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Randomized control trials

# Role of a prudent breakfast in improving cardiometabolic risk factors in subjects with hypercholesterolemia: A randomized controlled trial

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SUMMARY

*Background & aims:* It is unclear whether advising a prudent breakfast alone is sufficient to improve blood lipids and cardiometabolic risk factors in overweight hypercholesterolemic subjects. The aim of this study was to investigate whether a prudent low-fat breakfast (PB) rich in dietary fiber lowers low-density lipoprotein cholesterol (LDL-C) and other cardiometabolic risk factors in subjects with elevated LDL-cholesterol levels.

*Methods:* In a parallel, controlled, 12-week study, 79 healthy overweight subjects (all regular breakfast eaters) were randomly allocated to a group that received a PB based on Nordic foods provided *ad libitum* or a control group that consumed their usual breakfast. The primary outcome was plasma LDL-C. Secondary outcomes were other blood lipids, body weight, sagittal abdominal diameter (SAD), glucose tolerance, insulin sensitivity and inflammation markers (C-reactive protein [CRP] and tumor necrosis factor receptor-2 [TNF-R2]), and blood pressure. The PB was in accordance with national and Nordic nutrition recommendations and included oat bran porridge with low-fat milk or yogurt, bilberry or lingonberry jam, whole grain bread, low-fat spread, poultry or fatty fish, and fruit.

*Results:* No differences were found in LDL-C, other blood lipids, body weight, or glucose metabolism, but SAD, plasma CRP, and TNF-R2 decreased more during PB compared with controls ($p < 0.05$). In the overall diet, PB increased dietary fiber and β-glucan compared with controls ($p < 0.05$).

*Conclusions:* Advising a prudent breakfast for 3 months did not influence blood lipids, body weight, or glucose metabolism but reduced markers of visceral fat and inflammation.

The trial was registered in the Current Controlled Trials database (http://www.controlled-trials.com); International Standard Randomized Controlled Trial Number (ISRCTN): 84550872



## 1. Introduction

Eating breakfast has been associated with a reduced risk of obesity and cardiometabolic disease, potentially through mechanisms involved in energy balance and metabolism [1]. The morning meal may influence hormones and metabolic factors involved appetite regulation, energy utilization and storage, and blood glucose control [2].

Eating breakfast generally appears to be associated with favorable effects on cardiometabolic risk factors [3–5]. Surprisingly little data, however, are available on the role of the dietary composition of the breakfast. To our knowledge, no controlled study has investigated whether a breakfast with a food composition that is in line with general dietary recommendations has beneficial effects on cardiometabolic risk factors compared with a control breakfast in healthy individuals.

The American Heart Association recommends eating three meals per day—breakfast, lunch, and dinner—to help control binge, emotional, and nighttime eating [6]. A morning meal, preferably with high-fiber, carbohydrate-rich foods that contribute 20–25 energy percent (E%) within 1–2 h after an overnight fast is advised by the 2004 Nordic Nutrition recommendations [7].

Distinguishing between promoting breakfast consumption and promoting a prudent breakfast is important. Eating breakfast on a regular basis has been related to increased dietary quality of the entire day's diet [8–10]. Eating a prudent breakfast (PB) can improve the quality of the entire day's nutrient intake [9,11].

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One study in patients with type 2 diabetes investigated long-term metabolic effects of breakfast quality [12], but no studies have investigated the quality of a whole breakfast and its influence on cardiometabolic risk profiles in healthy adults. Therefore, intervention studies are needed to determine whether the quality of breakfast can improve cardiometabolic risk profiles in subjects who already eat breakfast. A diet that is in accordance with Nordic nutrition recommendations for all meals during the day has been shown to markedly lower low-density lipoprotein cholesterol (LDL-C) and improve several cardiovascular risk factors in hyperlipidemic subjects in 6 weeks [13]. The aim of the present randomized trial was to investigate whether the intake of a PB alone can reduce LDL-C levels and other cardiometabolic risk markers and improve fasting or postprandial glucose metabolism in healthy hypercholesterolemic individuals.

## 2. Material and methods

### 2.1. Subjects

Subjects were recruited by advertisements in local newspapers in Uppsala, Sweden, and the study was conducted between august 2009 and January 2010. After screening 79 overweight and mildly hypercholesterolemic but otherwise healthy men and women were included in the study (Fig. 1). The inclusion criteria were eating breakfast on a regular basis, 25–67 years of age, plasma LDL-C $\geq$3.0 mmol/L, body mass index (BMI) $\geq$25 and $\leq$31 kg/m, and hemoglobin concentration $\geq$120 g/L for women and $\geq$130 g/L for men. The exclusion criteria were use of lipid-lowering drugs, high blood pressure (BP) (defined as BP $>$ 155/95 mmHg), regular use of dietary supplements fortified with plant sterols or polyunsaturated fatty acids (e.g., omega-3), slimming or medically prescribed diet/medication, special diet (e.g., vegan or gluten-free), and aversion to eating porridge or having herring or mackerel for breakfast for 12 weeks. Written informed consent was provided by all subjects, and the study was approved by the regional ethical committee in Uppsala.

