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# High intake of regular-fat cheese compared with reduced-fat cheese does not affect LDL cholesterol or risk markers of the metabolic syndrome: a randomized controlled trial<sup>1,2</sup>

Farinaz Raziani,\* Tine Tholstrup, Marlene D Kristensen,<sup>3</sup> Matilde L Svanegaard, Christian Ritz, Arne Astrup, and Anne Raben

Department of Nutrition, Exercise, and Sports, University of Copenhagen, Copenhagen, Denmark

## ABSTRACT

**Background:** Regular-fat cheese contains a high amount of saturated fat. Therefore, dietary guidelines in many countries recommend the consumption of reduced-fat cheese as opposed to regular-fat cheese. However, the negative effect of regular-fat cheese is still under debate. **Objectives:** The aim was to compare the effects of regular-fat cheese with an equal amount of reduced-fat cheese and an isocaloric amount of carbohydrate-rich foods on LDL cholesterol and risk factors for the metabolic syndrome (MetS).

**Design:** The study was a 12-wk randomized parallel intervention preceded by a 2-wk run-in period. A total of 164 subjects with  $\geq 2$  MetS risk factors were randomly allocated to 1 of 3 intervention groups: regular-fat cheese (REG), reduced-fat cheese (RED), or a no-cheese, carbohydrate control (CHO) group. Subjects in the REG and RED groups replaced part of their daily habitual diet with 80 g cheese/10 MJ, whereas subjects in the CHO group did the same with bread and jam corresponding to 90 g and 25 g/10 MJ, respectively.

**Results:** A total of 139 subjects completed the intervention. The primary outcome, LDL cholesterol, was not significantly different between the REG and RED diets or between the REG and CHO diets. There was no significant difference in HDL cholesterol between the REG and RED diets, but HDL cholesterol tended to be higher with the REG diet than with the CHO diet ( $0.06 \pm 0.03$  mmol/L; *P* = 0.07). Insulin, glucose, and triacylglycerol concentrations as well as blood pressure and waist circumference did not differ significantly between the 3 diets.

**Conclusion:** A high daily intake of regular-fat cheese for 12 wk did not alter LDL cholesterol or MetS risk factors differently than an equal intake of reduced-fat cheese or an isocaloric amount of carbohydrate-rich foods. This trial was registered at www.clinicaltrials.gov as NCT02616471. *Am J Clin Nutr* 2016;104:973–81.

**Keywords:** saturated fat, dairy, triglycerides, insulin, glucose, blood lipids

## INTRODUCTION

Current dietary guidelines, including the Nordic Nutrition Recommendations 2012 and the US Dietary Guidelines for Americans 2015, recommend limiting the intake of foods high in saturated fat to reduce the risk of cardiovascular disease (CVD).<sup>4</sup> Regular-fat cheese (classified as a full-fat dairy product) would be expected to increase total cholesterol and LDL cholesterol. Accordingly, the guidelines recommend the replacement of full-fat cheese with reduced-fat alternatives. Although it is well established that the consumption of dairy fat from butter and cream causes an increase in LDL cholesterol (1–3), less is known about dairy fat from other foods. Observational studies on specific dairy products indicate that cheese consumption does not have any adverse effect on heart health and may, in fact, reduce the risk of coronary artery disease and/or stroke (4–9). Several randomized controlled trials (RCTs) have also shown that cheese, despite its high content of saturated fat, has a neutral or even beneficial effect on total cholesterol and/or LDL cholesterol compared with dairy products such as butter (10–12).

Insulin resistance has, in combination with abdominal obesity, been suggested to be one of most important risk factors for metabolic syndrome (MetS). Current evidence suggests that cheese consumption may improve impaired glucose tolerance (13) and decrease the risk of type 2 diabetes (T2D) (14). In addition, cheese consumption has been found to be inversely associated with the incidence of MetS (15, 16), although not consistently (17). These findings indicate that not all dairy products can be considered equal with regard to CVD and T2D risk. Furthermore, they emphasize the importance of considering whole foods and not

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<sup>&</sup>lt;sup>2</sup> Supplemental Tables 1 and 2 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

<sup>&</sup>lt;sup>3</sup> Present address: Novo Nordisk, Hillerød, Denmark.

<sup>\*</sup>To whom correspondence should be addressed. E-mail: fara@nexs.ku.dk.

<sup>&</sup>lt;sup>4</sup> Abbreviations used: CHO, carbohydrate control; CRP, C-reactive protein; CVD, cardiovascular disease; FFA, free fatty acid; GI, glycemic index; ITT, intention-to-treat; MetS, metabolic syndrome; RCT, randomized controlled trial; RED, reduced-fat cheese; REG, regular-fat cheese; T2D, type 2 diabetes.

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macronutrient composition alone when evaluating CVD risk markers, because these might be modified by the food matrix. A recent meta-analysis of RCTs found no association between fullfat and low-fat dairy intakes and cardiometabolic risk factors (18). To our knowledge, it has not yet been investigated how regular-fat cheese consumption affects blood lipids and other risk factors compared with reduced-fat cheese. Nonetheless, under free-living conditions, when a person reduces the intake of regular-fat cheese in an attempt to improve her or his health, it is likely that the person would compensate by either choosing reduced-fat cheese or by limiting the amount of cheese and eating something else instead, such as bread and a spread. The primary objective of the current study was to compare the effects of a high daily intake of regularfat cheese with an equal intake of reduced-fat cheese or an isocaloric amount of carbohydrate-rich foods on LDL cholesterol and MetS risk factors in a study population of men and women with  $\geq 2$ MetS risk factors. As a secondary objective, it was assessed whether cheese consumption affected women and men differently, as suggested by observational data (8). We hypothesized that the intake of regular-fat cheese would not be associated with increased LDL cholesterol or MetS risk factors compared with the intake of reduced-fat cheese.

