vs. 20% in the control group. We found a significant, albeit weak, dose-response relationship between weight loss and improvements in the apnoea-hypopnoea index in the palaeolithic diet group. One potential mechanism may be that palaeolithic diets, compared with low-fat diets, in previous randomised controlled trials have shown greater improvements in components of the
A reduction in body mass index corresponded to a reduction in the apnoea-hypopnoea index in the palaeolithic diet group ($r = 0.137$, $p = 0.037$) but not in the control low-fat diet group ($r = 0.005$, $p = 0.70$).

**Fig. 3** The association between change in body mass index and change in the apnoea-hypopnoea index (AHI) in the two dietary groups. A reduction in body mass index corresponded to a reduction in the apnoea-hypopnoea index in the palaeolithic diet group ($r = 0.137$, $p = 0.037$) but not in the control low-fat diet group ($r = 0.005$, $p = 0.70$).

**Fig. 4** Change in apnoea-hypopnoea index (AHI) and 8 kg weight loss. The box plot illustrates the difference in the change in AHI between participants who lost ≥8 kg vs. <8 kg from baseline to follow-up after 2 years regardless of dietary intervention.

A systematic review from 2013 concluded that lifestyle and dietary interventions improved obstructive sleep apnoea parameters but not sufficiently to normalise obstructive sleep apnoea. This prevalence is well in line with earlier population-based studies [2, 31] and thus constitutes a group of women running a major risk of sleep apnoea-related metabolic disorders, cardiovascular events and mortality [5–13, 32].

A reduction in body mass index corresponded to a reduction in the apnoea-hypopnoea index in the palaeolithic diet group ($r = 0.137$, $p = 0.037$) but not in the control low-fat diet group ($r = 0.005$, $p = 0.70$).
was found between weight reduction and daytime sleepiness in the present trial.

One limitation is the small sample size and the large variability in the apnoea-hypopnea index, as women both with and without sleep apnoea at baseline were included. Another limitation is the use of simplified sleep apnoea recordings instead of polysomnography including an EEG for sleep scoring. We did not control for abstinence from alcohol and caffeine before the sleep apnoea recordings, which could have affected the results. The high adherence to the palaeolithic diet, with a low drop-out rate from the study over a period of 2 years, is a strength in the present study. Further studies with large sample sizes are needed before a palaeolithic diet can be recommended to people with obstructive sleep apnoea.

CONCLUSIONS
A substantial decrease in body weight of 8 kg was needed to achieve a reduction in sleep apnoea in women who are overweight after menopause. The palaeolithic diet was more effective for weight reduction than a control low-fat diet and the reduction in sleep apnoea was related to the degree of weight decrement within this diet group. The study sample size was limited and further studies are warranted.

DATA AVAILABILITY
All data that support the findings are available on request to the corresponding authors within reason. Material and correspondence requests should be made to the corresponding author.

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AUTHOR CONTRIBUTIONS
TO, CL, BL, KAF, CM and MR designed the study, while CS, CM and MR collected data and KAF, EL, JS, TO and MR played an important role in interpreting the results. KAF, EL, To and MR drafted the paper and JS, CL, BL, CM and CV revised the paper. All the authors agreed to be accountable for every aspect of the work of ensuring that questions related to the accuracy or integrity of any part of the work have been appropriately investigated and resolved.

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COMPETING INTERESTS
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