### 2.2. Outcome measures

The primary outcome measure was plasma LDL-C concentrations. Secondary outcomes were body weight, plasma total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), LDL-C/HDL-C ratio, triglycerides (TGs), Apo lipoprotein A1 and B (ApoA1 and ApoB), ApoB/ApoA1 ratio, glucose tolerance, hemoglobin A1c (HbA1c), insulin sensitivity, sagittal abdominal diameter (SAD), tumor necrosis factor receptor-2 (TNF-R2), C-reactive protein (CRP), and blood pressure.

### 2.3. Study design

The study was a parallel, randomized, controlled, intervention study in free-living subjects (Fig. 1). Subjects were randomly assigned to one of two groups for 12 weeks: control breakfast or PB. The sole intervention of this study was the instruction to eat a breakfast composed of healthy Nordic foods, in accordance with Nordic dietary recommendations [13]. Participants in the PB were provided with all breakfast items. Beverages were, however, not provided to the PB. The intervention group was encouraged to otherwise maintain their usual lifestyle. The control group was encouraged to maintain their usual breakfast habits and maintain their usual dietary or lifestyle habits during the study. The subjects in the control group were offered the PB for 3 weeks after completing the study. This offer was made in an attempt to decrease the number of drop-outs in the control group.

Subjects that met the eligibility criteria and signed the informed consent were assigned a randomization number. Randomization was performed by personnel at Good Food Practice (GFP). A study nurse enrolled and assigned participants into the study in accordance with the randomization procedure. A randomization treatment code list was generated by an independent contract research organization (Good Food Practice), unavailable to all study investigators. The first eligible subject received the first number in the randomization number list, and the second subject received the second number, and so on. The investigational products were sent

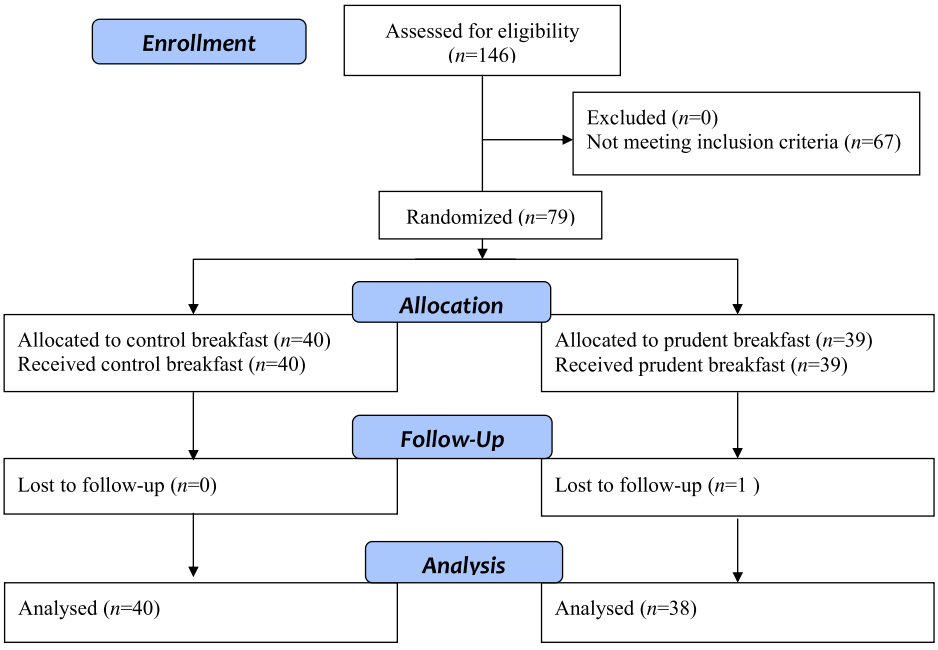


**Fig. 1.** Flow diagram of the phases of the randomized trial.

to GFP and were stored at GFP until distribution. The protocol for this trial and supporting CONSORT checklist are available as Supporting information.

## 3. Intervention

### 3.1. Prudent breakfast

As shown in Table 1, the PB included porridge (oat bran) with low-fat milk or yogurt, a choice of bilberry or lingonberry jam, raisin, fruit, whole-grain bread, low-fat spread that is high in polyunsaturated fatty acids, turkey meat, and pickled herring or mackerel in tomato for use on the whole-grain bread (Table 1).