## METHODS

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## Study design

This study was a 12-wk randomized parallel-intervention study preceded by a 2-wk run-in period. During the 2-wk run-in period, subjects received 250 mL skimmed milk/d (0.1%; Arla) and were asked to refrain from consuming other dairy products. Subjects were then randomly allocated to 3 intervention groups: regular-fat cheese (REG), reduced-fat cheese (RED), or a noncheese, carbohydrate control (CHO) by means of randomization sequences stratified by sex and smoking status and generated by using R (19). Conditions before and on sampling days were standardized. Thus, subjects were requested to be fasting for 12 h (maximum of 0.5 L water allowed), not to perform extreme physical activity for 24 h, and not drink alcohol for 24 h before the blood sampling. Fasting blood samples were drawn after the 2-wk run-in period at baseline (week 0) and after the 12-wk intervention period. In addition to blood samples, anthropometric variables (weight, height, and waist circumference), blood pressure, and body composition were measured. The study was carried out at the Department of Nutrition, Exercise, and Sports, Faculty of Sciences, University of Copenhagen, Frederiksberg, Denmark, from February 2014 to May 2015 and was approved by the Municipal Ethical Committee of Copenhagen (H-4-2013-099). Due to logistical issues, the study had 4 study periods. The first period was from February to July 2014, the second period was from September to December 2015, the third period was from November 2014 to January 2015, and the fourth period was from January to May 2015.

## Subjects

Subjects were recruited for the study through advertisements in local newspapers. A total of 193 subjects were selected for screening, and 164 were randomly assigned as study participants (see **Figure 1** for participant flowchart). Inclusion criteria were 18–70 y of age, BMI (in kg/m<sup>2</sup>) of 18.5–37.5, waist circum-

ference >80 cm for women and >94 cm for men, and  $\geq 1$  additional established risk factor for the MetS by using the following criteria: systolic blood pressure >130 mm Hg and/or diastolic blood pressure >85 mm Hg, triacylglycerols >1.7 mmol/L, HDL cholesterol <1.00 mmol/L for men and <1.3 mmol/L for women, and/or glucose >5.6 mmol/L. Exclusion criteria were chronic diseases (known T2D, CVD, or other chronic diseases that could affect the study outcome), milk allergy, the use of prescription medicine that could affect the results of the study (e.g., lipid-lowering agents), >10 h of strenuous physical activity/wk, drug and alcohol abuse, blood donation <1 mo before study commencement or during the study period, simultaneous participation in other clinical studies, pregnant or lactating woman or women who were planning to become pregnant during the intervention, or inability to comply with the procedures required by the protocol. A total of 6 subjects were smokers, and they did not change smoking habits during the intervention. Subjects were asked to refrain from dietary supplements and blood donation during the entire intervention. In addition, they were asked to maintain their usual physical activity levels and alcohol habits throughout the intervention. All of the subjects gave their informed consent in writing after receiving written and oral information about the study. Habitual physical activity level was assessed by using a validated physical activity questionnaire. Physical activity as well as basal metabolic rate, on the basis of age, sex, and weight, were used to calculate the subject's energy requirement and thereby the amount of test food to consume (20).

## **Experimental diets**

Subjects in the REG and RED groups were provided with equal amounts of regular-fat Danbo (25% fat; Riberhus; Arla) and cheddar (32% fat; Sharp Cheddar; Lactalis) cheeses and reduced-fat Danbo (13% fat; Riberhus) and cheddar (16% fat; Sharp Cheddar) cheeses, respectively. In the CHO group, cheese was replaced with white-wheat bread (Kohberg) and sugarsweetened jam (Fynbo). The subjects could choose between 5 different flavors of jam, including strawberry, raspberry, blueberry, blackcurrant, and orange, all containing 50 g fruit/100 g and 45 g added sugar/100 g. The cheese supplied in the REG group contained an amount of energy similar to the bread and jam supplied to the CHO group. The cheese supplied in the RED group contained  $\sim 17\%$  less energy than the cheese in the REG group. Subjects in all 3 groups were also provided with 250 mL skimmed milk/d (0.1% fat; Arla) throughout the intervention and were asked not to consume any other dairy products in this period. The subjects were guided in how to substitute the cheese or bread for food items from their habitual diets. Subjects were given a list of food items equaling the energy content of the test foods, and it was then up to the individual subject to decide which food items to replace. The remaining part of the subjects' habitual diet was not controlled, and they were asked to maintain their usual diets. Subjects were allocated to an energy level of 8, 10, 12, or 14 MJ depending on their estimated energy requirement. The daily amounts of cheese provided corresponded to 80 g  $\cdot$  d<sup>-1</sup>  $\cdot$  10 MJ<sup>-1</sup>, whereas the daily amounts of bread and jam corresponded to 90 and 25 g  $\cdot$  d<sup>-1</sup>  $\cdot$  10 MJ<sup>-1</sup>, respectively. The composition of the 3 intervention diets is shown in Table 1.



FIGURE 1 Participant flowchart. CHO, carbohydrate control; RED, reduced-fat cheese; REG, regular-fat cheese.

During the run-in period before baseline measurements and in week 12 of the intervention, subjects completed a 3-d dietary food record to provide information about their dietary intake during the intervention. Two weekdays and 1 weekend day were included in the dietary record to take into account any differences in nutrient intake during weekdays and weekend days. Subjects were instructed not to let the recording influence their food consumption. At the beginning of the intervention, subjects received a scale and a study food diary in which they were asked to note the weight of all of the intervention food not consumed, together with an explanation of why consumption had been avoided. Subjects attended the department each week to collect the intervention food and were asked to bring their food diaries for compliance control. Compliance was measured as a percentage of test food consumed compared with test food handed out to the subjects.