## 4. Dietary assessment

Although the intervention concerned breakfast only we also collected dietary intake data during the whole day, thus we wanted to investigate if the breakfast intervention influenced total dietary intake in both groups. Participants in the control group and PB completed a 3-day food record at baseline and after 12 weeks to obtain data on the overall dietary intake during the study period [14]. The food record was a pre-coded menu book that was evaluated by the National Food Administration in Sweden and was supplemented with whole-grain and high-fiber products for the present study. To monitor dietary compliance in the PB group, the subjects received a study diary that included a list and amounts of foods to be included in the PB. The subjects were asked to fill in the date and mark the foods they consumed and any possible failure to consume the food items in the PB. Dietist XP version 3.0, a computer program based on the Swedish National Food Administration database (2005-02-01), was used to calculate the nutrient content of the PB and the 3-day food record. The Glycemic Index (GI) for the control breakfast from the 3-day food record at 12 weeks, and GI for the planned PB (Table 1), was calculated according to FAO/WHO [15]. Foods containing less than 15 g carbohydrates per 100 g was excluded.

**Table 1**
Quantity and frequency of food items included in the prudent breakfast.

| | Quantity | Frequency |
|---|---|---|
| **Porridge** | | |
| Oat bran. As an alternative to porridge, oat bran-enriched muesli could be eaten | 40 g per serving (corresponding to 3 g β-glucan per day) | Oat bran porridge: 5–7 days per week<br>Oat bran enriched muesli: Not more than 2 days per week |
| Low-fat milk or yogurt | Maximal amount, 4 dl | Each breakfast |
| Jam, raisins | 1–2 tbsp (17 g) of each | Each breakfast |
| Fresh or frozen fruit or berries | Corresponding to 1 fruit | Each breakfast |
| Psyllium | 1.5 tsp (7 g) | 7 days per week |
| Linseed | 1.5 tsp (7 g) | 7 days per week |
| Table salt | Do not exceed recipe on package | Use low-sodium table salt |
| **Sandwich** | | |
| Soft or hard whole-grain bread, 50% whole grain as dry matter | One soft slice (40 g) or two hard slices (24 g) | Each breakfast. Subjects had to eat bread until satiated. Subjects were allowed to have more or less bread to regulate satiety. |
| Low-fat spread (38% fat) | 5 g per slice of bread | |
| Turkey meat | One slice (20 g) | 4 days per week |
| Pickled herring or mackerel | Two to three pieces (10–15 g) of herring or 1 tbsp mackerel | 3 days per week |

## 5. Biochemical assessment

The analyses included in the lipid profile were fasting LDL-C, TC, HDL-C, and TG. An oral glucose tolerance test (OGTT) was performed, i.e. 75 g glucose dissolved in 350 ml water. Plasma glucose and serum insulin were measured at 0, 30, 60, 90, and 120 min.

## 6. Clinical assessment

The subjects visited the clinic in the morning after a 12-h fast. Body weight was measured (kg) on a digital scale with subjects wearing light clothing and no shoes. Height was measured to the nearest 0.5 cm. BMI was calculated as weight (kg) divided by height (m) squared.

SAD, a valid marker of visceral fat [18,19], was measured after a normal expiration to the nearest 0.1 cm in the supine position with bent legs on a firm examination table, without clothes in the measurement area [14]. At the level of the iliac crest, the SAD was measured using a ruler and water level. The SAD was the distance between the examination table and the horizontal level [16]. BP was measured oscillometrically (Omron M4-1, Omron Healthcare Europe B.V, Hofddorp, The Netherlands) in a sitting position on the right arm after a resting period of 3–5 min. BP was calculated as the average of three measurements.

## 7. Biochemical analysis

Blood samples were drawn from an antecubital vein using vacutainer tubes. The samples were handled according to sample treatment instructions provided by the Centre for Laboratory Medicine, Clinical Chemistry, Uppsala University Hospital, which performed the analyses according to their routine practice. Plasma LDL-C, TC, HDL-C, TG, and glucose were measured by enzymatic reactions, and plasma high sensitivity CRP, ApoA1 and ApoB were measured using immunoturbidometric assays and an Architect C 8000 instrument from Abbott (Abbott Park, IL, USA). Serum insulin was measured using a sandwich immunosorbent assay on a Cobas E601 immunology analyzer from Roche (Mannheim, Germany). Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) was calculated as plasma insulin × glucose/22.5 [17].

Soluble TNF-R2 (or Type A, type α, or 75 kDa) was measured in plasma by commercial sandwich ELISA (DY726, R&D Systems, Minneapolis, MN, USA). The concentrations in the samples were determined by comparing the optical density of the sample with the standard curve. The assay had a total coefficient of variation (CV) of approximately 7% and was calibrated against highly purified recombinant human peptides.

## 8. Statistical analyses

The data are expressed as mean ± standard deviation (SD) or standard error of mean (SEM), and median (interquartile range). For dietary intake data, the distribution was examined by the Shapiro–Wilks test. Non-normally distributed variables were logarithmically transformed; if they did not achieve normality, then nonparametric tests were used. Statistical analyses for dietary intake were based on intention-to-treat principles.

Differences between groups in dietary intake were analyzed using an unpaired two-tailed *t*-test for normally distributed data and an independent-sample Mann–Whitney *U*-test for non-normally distributed data. Linear mixed-effects models were used to assess effects of treatment on cardiometabolic risk factors during the intervention. Restricted maximum likelihood method was used to fit models and missing observations were ignored. The risk factor of interest was included in the model as dependent variable while

subject was a random effect. In the crude model, study group, time point (baseline or end of the intervention) and the study group * time point interaction was included as covariates. Analyses were also performed using extended models including age, sex, and body weight as additional covariates. The *p*-values presented represent those of the models' study group * time point interaction term and display the statistical significance of study group effects on risk factors during the intervention. Observations with CRP ≥10 mg/L were excluded before analyses of CRP and TNF-R2.

The AUCs for insulin and glucose concentrations during the OGTT were calculated according to the trapezoid rule. Correlations were tested using Pearson's correlation and linear regression analyses.

For nutrient data, paired *t*-tests were used to explore within-group changes between baseline and at 12 weeks. Nutrients, not normally distributed after logarithmically transformation data, are presented as median 25th and 75th percentiles (interquartile range).

We calculated statistical power based on dose-response studies using β-glucan as well as our previous trial where the present breakfast was included in a whole diet [13,18,19]. Based on our previous study using a comparable PB to the current one, it was estimated that detecting a difference between groups in LDL-C of 0.4 mmol/L, with an estimated SD of 0.60, $n = 36$ subjects were needed in each group with a power of 80% ($\alpha = 0.05$). A *p*-value <0.05 was considered statistically significant for the primary outcome measure. *P*-values for secondary endpoints are considered as supportive to the primary analysis. Statistical analyses were performed using IBM SPSS 19 software.

## 9. Results

Of the 79 subjects randomly assigned to the two groups (31 men and 48 women), one subject dropped out from the study (Fig. 1). With the exception of ApoA1 and serum insulin (AUC), no significant differences were found between the PB and control breakfast groups at baseline with regard to clinical characteristics (Table 2).

**Table 2**
Baseline characteristics after randomization.[a]

| Characteristics | Control breakfast ($n = 40$) | Prudent breakfast ($n = 38$) | *p* |
|---|---|---|---|
| Age (years) | 54.4 ± 9 | 54.9 ± 7.8 | |
| Sex, men/women, *n* (%) | 17/23 (42/58) | 14/25 (36/64) | |
| Body weight (kg) | 84.7 ± 13.1 | 82.5 ± 10.2 | 0.408 |
| Body mass index (kg/m$^2$) | 28.5 ± 2.4 | 28.2 ± 2.5 | 0.585 |
| Plasma LDL-C (mmol/L) | 4.1 ± 0.7 | 4.2 ± 0.8 | 0.778 |
| Plasma total cholesterol (mmol/L) | 6.3 ± 0.9 | 6.5 ± 1.1 | 0.330 |
| Plasma HDL-C (mmol/L) | 1.4 ± 0.3 | 1.5 ± 0.4 | 0.148 |
| LDL-C/HDL-C ratio | 3.2 ± 0.8 | 3.0 ± 0.8 | 0.284 |
| Plasma triglycerides (mmol/L) | 1.53 ± 1.04 | 1.6 ± 0.7 | 0.703 |
| Plasma ApoA1 (g/L) | 1.4 ± 0.2 | 1.5 ± 0.2 | 0.034 |
| Plasma ApoB (g/L) | 1.1 ± 0.2 | 1.2 ± 0.2 | 0.693 |
| ApoB/ApoA1 ratio | 0.83 ± 0.23 | 0.78 ± 0.21 | 0.277 |
| Plasma glucose (mmol/L) 0 min | 5.3 ± 0.6 | 5.4 ± 0.8 | 0.988 |
| Plasma glucose (AUC) | 915 ± 236 | 818 ± 133 | 0.09 |
| Serum insulin (mU/L) 0 min | 8.4 ± 4.4 | 8.8 ± 5.4 | 0.872 |
| Serum insulin (AUC) | 7497 ± 4769 | 4742 ± 2308 | 0.012 |
| HOMA-IR | 2.0 ± 1.2 | 2.2 ± 1.7 | 0.822 |
| Sagittal abdominal diameter (cm) | 22.3 ± 2.0 | 22.4 ± 2.1 | 0.922 |
| C-reactive protein (mg/L)[b] | 1.9 ± 1.4 | 2.2 ± 1.8 | 0.424 |
| Systolic blood pressure (mmHG) | 124 ± 13.1 | 125.8 ± 11.5 | 0.404 |
| Diastolic blood pressure (mmHG) | 76.8 ± 7.7 | 79.0 ± 7.7 | 0.208 |

[a] The data are expressed as the mean ± SD.
[b] Subjects with baseline CRP ≥10 mg/L were excluded.

No difference in HbA1c was found between groups ($p = 0.92$; data not shown). No adverse events were reported in either group.