## Analytic procedures

#### Blood samples

Blood samples were drawn for the measurement of serum blood lipids (total, LDL, and HDL cholesterol and triacylglycerols), serum C-reactive protein (CRP), free fatty acids (FFAs), plasma glucose, and serum insulin. LDL and HDL cholesterol were assessed by using an enzymatic colorimetric procedure (ABX Pentra LDL Direct CP and ABX Pentra HDL Direct CP, respectively; Horiba ABX). Total cholesterol and triacylglycerol concentrations were assessed in serum by enzymatic procedures (cholesterol oxidase-phenol 1 aminophenazone and glycerol-3phosphate oxidase-phenol 1 aminophenazone, respectively). The analysis was carried out with an ABX Pentra 400 Chemistry Analyzer. Interassay CVs for total cholesterol, LDL cholesterol, HDL cholesterol, and triacylglycerols were 2.4%, 2.7%, 2.0%, and 3.5%, respectively. Intra-assay CVs for total cholesterol, LDL cholesterol, HDL cholesterol, and triacylglycerols were 0.9%, 0.7%, 1.2%, and 3.8%, respectively. CRP concentrations were

measured by using a high-sensitivity immunometric assay (ABX Pentra CRP CP). Inter- and intra-assay CVs for CRP were 3.4% and 2.3%, respectively. FFAs were assessed by using an enzymatic colorimetric procedure (ABX Pentra FFA CP). Inter- and intraassay CVs for FFAs were 2.0% and 1.7%, respectively. Glucose concentrations were measured with an enzymatic procedure (ABX Pentra Glucose HK CP) and were analyzed with an ABX Pentra 400 Chemistry Analyzer. Inter- and intra-assay CVs for plasma glucose were 2.5% and 0.8%, respectively. Insulin was measured by chemiluminescent immunoassay with an Immulite 1000 (Siemens Medical Solution Diagnostics). Inter- and intra-assay

#### TABLE 1

Nutrient composition of the test foods<sup>1</sup>

	Group					
	RE	EG	R	ED	СН	0
	Riberhus	Cheddar	Cheasy	Cheddar	Bread	Jam
Daily amount, g	40	40	40	40	90	25
Energy, kJ/d	528	666	378	614	954	219
Energy density, kJ/100 g	3.2	3.9	2.3	3.7	2.5	2.1
Fat, g/d	10.2	13.2	5.4	9.6	1.8	0.1
Saturated fat, g/d	6.3	8.1	3.3	5.6	0.2	_
Monounsaturated fat, g/d	2.8	4.6	1.3	3.3	_	_
Polyunsaturated fat, g/d	0.3	0.7	0.1	0.3		_
Protein, g/d	8.8	10	10.4	15.2	6.3	0.1
Carbohydrates, g/d	0.2	_	0.2	_	45	12.5
Total sugar, g/d		_		_	0.9	11.3
$\mathrm{GI}^2$		_	_	_	71	51
GL		_		_	35.5	25.5
Calcium, mg/d	267	285	309	285	33	25
Sodium, g/d	0.6	0.7	0.6	0.7	0.9	_

<sup>1</sup>Values are per a 10-MJ diet. Nutrition information was provided by the manufacturer (Arla, Lactalis, and Kohberg). CHO, carbohydrate control; GI, glycemic index; GL, glycemic load; RED, reduced-fat cheese; REG, regular-fat cheese. <sup>2</sup>Data are from reference 21.

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CVs for insulin were 3.5% and 4.2%, respectively. Insulin resistance was calculated by using HOMA-IR with the following formula:

HOMA-IR = [fasting serum insulin (
$$\mu$$
IU/mL)  
× [fasting plasma glucose (mmol/L)] ÷ 22.5 (1)

## Anthropometric measures

Fasting body weight was measured after the run-in period (week 0), halfway through the intervention (week 6), and postintervention (week 12) to the nearest 0.1 kg with subjects wearing light clothing and having emptied their bladder in advance (Lindeltronic 8000 scale; Lindells). Height was measured after the run-in (week 0) without shoes to the nearest 0.5 cm with a wall-mounted stadiometer (Seca). Waist and hip circumferences were measured after the run-in period (week 0), halfway through the intervention (week 6), and postintervention (week 12) with a flexible nonelastic tape around subjects while dressed in underwear and standing in an upright position with 25-30 cm distance between their feet. Waist circumference was measured horizontally at the midpoint between the lower rim of the ribs and the top of the iliac crest. Hip circumference was measured at the level of trochanter major and pubic symphysis. The average of 2 consecutive measurements rounded to the nearest 0.5 cm was used.

A dual-energy X-ray absorptiometry scanner (GE Prodigy) was used for the determination of body composition (fat mass and lean body mass) after the run-in period (week 0) and postintervention (week 12). Subjects were scanned in a fasting condition while wearing light clothing. Their feet were wrapped in fabric enclosed by Velcro straps to maintain the same position during the duration of the scan. All scans were performed at an appropriate scanning speed according to the subject's body weight and sagittal diameter. Quality control and calibration were performed before each scan by using a Lunar Aluminum Spine Phantom (GE Prodigy).

## Blood pressure

Fasting blood pressure was measured after the run-in period (week 0), halfway through the intervention (week 6), and postintervention (week 12). After 5 min of rest in a reclined position with an empty bladder, 3 consecutive measurements were performed by using an automatic sphygmomanometer (UA-787; A&D Co. Ltd.). A cuff of the appropriate size was placed directly on the skin 2 cm from the elbow. Conversation during measurement was not allowed. All of the measurements were recorded and the mean of the last 2 measurements was used.

## Sample size calculation

The power calculation was based on a previous study in which a difference of  $0.25 \pm 0.46$  mmol/L in LDL cholesterol was observed between a regular-cheese diet and a cheese diet with conjugated linoleic acid (22). To detect a similar difference in our study, 57 subjects had to be included in each intervention group (assuming a significance level of 5% and 80% power). In addition, sample size was recalculated after the first period. The

updated sample size calculation was based on estimated means and residual SEs, which were obtained from an interim analysis by using an ANCOVA model fitted to LDL-cholesterol measurements from the 38 subjects in period 1. The model included adjustments for baseline LDL cholesterol, age, sex, and change in body fat. To detect significant differences in LDL cholesterol between the intervention groups (significance level of 5% and 80% power), a total of 48 subjects were needed in each group. Thus, 144 subjects were needed to complete the study. A total of 168 subjects were enrolled in the study to allow for a 15% drop-out rate.