### 9.1. Effects of the prudent breakfast on dietary intake

When comparing breakfast intake at 12 weeks (Table 3) with breakfast intake at baseline in PB, significant increases were observed in the intake of protein as a percentage of energy (E%), dietary fiber, β-glucan, and polyunsaturated fat ($p < 0.05$). Significant decreases were observed in total fat (E%), saturated fat, monounsaturated fat, dietary cholesterol, and sodium ($p < 0.05$). No differences in energy intake, carbohydrates (E%), and whole grain intake were observed (Table 3). Significant changes in whole-day nutrient intake were found with regard to alcohol (E%), carbohydrate (E%), dietary fiber, and β-glucan from baseline to 12 weeks in the PB group compared with the control group (Table 4). GI for the control breakfast from the 3-day food record at 12 weeks was 75 ± 0.23 and for the planned PB, GI was 56 (Table 3).

### 9.2. Effects on cardiometabolic risk factors

No significant group differences in effects on plasma LDL-C, TC, HDL-C, the HDL/LDL ratio, TG, or the ApoB/ApoA1 ratio were found (Table 5). No differences were observed between groups in body weight, plasma glucose, serum insulin, glucose and insulin AUC, HOMA-IR, or systolic and diastolic BP (all $p > 0.14$). HbA1c was not influenced by the diets (data not shown).

SAD (Table 5) and plasma levels of CRP and TNF-R2 (Fig. 2(a) and (b)) were significantly decreased by the PB compared with the control breakfast ($p < 0.05$). The absolute changes in CRP and TNF-R2 between baseline and 12 weeks were 0.66 ± 0.30 (+37%) for the control breakfast and −0.71 ± 0.27 (−30%) for the PB and 359 ± 118 (+9%) for the control breakfast and 66 ± 88 (+2%) for the PB, respectively. The change in CRP was weakly associated with the change in TNF-R2 ($r = 0.38$, $p < 0.05$, $n = 64$).

**Table 3**
Daily energy and nutrient intake of actually consumed prudent breakfast in the control breakfast group[a] and prudent breakfast group during 12 weeks.[b]

| | Control breakfast ($n = 40$) | Prudent breakfast ($n = 38$) |
|---|---|---|
| Energy (kcal) | 386 ± 142 | 356 ± 49 |
| Protein (E%) | 19 ± 6 | 23±1[c] |
| Carbohydrates (E%) | 50 ± 11 | 52 ± 2 |
| Dietary fiber (g) | 5 ± 2.6 | 12 ± 1.5[c] |
| β-glucan (g) | 0.2 ± 0.3 | 2.0 ± 0.3[c] |
| Whole grain (g) | 22 ± 15 | 14 ± 4 |
| Fat (E%) | 30 ± 9 | 25±1[d] |
| Saturated fat (E%) | 13 ± 5 | 6 ± 0[d] |
| Monounsaturated fat (E%) | 9 ± 4 | 6 ± 1[d] |
| Polyunsaturated fat (E%) | 4 ± 2 | 8 ± 1[c] |
| Dietary cholesterol (mg) | 82 ± 105 | 20 ± 13[d] |
| Sodium (mg) | 557 ± 366 | 317 ± 66[d] |
| Glycemic Index[e] | 75 ± 0.23 | 56 |

[a] The data are expressed as mean ± SD, and is based on a 3-day food record. Paired *t*-test was used to assess changes within groups between baseline and at 12 weeks.
[b] The data are expressed as mean ± SD, and is based on the study diary. Paired *t*-test was used to assess changes within groups between baseline and at 12 weeks.
[c] Significant increases were observed in the intake of protein as a percentage of energy (E%), dietary fiber, β-glucan, and polyunsaturated fat ($p < 0.05$) when comparing breakfast intake at 12 weeks with breakfast intake at baseline within PB.
[d] Significant decreases were observed in total fat (E%), saturated fat, monounsaturated fat, dietary cholesterol, and sodium ($p < 0.05$). No differences in energy intake, carbohydrates (E%), and whole grain intake were observed.
[e] GI for the control breakfast was calculated as a mean of 12 weeks and GI for the PB, was for the planned PB.

**Table 4**
Nutrient intake at baseline and 12 weeks in the control group and prudent breakfast group.[a,b]

| Nutrients | Control breakfast | | | Prudent breakfast | | | |
|---|---|---|---|---|---|---|---|
| | Baseline $n = 40$ | 12 weeks $n = 40$ | $p^c$ | Baseline $n = 38$ | 12 weeks $n = 38$ | $p^c$ | $p^d$ |
| Energy (kcal/day) | 1819 ± 517 | 1917 ± 498 | 0.18 | 1886 ± 488 | 1921 ± 366 | 0.724 | 0.581 |
| Protein (E%) | 17 ± 3 | 17 ± 2 | 0.320 | 16 ± 2 | 18 ± 2 | 0.012 | 0.378 |
| Alcohol[e] (E%) | 0.00(0.00–0.04) | 0.04(0.00–0.08) | <0.05 | 0.03(0.00–0.07) | 0.02(0.00–0.04) | 0.21 | <0.05 |
| Carbohydrates (E%) | 45 ± 6 | 42 ± 6 | <0.05 | 43 ± 6 | 44 ± 5 | 0.401 | <0.05 |
| Dietary fiber (g/day) | 20 ± 6 | 21 ± 7 | 0.093 | 20 ± 5 | 26 ± 7 | 0.000 | <0.05 |
| β-glucan[e] (g/day) | 0.00(0.00–0.40) | 0.40(0.00–1.80) | <0.05 | 0.00(0.00–0.40) | 1.80(0.30–2.60) | 0.000 | <0.05 |
| Whole grain (g/day) | 37 ± 22 | 35 ± 24 | 0.527 | 35 ± 24 | 40 ± 18 | 0.335 | 0.250 |
| Fat (E%) | 36 ± 6 | 35 ± 6 | 0.682 | 35 ± 5 | 34 ± 5 | 0.647 | 0.980 |
| Saturated fat[e] (E%) | 13(11–15) | 13(12–15) | 0.789 | 13(12–15) | 13(10–15) | 0.053 | 0.093 |
| Monounsaturated fat (E%) | 14 ± 4 | 12 ± 2 | 0.29 | 12 ± 2 | 12 ± 2 | 0.989 | 0.387 |
| Polyunsaturated fat (E%) | 6 ± 2 | 6 ± 2 | 0.325 | 5.6 ± 2 | 5.9 ± 2 | 0.196 | 0.764 |
| Dietary cholesterol[e] (mg/day) | 264(193–350) | 270(232–358) | 0.388 | 309(241–386) | 284(230–319) | 0.096 | 0.080 |
| Sodium (mg/day) | 2854 ± 1107 | 2839 ± 939 | 0.576 | 2863 ± 755 | 2939 ± 728 | 0.510 | 0.936 |

[a] The data are expressed as mean ± SD for normally distributed variables and median (interquartile range) for non-normally distributed variables after logarithmic transformation.
[b] Data is based on 3-day food records.
[c] Differences within group were analyzed using paired samples *t*-test.
[d] Differences in change between groups were analyzed using an unpaired two-tailed *t*-test for normally distributed data and an independent-sample Mann–Whitney *U*-test for non-normally distributed data.
[e] Variables that were not normally distributed after logarithmic transformation.

## 10. Discussion

The present randomized controlled trial investigated whether a PB alone improves cardiometabolic risk factors compared with a control group that consumed their usual breakfast. In contrast to our hypothesis, however, a PB in line with a healthy Nordic diet rich in dietary fiber and unsaturated fats and low in total fat had no effect on blood lipids, glucose metabolism, or body weight. However, significant reductions of SAD, a marker of visceral fat, and circulating plasma inflammation markers were found in the PB group compared with controls. CRP concentrations were reduced by 23% after PB despite groups were weight stable.

Previous studies of the effects of eating breakfast on health mainly explored the effect of eating breakfast *per se* compared with skipping breakfast, suggesting that omitting breakfast both in the short-term [3] and long-term [5] increases LDL-C and fasting insulin concentrations. However, in a six month parallel designed randomized study, investigating the effects of high- versus low GI cereal breakfast, or a MUFA rich breakfast in subjects with type 2 diabetes, no significant differences between groups in fasting LDL-cholesterol, triglycerides, glycaemia or body weight were observed [12]. Thus, those findings in patients with diabetes accord well with the current study in healthy subjects. The ratio of total to HDL-cholesterol was however higher in patients who consumed the high-GI cereal than in the MUFA group at 3 months but not at 6 months in that study [12]. In the present study, all of the subjects were regular breakfast eaters because our aim was to investigate the role of breakfast nutrient quality. Breakfast is recommended to contribute to 20–25% of energy intake [7], and breakfast is only one part of the entire day's diet. Comparisons of the nutrient composition of the PB between baseline and at 12 weeks indicated significant changes in several nutrients, including protein, dietary

**Table 5**
Changes in cardiometabolic risk factors from baseline to 12 weeks during control breakfast and prudent breakfast.