#### Statistical analysis

All of the statistical analyses were performed by using R (R Core Team, 2015) (19). For all outcomes except for dietary records, the effect of the intervention was evaluated by means of an intention-totreat (ITT) analysis with the use of linear mixed models based on all subjects completing the run-in period. Missing values and outliers were imputed by means of baseline observation carried forward, and if needed, simple mean imputation was used for missing baseline outcome values. In addition, complete-case analyses were carried out to gauge the efficacy of the intervention (only complete-case analyses were carried out for dietary records). All of the models included adjustments for baseline outcome, age, sex, BMI, and change in body fat as fixed effects, whereas differences between periods were modeled by means of random effects. For each outcome, 2 pairwise comparisons were evaluated-the REG compared with the RED diet and the REG compared with the CHO diet-by using post hoc t tests based on the linear mixed models. The resulting 2 P values were adjusted for multiplicity (23). For the primary outcome, P values were adjusted for the interim analysis used for recalculation of the sample size (24). Model checking of assumptions of variance homogeneity and normality was carried out by means of residual and normal probability plots. Results are presented as means  $\pm$  SEMs. A significance level of 0.05 was used.

## RESULTS

## Subjects

Of the 164 subjects randomly assigned to the study, 150 subjects (100 women and 50 men) entered the 12-wk intervention period and 139 subjects (92 women and 47 men) completed the 12-wk intervention. Five subjects (4 women and 1 man) in the REG group, 3 subjects (1 woman and 2 men) in the RED group, and 3 subjects (3 women) in the CHO group dropped out during the intervention. The main reasons for discontinued intervention were personal practical problems, illness unrelated to the study, and inability to follow study protocol. The baseline characteristics of subjects who completed the study are listed in **Table 2**. Baseline characteristics of dropouts did not differ from those of study completers (data not shown).

#### Lipids and cholesterol homeostasis

Changes from baseline as well as differences between groups for total, LDL, and HDL cholesterol; ratios of total cholesterol to HDL cholesterol and LDL cholesterol to HDL cholesterol; triacylglycerols; and FFAs are shown in **Table 3**. The ITT analyses showed no significant differences for these outcomes between the REG and RED diets or between the REG and CHO diets (all

**TABLE 2**Subject baseline characteristics1

		Group	
	REG $(n = 50)$	RED $(n = 51)$	CHO $(n = 49)$
Sex, n (%)			
Female	32 (64)	35 (69)	33 (67)
Male	18 (36)	16 (31)	16 (33)
Age, y	$53.8 \pm 13.7$	$50.6 \pm 12.9$	$55.6 \pm 10.3$
Weight, kg	$85.4 \pm 13.4$	84.1 ± 13.7	$84.5 \pm 15.1$
BMI, kg/m <sup>2</sup>	$29.3 \pm 3.6$	$28.1 \pm 3.5$	$28.6 \pm 3.5$
Waist circumference, cm	$98.9 \pm 10.3$	$97.0 \pm 11.4$	$96.6 \pm 10.9$
Smoking, $n$ (%)	1 (2)	4 (8)	1 (2)
Energy requirement, MJ/d	$10.5 \pm 1.8$	$10.4 \pm 2.0$	$10.3 \pm 2$
Cholesterol, mmol/L			
Total	$5.21 \pm 0.93$	$5.25 \pm 1.03$	$5.24~\pm~0.96$
LDL	$3.34 \pm 0.81$	$3.36 \pm 0.88$	$3.40 \pm 0.84$
HDL	$1.39 \pm 0.37$	$1.42 \pm 0.33$	$1.46 \pm 0.32$
Triacylglycerols, mmol/L	$1.31 \pm 0.59$	$1.26 \pm 0.53$	$1.18\pm0.56$
Insulin, pmol/L	$78.3 \pm 51.4$	$73.6 \pm 56.2$	$68.4 \pm 39.0$
Glucose, mmol/L	$5.77 \pm 0.47$	$5.78 \pm 0.71$	$5.84 \pm 0.53$
HOMA-IR	$2.93 \pm 1.99$	$2.81 \pm 2.51$	$2.63 \pm 1.69$
Systolic blood pressure, mm Hg	131.7 ± 15.1	128.5 ± 15.2	129.7 ± 14.9
Diastolic blood pressure, mm Hg	84.7 ± 9.1	83.1 ± 9.5	85.0 ± 8.6

<sup>1</sup>Values are means  $\pm$  SDs unless otherwise indicated. n = 150. CHO, carbohydrate control; RED, reduced-fat cheese; REG, regular-fat cheese.

 $P \ge 0.07$ ). Complete-case analyses showed similar results (**Supplemental Table 1**). There were no differences between men and women for any of the blood lipid measurements in either the ITT analyses or the complete-case analyses.

## Glucose homeostasis and CRP

Changes in mean serum concentrations of insulin, glucose, and CRP and calculated HOMA-IR are also shown in Table 3. ITT analyses showed no significant differences for any of these

#### TABLE 3

Fasting blood values at week 12 and changes from baseline<sup>1</sup>

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outcomes between the REG and RED diets or between the REG and CHO diets (all  $P \ge 0.12$ ). Complete-case analyses showed similar results (Supplemental Table 1).

#### Anthropometric measures and blood pressure

Changes in mean anthropometric measures, body composition, and blood pressure are shown in **Table 4**. ITT analyses showed no significant differences in body weight, fat mass, lean body mass, waist circumference, or blood pressure between the REG and RED diets or between the REG and CHO diets (all  $P \ge 0.16$ ). Complete-case analyses showed similar results (**Supplemental Table 2**).

## Dietary intake and compliance

On the basis of daily completed food diaries and weekly conversations, compliance in all 3 groups was considered good (>95%) with regard to adherence to assigned intervention foods and refraining from other dairy products. There were no significant differences in compliance between the 3 diet groups in amount of test food consumed (REG group:  $98.9\% \pm 0.3\%$ ; RED group:  $98.8\% \pm 0.4\%$ ; CHO group:  $99.3\% \pm 0.3\%$ ).