| Characteristics | Control breakfast ($n = 40$) | Prudent breakfast ($n = 38$) | $p^a$ | $p^b$ |
|---|---|---|---|---|
| Body weight (kg) | 0.62 ± 0.29 | 0.28 ± 0.23 | 0.316 | n/a |
| Plasma LDL-C (mmol/L) | −0.005 ± 0.06 | −0.07 ± 0.09 | 0.528 | 0.494 |
| Plasma total cholesterol (mmol/L) | −0.002 ± 0.07 | −0.11 ± 0.10 | 0.369 | 0.436 |
| Plasma HDL-C (mmol/L) | 0.05 ± 0.02 | 0.003 ± 0.02 | 0.078 | 0.099 |
| LDL-C/HDL-C ratio | −0.09 ± 0.06 | −0.07 ± 0.08 | 0.725 | 0.798 |
| Plasma triglycerides (mmol/L) | 0.04 ± 0.05 | 0.06 ± 0.10 | 0.641 | 0.588 |
| Plasma ApoA1 (g/L) | 0.04 ± 0.02 | 0.04 ± 0.02 | 0.663 | 0.964 |
| Plasma ApoB (g/L) | 0.004 ± 0.01 | −0.023 ± 0.02 | 0.363 | 0.392 |
| ApoB/ApoA1 ratio | −0.02 ± 0.01 | −0.034 ± 0.02 | 0.661 | 0.775 |
| Plasma glucose (mmol/L) 0 min | 0.00(−0.18 to 0.30) | 0.10(−0.10 to 0.20) | 0.808 | 0.795 |
| Plasma glucose (AUC)[c] | −27.8(−117.8 to 62.6) | −12.0(−130.5 to 30.0) | 0.511 | 0.502 |
| Serum insulin (mU/L) 0 min | 0.40(−0.40 to 1.80) | −0.20(−2.10 to 1.60) | 0.123 | 0.135 |
| Serum insulin (AUC)[d] | −285(−1484 to 1646) | −374(−1755 to 519) | 0.579 | 0.432 |
| HOMA-IR | 0.27 ± 0.20 | −0.12 ± 0.13 | 0.128 | 0.141 |
| Sagittal abdominal diameter (cm) | 0.24 ± 0.19 | −0.38 ± 0.18 | 0.038 | 0.034 |
| Systolic blood pressure (mmHG) | 2.6 ± 1.18 | 1.9 ± 1.20 | 0.535 | 0.576 |
| Diastolic blood pressure (mmHG) | 2.2 ± 0.80 | 0.62 ± 0.85 | 0.386 | 0.396 |

The data are mean ± SEM, and median (interquartile range). Differences between groups are assessed by Linear mixed effects models.
[a] Crude model without adjusmtents.
[b] Crude model adjusted for age, sex and body weight.
[c] Plasma glucose AUC: control breakfast, $n = 34$; prudent breakfast, $n = 35$.
[d] Serum insulin AUC: control breakfast, $n = 30$; prudent breakfast, $n = 34$.

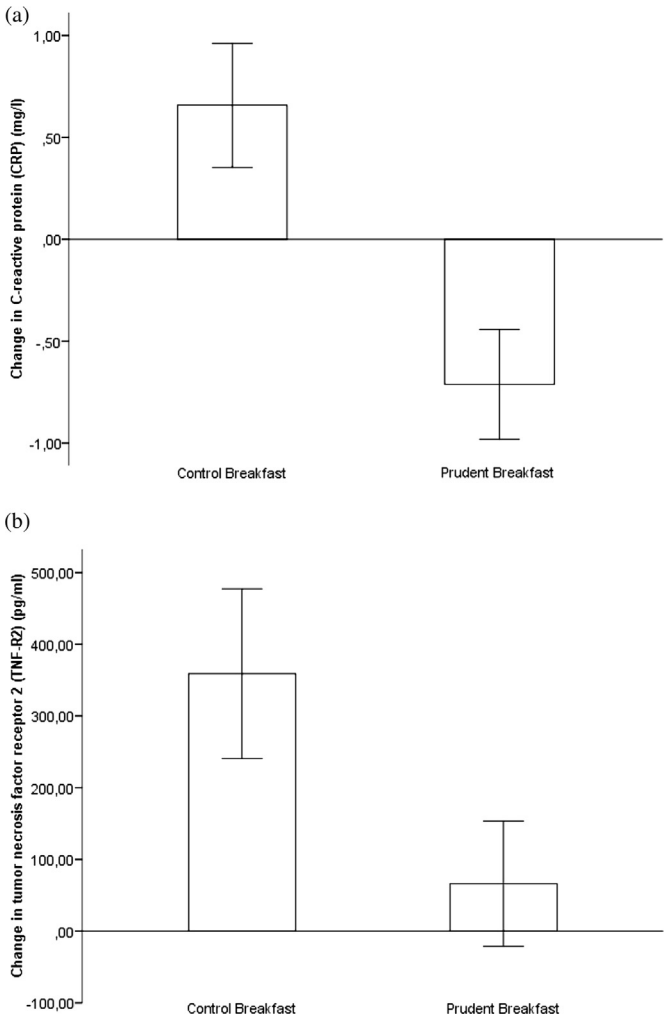


**Fig. 2.** (a) Change in C-reactive protein (CRP) during the intervention in participants in the control breakfast and prudent breakfast groups, mean ± SEM. CRP was significantly decreased by the PB compared with the control breakfast ($p < 0.05$). (b) Change in tumor necrosis factor receptor 2 (TNF-R2; pg/ml) during the intervention in participants in the control breakfast and prudent breakfast groups, mean ± SEM. TNF-R2 was significantly decreased by the PB compared with the control breakfast ($p < 0.05$).

fiber, β-glucan, total fat, saturated fat, monounsaturated fat, polyunsaturated fat, dietary cholesterol, and sodium. The PB group also exhibited significant changes in the entire day's nutrient intake of alcohol (E%) carbohydrates (E%), dietary fiber, and β-glucan from baseline to 12 weeks compared with the control group. Despite the significant change from baseline in β-glucan intake in the entire day's nutrient intake during PB, β-glucan intake (1.8 g) did not reach the planned intake of 3 g per day in the PB. Because of the dose-dependent effect of β-glucan on LDL-C and TC, we expected that the intake of 2 g β-glucan in the PB intervention would alone decrease LDL-C and TC by −0.11 and −0.09 mmol/L, respectively [19]. Furthermore, the low content of saturated fat and high content of unsaturated fats and fiber in the PB was expected to lower LDL-C in addition to β-glucan. Negliable changes were however observed in the present study, −0.07 mmol/L for LDL-C and −0.11 mmol/L for TC.