## **Dietary records**

Results from the 3-d weighted dietary records in week 12 are shown in **Table 5**. No differences were observed in energy intake between groups. Fat intakes (in grams and percentage of energy) were significantly higher with the REG diet than with the RED diet (P < 0.05) and the CHO diet (P < 0.001). Saturated fat was significantly higher with the REG diet than with the RED (P < 0.01) and CHO (P < 0.001) diets. The amount of MUFAs was significantly higher with the REG diet than with the CHO diet (P < 0.01), whereas PUFAs did not differ between the diets. The intake of carbohydrate was greater with the CHO diet than with the REG (P < 0.001) and RED (P < 0.001) diets. However, dietary fiber did not differ between the diets. As

	REG $(n = 50)$		RED $(n = 51)$		CHO $(n = 49)$		Р	
	Week 12	Change from baseline	Week 12	Change from baseline	Week 12	Change from baseline	REG vs. RED	REG vs. CHO
LDL-C, mmol/L	$3.51 \pm 0.11$	$0.17 \pm 0.07$	$3.45 \pm 0.13$	$0.09 \pm 0.08$	$3.43 \pm 0.11$	$0.03 \pm 0.06$	0.42	0.17
HDL-C, mmol/L	$1.45 \pm 0.06$	$0.06 \pm 0.02$	$1.46 \pm 0.04$	$0.05 \pm 0.02$	$1.46 \pm 0.05$	$0.01 \pm 0.03$	0.86	0.07
TC, mmol/L	$5.40 \pm 0.14$	$0.18 \pm 0.07$	$5.28 \pm 0.15$	$0.03 \pm 0.09$	$5.24 \pm 0.13$	$0.00\pm0.08$	0.14	0.11
Triacylglycerols, mmol/L	$1.42 \pm 0.11$	$0.11 \pm 0.09$	$1.23 \pm 0.07$	$-0.03 \pm 0.07$	$1.30 \pm 0.10$	$0.11 \pm 0.06$	0.11	0.88
FFAs, µmol/L	$510 \pm 31$	$28 \pm 25$	$494 \pm 24$	$-42 \pm 34$	$503 \pm 25$	6 ± 21	0.34	0.54
LDL-C:HDL-C	$2.54 \pm 0.12$	$0.02 \pm 0.05$	$2.49 \pm 0.13$	$-0.04 \pm 0.05$	$2.47 \pm 0.13$	$-0.01 \pm 0.05$	0.06	0.69
TC:HDL-C	$3.92 \pm 0.18$	$0.01 \pm 0.10$	$3.76 \pm 0.15$	$-0.14 \pm 0.06$	$3.72 \pm 0.13$	$-0.05 \pm 0.06$	0.23	0.71
Insulin, pmol/L	$90.0 \pm 8.3$	$11.7 \pm 4.2$	$81.2 \pm 8.2$	$7.5 \pm 4.5$	$78.2 \pm 8.0$	$9.8 \pm 5.4$	0.72	0.57
Glucose, mmol/L	$5.78 \pm 0.08$	$0.01 \pm 0.06$	$5.81 \pm 0.10$	$0.04 \pm 0.06$	$5.78 \pm 0.08$	$-0.05 \pm 0.05$	0.39	0.88
HOMA-IR	$3.43 \pm 0.35$	$0.51 \pm 0.20$	$3.13 \pm 0.36$	$0.33 \pm 0.20$	$2.96 \pm 0.31$	$0.34 \pm 0.19$	0.68	0.46
CRP, mg/L	$2.39\pm0.30$	$0.54 \pm 0.28$	$2.17 \pm 0.30$	$0.44 \pm 0.17$	$1.75 \pm 0.27$	$0.05 \pm 0.25$	0.80	0.12

<sup>1</sup>All values are means  $\pm$  SEMs. Significant differences between groups are based on linear mixed models with baseline values as covariates and adjustments for age, sex, BMI, and change in body fat. Pairwise comparisons were made by using a post hoc *t* test on the linear mixed model with *P* values adjusted for multiplicity. CHO, carbohydrate control; CRP, C-reactive protein; FFA, free fatty acid; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; RED, reduced-fat cheese; REG, regular-fat cheese; TC, total cholesterol.

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## TABLE 4

Fasting values of anthropometric measurements, body composition, and blood pressure at week 12 and changes from baseline<sup>1</sup>

	REG $(n = 50)$		RED ( <i>n</i> = 51)		CHO ( <i>n</i> = 49)		Р	
	Week 12	Change from baseline	Week 12	Change from baseline	Week 12	Change from baseline	REG vs. RED	REG vs. CHO
Body weight, kg	85.6 ± 1.9	$0.1 \pm 0.2$	84.1 ± 2.0	$0.1 \pm 0.2$	84.6 ± 2.2	$0.1 \pm 0.2$	0.80	0.85
WC, cm	$99.0 \pm 1.4$	$0.1 \pm 0.4$	$97.3 \pm 1.6$	$0.2 \pm 0.4$	$97.0 \pm 1.5$	$0.1 \pm 0.4$	0.88	0.62
BMI, kg/m <sup>2</sup>	$29.3 \pm 0.5$	$0.0 \pm 0.1$	$28.1 \pm 0.5$	$0.03 \pm 0.1$	$28.7 \pm 0.5$	$0.1 \pm 0.1$	0.74	0.93
Fat mass, kg	$31.9 \pm 1.2$	$-0.1 \pm 0.2$	$32.4 \pm 1.2$	$0.3 \pm 0.2$	$32.1 \pm 1.3$	$-0.3 \pm 0.2$	0.30	0.56
Fat, %	$37.6 \pm 1.1$	$-0.2 \pm 0.2$	$38.5 \pm 0.9$	$0.2 \pm 0.2$	$38.0 \pm 1.2$	$-0.4 \pm 0.2$	0.17	0.57
Lean body mass, kg	$50.4 \pm 1.5$	$0.3 \pm 0.2$	$48.4 \pm 1.3$	$-0.1 \pm 0.2$	$49.2 \pm 1.6$	$0.2 \pm 0.2$	0.16	0.71
Systolic BP, mm Hg	$130.5 \pm 1.9$	$-1.1 \pm 1.4$	$125.2 \pm 2.2$	$-3.2 \pm 1.3$	$127.7 \pm 1.8$	$-2.0 \pm 1.5$	0.17	0.21
Diastolic BP, mm Hg	$83.3 \pm 1.1$	$-1.4 \pm 0.7$	$81.1 \pm 1.3$	$-2.0\pm0.7$	$83.1 \pm 1.1$	$-1.9 \pm 0.7$	0.50	0.77

<sup>1</sup>All values are means  $\pm$  SEMs. Significant differences between groups are based on linear mixed models with baseline values as covariates and adjustments for age, sex, BMI, and change in body fat. Pairwise comparisons were made by using a post hoc *t* test on the linear mixed model with *P* values adjusted for multiplicity. BP, blood pressure; CHO, carbohydrate control; RED, reduced-fat cheese; REG, regular-fat cheese; WC, waist circumference.

expected, calcium intake was significantly higher with the REG diet than with the CHO diet (P < 0.001).

## DISCUSSION

Our results showed that daily consumption of 64–112 g regularfat cheese for 12 wk did not modify LDL cholesterol or MetS risk factors differently than equal amounts of reduced-fat cheese or carbohydrate-rich foods. These findings are consistent with our hypothesis that cheese consumption, both regular-fat and reduced-fat, has a neutral effect on metabolic risk factors. The fact that subjects in all 3 groups remained weight-stable throughout the intervention indicates that the observed effects were independent of changes in body weight. Our results are in line with a recently published Norwegian study, which showed no changes in LDL cholesterol or any of the MetS factors after 8 wk of cheese intake with different fat contents compared with a control group (25). Our results are also in accordance with a study by Thorning et al. (26), who found no difference be-

tween a high-fat cheese diet and a carbohydrate-rich diet on concentrations of total cholesterol, LDL cholesterol, triacylglycerols, insulin, or glucose. However, they observed a 5% higher HDL-cholesterol concentration (P = 0.012) with the cheese diet than with the carbohydrate-rich diet. In our study, a small increase in HDL cholesterol was observed with the REG diet compared with the CHO diet, although this increase was not significant (P = 0.07). This partly reflects the well-characterized impact of total fat on HDL metabolism. Other studies have shown that cheese intake is associated with higher HDL-cholesterol concentrations (27, 28). These findings are in accordance with a meta-analysis that showed that the replacement of all classes of dietary fat with carbohydrates yields unfavorable changes in HDL cholesterol, with significant decreases in some HDL subgroups (29, 30). According to the literature, a high concentration of circulating HDL cholesterol is considered beneficial with regard to cardiovascular health, although the mechanism for the apparent beneficial effect is not fully understood (31-33). Thus, it is reasonable to consider that

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Daily consumption of energy and macronutrients for the REG, RED, and CHO diets during the 12-wk intervention<sup>1</sup>

				P		
	REG $(n = 39)$	RED $(n = 46)$	CHO $(n = 44)$	REG vs. RED	REG vs. CHO	
Total energy, kJ	9098 ± 362	9073 ± 429	8000 ± 340	0.81	0.07	
Energy density, kcal/g	$0.9 \pm 0.1$	$0.8 \pm 0.1$	$0.8 \pm 0.1$	0.72	0.87	
Fat, % of energy	$36.6 \pm 1.1$	$32.2 \pm 0.8$	$29.8 \pm 1.0$	< 0.01	< 0.001	
Fat, g	$90.8 \pm 5.2$	$78.5 \pm 4.0$	$65.4 \pm 3.7$	< 0.05	< 0.001	
Saturated fat, g	$34.3 \pm 2.3$	$27.4 \pm 1.2$	$19.1 \pm 1.4$	< 0.01	< 0.001	
Monounsaturated fat, g	$30.1 \pm 2.1$	$27.1 \pm 1.6$	$23.9 \pm 1.6$	0.10	< 0.01	
Polyunsaturated fat, g	$13.7 \pm 1.0$	$13.0 \pm 0.8$	$13.3 \pm 0.9$	0.40	0.60	
Carbohydrate, % of energy	$40.5 \pm 1.4$	$43.2 \pm 1.1$	$49.4 \pm 1.2$	0.06	< 0.001	
Dietary fiber, g/d	$23.2 \pm 1.3$	$22.7 \pm 1.2$	$22.4 \pm 1.6$	0.72	0.68	
Protein, % of energy	$19.2 \pm 0.6$	$20.6 \pm 0.6$	$18.4 \pm 0.6$	0.11	0.17	
Alcohol, g	$11.5 \pm 1.8$	$12.9 \pm 1.7$	$7.1 \pm 1.6$	0.92	0.26	
Calcium, mg	$1281 \pm 70$	$1328 \pm 55$	$728 \pm 33$	0.56	< 0.001	

<sup>1</sup>All values are means  $\pm$  SEMs. n = 129 (10 subjects had dietary records considered nonsufficient and were therefore removed from the model). Data were assessed by using a 3-d weighted dietary record estimated with the use of Dankost 3000 dietary assessment software (Dankost). Significant differences were based on linear mixed models with values for average daily consumption at week 0 for all variables included as covariates. Pairwise comparisons were based on a post-hoc *t* test with *P* values adjusted for multiplicity. CHO, carbohydrate control; RED, reduced-fat cheese; REG, regular-fat cheese. unbeneficial changes in LDL cholesterol caused by SFAs are counteracted by their favorable effect on HDL cholesterol. This hypothesis might be a possible explanation for the less harmful effect of saturated fat in relation to CVD shown in several current meta-analyses (31, 34, 35).