Thus, despite changes in the breakfast and some significant changes in overall dietary intake, a lack of effect was found on LDL-C, the primary outcome of the study. These dietary changes of the breakfast may have been too small to influence LDL-C. We previously showed that a similar dietary intervention that included all meals of the day had profound effects on body weight, blood lipids, and several other cardiometabolic risk factors [13].

Food intake in the morning may be particularly satiating and can reduce the total amount of energy ingested during the day, thereby preventing obesity [8]. In the present study, no significant changes in entire-day energy intake, body weight, BMI, or waist measurement were observed. However, a significant reduction of the SAD was found, possibly indicating reduced visceral fat content that is not captured by changes in waist girth [20,21]. The latter is subjected to higher measurement error than the SAD and thus less sensitive to small changes in abdominal fat content [22]. Nevertheless, this finding should be interpreted with caution because no trend toward a lower waist girth was found in the PB group. The reduced levels of CRP and TNF-R2, despite lack of weight change, are an interesting finding that may accord with the reduced SAD. A close link has been reported between visceral fat and low-grade systemic inflammation [23]. The dietary components responsible for this effect are unclear, but may involve improved fat quality of the diet. E.g. polyunsaturated fatty acids (both n-3 and n-6) in place of saturated fats can reduce the visceral fat-to-subcutaneous fat ratio and reduce inflammation markers, such as TNF-R2, as shown in a recent dietary fat modification study [24]. Dietary fiber, another key component of the PB, may also influence inflammation markers as shown in recent controlled interventions in which reduced CRP concentrations were observed after high-fiber diets [25,26]. The mechanisms for such associations are unclear but may involve fiber-induced increase of short-chain fatty acids (e.g.butyrate) in colon, which may counteract inflammatory processes, whereas a high-fat diet might instead reduce the production of butyrate [27]. The main source of dietary fiber in PB was oats and as the source of dietary fiber may be of importance in reduction of inflammatory markers the breakfast composition might have contributed to the change in inflammatory markers in PB [26]. The significantly lower level of two independent inflammation markers in the current study suggests that this finding was unlikely caused by chance. Indeed, a direct association was found between CRP and TNF-R2. One could speculate that apart from a role of dietary fiber as indicated above, a reduction in saturated fat and increase in polyunsaturated fat might lower certain systemic inflammation markers [24], possibly by influencing inflammatory gene expression An increased intake of fish might also inhibit inflammatory process, although the evidence is inconsistent [28].

No effects on fasting insulin sensitivity, glucose tolerance, or insulin response in the OGTT were found. Improving glucose metabolism in non-diabetic subjects by altering breakfast habits alone is likely difficult to achieve without caloric restriction and weight loss. The present study has some limitations. As our study was powered to detect a difference between groups of 0.4 mmol/l in LDL-C, the present sample size may not be sufficient to detect smaller differences. However, if that would have been the case, such small effect on LDL-C would most likely be of little clinical importance. We did not monitor physical activity in the groups. However, both groups were encouraged to maintain their usual lifestyle, including their level of physical activity, during the study. We did not perform an intermediary dietary evaluation during the study (besides at baseline and 12-weeks) which may be a possible limitation since subjects could have changed their intake in that intermediate period during the three months of the study.

The strengths of the study include the randomized controlled design, exceptionally low drop-out rate, and inclusion of both men and women. Also, the study provided all food to the PB subjects. The latter allowed us to monitor compliance with study breakfast more accurately by using a study diary that recorded any deviations from the planned breakfast.

In conclusion, advising a PB based on Nordic foods rich in dietary fiber and low in fat had no favorable effects on blood lipids, glucose metabolism, or body weight but reduced markers of visceral fat and inflammation.

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## Statement of authorship

VA, UR, and GFP designed the study. GFP and VA conducted the research. VA UR and MM performed the statistical analysis, and AL performed biochemical analyses. VA and UR wrote the paper, and VA, UR, AL, AR and MM reviewed the draft and gave valuable input to the draft and interpreted data. VA, UR had primary responsibility for the final content. All authors read and approved the final manuscript.

## Conflict of interest

VA is a PhD student at Uppsala University, Sweden. VA and AR were employed by Lantmännen R&D at the time of the study. Lantmännen group is owned by Swedish farmers and operates within the food, energy and agricultural industries. UR was funded by the Swedish Research Council and Zetterling Foundation. UR and AL have no conflict of interest. The sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript.

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## Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.clnu.2014.04.009.

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