The present study was designed to assess the effects of 12 wk of high cheese consumption under conditions similar to real life, without controlling the subjects' habitual diet and by using manufactured products normally consumed by the Danish population. According to the subjects' dietary records, subjects in the REG group consumed 7.7% of energy from SFAs from other nondairy sources, whereas subjects in the RED and CHO groups consumed 6.2% and 8.8% of energy from SFAs from other nondairy sources, respectively. An interesting finding in the current study was that, despite a significant increase in SFA intake (primarily due to the regular-fat cheese) during the REG diet compared with the RED and CHO diets, LDL cholesterol did not differ between the diets. This finding could partly be explained by the fact that MUFA intake was significantly higher with the REG diet than with CHO diet. MUFAs have been suggested to reduce LDL cholesterol instead of carbohydrates (36, 37). Thus, the higher intakes of MUFAs during the REG intervention period could possibly have diminished the effect of SFAs on LDL cholesterol. Energy intake remained similar during the intervention in all 3 groups, suggesting that subjects in the RED and CHO groups replaced energy from saturated fat with other sources, mainly carbohydrates. The health effects of replacing saturated fat depend highly on what is consumed instead. PUFAs, but not carbohydrates, have been associated with a reduced risk of coronary artery disease (38).

Intervention studies on specific regular-fat dairy products compared with reduced-fat products are limited. However, several RCTs have explored how the food matrix modulates the effect of dairy fat on CVD risk markers by comparing cheese with butter (10–12, 39–41). A meta-analysis of 5 RCTs concluded that, despite a similar intake of saturated fat, cheese consumption significantly decreased LDL cholesterol by 6.5% and HDL cholesterol by 3.9% compared with butter (42). These results emphasize the importance of considering whole foods when evaluating CVD risk markers, because they might be modified by food matrix.

Despite a significantly higher intake of carbohydrates during the CHO diet in our study, fasting triacylglycerol concentrations did not differ significantly from the REG and RED diets. This result was interesting because the control diet mainly consisted of medium- and high-glycemic index (-GI) carbohydrate-rich foods (white bread and jam), which have been shown to increase triacylglycerol concentrations in some studies (36, 43). However, this finding might be due to the weightmaintenance design of the current study. Sloth et al. (44) found no differences in triacylglycerol concentrations with a high-carbohydrate diet with a low GI than with a highcarbohydrate diet with a high GI in a 10-wk parallel study. Here, ad libitum intake was allowed, and both diet groups experienced a small decrease in body weight, in contrast to the present study. Moreover, cheese has been suggested to decrease triacylglycerol by inhibiting stearoyl-CoA desaturase, a ratelimiting enzyme in the synthesis of triacylglycerol (45); however, we did not observe lower triacylglycerol concentrations with the 2 cheese diets.

The current study found no difference in fasting glucose, insulin, or HOMA-IR between the REG and RED groups. However, it seems that the effect of cheese intake on T2D risk markers is inconsistent. In healthy subjects, a current study found higher fasting plasma glucose after cheese consumption than after butter consumption (12), whereas another found lower insulin concentrations after cheese consumption than after a nondairy control diet (41). Finally, a third study found higher postprandial glucose concentrations after cheese intake (39), whereas others observed no effect of cheese on glucose or insulin values (10). Thus, the effect of cheese intake on indicators of insulin sensitivity requires further exploration. In a recent study in pigs, Thorning et al. (46) investigated how cheese with different ripening times affects blood lipid, glucose, and insulin concentrations. Short-term ripened cheddar caused higher serum insulin concentrations than did longterm ripened cheddar, indicating that insulin responses to cheese consumption may depend on the ripening duration of the cheese. LDL cholesterol was not affected by ripening time, nor were total cholesterol, HDL-cholesterol, or triacylglycerol concentrations. Therefore, it is unlikely that ripening duration is involved in the observed effect of cheese intake on blood lipids. However, these results have yet to be confirmed in human subjects.

The strength of the current study was its long duration and the relatively large sample size compared with similar trials. The current study also strived to imitate real-life settings by not matching the diets for energy content or macronutrient composition, making it possible to directly compare regular-fat cheese and reduced-fat cheese as whole foods. Limitations of the present study include the fact that subjects were free-living; thus, potential confounding by other dietary and lifestyle factors was present. It was also not possible to blind the study to subjects and staff due to the nature of the diets. However, the laboratory technicians conducting the blood analyses were not aware of the intervention allocation.

In conclusion, our results indicate that the consumption of regular-fat cheese in high daily amounts does not affect serum lipid concentrations, fasting glucose and insulin concentrations, blood pressure, or waist circumference differently than do reduced-fat cheese or carbohydrate-rich foods in a population with  $\geq 2$  MetS risk factors. Our results suggest that, for most individuals, it is reasonable to include regular-fat cheese as part of a healthy diet.

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The authors' responsibilities were as follows-AA and AR: designed the study; FR, MDK, and MLS: conducted the study; FR and CR: performed the statistical analyses, FR: performed the randomization, wrote the manuscript, and had primary responsibility for the final content of the manuscript; TT and AR: supplied valuable knowledge and scientific consultation throughout the study; and all authors: read and approved the final manuscript. AA has received research grants from Arla Foods AMBA, Denmark; The Danish Dairy Research Foundation, Denmark; Global Dairy Platform, USA; and the Danish Agriculture and Food Foundation, Denmark. TT has received research grants from Arla Foods AMBA, Denmark; The Danish Dairy Research Foundation; and the Dairy Institute, Rosemont, IL. AR has received research funding from the Dairy Research Industry, Rosemont, IL, and The Danish Agriculture and Food Council, Denmark. None of the other authors declared a conflict of interest. The sponsors were invited to comment on the study design, but the researchers made the final decisions. The sponsors had no influence on the execution of the study, the analysis and interpretation of data, or on the final manuscript.

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# **Consumer Education Project of Milk SA - CPD activity for Dietitians**

You can obtain 1 CEU for reading the review article "High intake of regular-fat cheese compared with reduced-fat cheese does not affect LDL cholesterol or risk markers of the metabolic syndrome:

a randomized controlled trial" and answering the accompanying questions.

The article has been accredited for 1 CEU for dietitians, Ref number: DT/A01/2017/00105 HOW TO EARN YOUR CEU's

- 1. Complete your personal details below.
- 2. Read the article titled "High intake of regular-fat cheese compared with reduced-fat cheese does not affect LDL cholesterol or risk markers of the metabolic syndrome: a randomized controlled trial" Raziani F et al. 2016. American Journal of Clinical Nutrition 104:973-81 of the Education Project of Milk SA and answer the auestions.
- 3. Indicate your answers to the questions by making an "X" in the appropriate block at the end.
- 4. You will earn 1 CEU if you answer 70% or more of the questions correctly. A score of less than 70% will unfortunately not earn you any CEU's.
- 5. Make a photocopy for your own records in case your answers do not reach us.
- 6. Cut and paste the area indicated below into an e-mail message and e-mail it to maretha@dairycep.co.za or post to P.O. Box 36332 Menlo Park 0102
- 7. The closing date for this activity is 30 December 2017. Answer sheets received after this date will not be processed. Certificates will be sent within two months from receipt of the answer sheet.

# PLEASE ANSWER ALL THE QUESTIONS

(There is only one correct answer per question.)

1. Several randomized controlled trials have shown that cheese, despite its high content of saturated fat, has a effect on total cholesterol and/or LDL cholesterol compared

with dairy products such as butter.

[a] neutral or protective

[b] beneficial

[c] neutral or beneficial

2. The study was designed using a 12-wk randomized parallel-intervention study preceded by a 2-wk run-in period, consisting of 164 subjects and using exclusion criteria including: chronic diseases (known T2D, CVD, or other chronic diseases that could affect the study outcome), milk allergy, the use of prescription medicine such as, lipid-lowering agents, <10 h of strenuous physical activity/wk. alcohol abuse, blood donation. <1 month before study commencement, simultaneous participation in other clinical studies and pregnant or lactating woman.

[a] true

[b] false

3. Changes from baseline values at 12 weeks for regular fat cheese

[a] LDL 0.09 ± 0.08 mmol/L; HDL 0.05 ± 0.02 mmol/L; TC 0.03 ± 0.09 mmol/L; LDL:HDL 0.03 ± 0.09 mmol/L [b] LDL 0.03 ± 0.06 mmol/L; HDL 0.01 ± 0.03 mmol/L; TC 0.00 ± 0.08 mmol/L; LDL:HDL -0.01 ± 0.05 mmol/L [c] LDL 0.17 ± 0.07 mmol/L; HDL 0.06 ± 0.02 mmol/L; TC 0.18 ± 0.07 mmol/L; LDL:HDL 0.02 ± 0.05 mmol/L

\_\_g regular-fat cheese for 12 wk did not modify 4. Results showed that daily consumption of LDL cholesterol or Metabolic Syndrome risk factors differently than equal amounts of reduced-fat cheese or carbohydrate-rich foods.

- [a] 23g 36g [b] 64g - 112g
- [c] 47g 62g

5. The daily consumption of energy and macro nutrients for the regular-fat cheese diets during the 12we intervention was:

[a] Total energy 8000 ± 340; 29.8 ± 0.1% Fat ; 19.1 ± 1.4g Sat fat; 49.4 ± 1.3% CHO; 18.4 ± 0.6% Prt [b] Total energy 9098 ± 362; 36.6 ± 1.1% Fat ; 34.3 ± 2.3g Sat fat; 40.5 ± 1.4% CHO; 19.2 ± 0.6% Prt [c] Total energy 9073 ± 429; 32.2 ± 0.8% Fat ; 27.4 ± 1.2g Sat fat; 43.2 ± 1.1% CHO; 20.6 ± 0.6% Prt

6. Some meta-analysis studies showed that the replacement of all classes of dietary fat with carbohydrates yields favourable changes in HDL cholesterol, with significant increases in some HDL subgroups.

[a] true [b] false

**7.** A meta-analysis of 5 randomized control trails concluded that, despite a similar intake of saturated fat, cheese consumption significantly \_\_\_\_\_\_ LDL cholesterol and HDL cholesterol by 3.9% compared with butter. These results emphasize the importance of considering whole foods when evaluating CVD risk markers, because they might be modified by food matrix.

[a] decrease by 6.5% [b increase by 6.5%

[c] increase by 3.9%

**8.** Cheese has been suggested to \_\_\_\_\_\_ triacylglycerol by inhibiting stearoyl-CoA desaturase, a rate-limiting enzyme in the synthesis of triacylglycerol; however, this study did not observe lower triacylglycerol concentrations with either the 2 cheese diets.

- [a] maintain
- [b] increase

[c] decrease

**9.** Short-term ripened cheddar caused \_\_\_\_\_\_ serum insulin concentrations than did long term ripened cheddar, indicating that insulin responses to cheese consumption may depend on the ripening duration of the cheese.

- [a] stable
- [b] higher
- [c] lower

10. The consumption of regular-fat cheese in high daily amounts does not affect serum lipid concentrations, fasting glucose and insulin concentrations, blood pressure, or waist circumference differently than do reduced-fat cheese or carbohydrate-rich foods. The results suggest that, for most individuals, it is \_\_\_\_\_\_ to include regular-fat cheese as part of a healthy diet.
[a] undesirable
[b] reasonable
[c] advisable

# **Consumer Education Project of Milk SA - CPD activity for Dietitians**

"High intake of regular-fat cheese compared with reduced-fat cheese does not affect LDL cholesterol or risk markers of the metabolic syndrome: a randomized controlled trial" Ref number: DT/A01/2017/00105 Cut and paste the section below into an e-mail message

PLEASE WRITE <u>CLEARLY</u>	
HPCSA number: DT	
Surname as registered with HPCSA:	Initials:
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(*NB: Supply email address for certif	icate delivery – please write in clear BLOCK LETTERS)
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I hereby declare that this is my own	unassisted work.

Please make an "X" in the appropriate block for each question:

a[] b[]c[]
 a[] b[]
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 a[] b[]c[]