Associations of the Baltic Sea diet with cardiometabolic risk factors – a meta-analysis of three Finnish studies
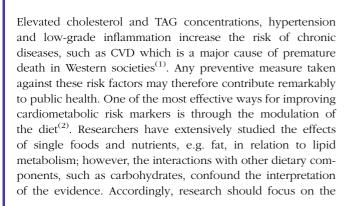
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Abstract

Dyslipidaemia, hypertension and low-grade inflammation increase the risk of CVD. In the present meta-analysis, we examined whether adherence to a healthy Nordic diet, also called the Baltic Sea diet, may associate with a lower risk of these cardiometabolic risk factors. In 2001–2007, three cross-sectional Finnish studies were conducted: the Dietary, Lifestyle and Genetic Determinants of Obesity and Metabolic Syndrome study (*n* 4776); Health 2000 Survey (*n* 5180); Helsinki Birth Cohort Study (*n* 1972). The following parameters were assessed in these three studies: blood pressure, total, HDL- and LDL-cholesterol, TAG and high-sensitivity C-reactive protein (hs-CRP); a validated FFQ was used to assess the participants' dietary intakes. The Baltic Sea Diet Score (BSDS) was developed based on the healthy Nordic diet. All studies assessed confounding variables, such as physical activity and BMI, based on standardised questionnaires and measurements. The random-effects meta-analysis provided summary estimates for OR and 95% CI by the BSDS quintiles. In the meta-analysis, the risk of elevated hs-CRP concentration was lower among men (OR 0·58, 95% CI 0·43, 0·78) and women (OR 0·73, 95% CI 0·58, 0·91) in the highest BSDS quintile than among those in the lowest BSDS quintile. In contrast, the risk of lowered HDL-cholesterol concentration was higher among women (OR 1·67, 95% CI 1·12, 2·48) in the highest BSDS quintile than among those in the lowest BSDS quintile. However, no other associations were found. In conclusion, the associations between the adherence to the healthy Nordic diet and cardiometabolic risk factors are equivocal. Longitudinal studies are needed to further examine this hypothesis.

Key words: Baltic Sea diet: Nordic diet: C-reactive protein: Meta-analyses: Pooling

Elevated cholesterol and TAG concentrations, hypertension and low-grade inflammation increase the risk of chronic diseases, such as CVD which is a major cause of premature death in Western societies[1]. Any preventive measure taken against these risk factors may therefore contribute remarkably to public health. One of the most effective ways for improving cardiometabolic risk markers is through the modulation of the diet[2]. Researchers have extensively studied the effects of single foods and nutrients, e.g. fat, in relation to lipid metabolism; however, the interactions with other dietary components, such as carbohydrates, confound the interpretation of the evidence. Accordingly, research should focus on the overall diet. For such purposes, nutritionists have developed dietary scores that have been increasingly used in epidemiological studies[3]. Instead of using data-driven approaches to identify dietary patterns that exist among study participants, the dietary score method was employed, which is a hypothesis-oriented approach that predefines the diet and then assesses how well the participants adhere to it.

The most well-known dietary score, the Mediterranean Diet Score, is based on the traditional diet of the Mediterranean countries[4]. Strong evidence exists that this diet improves metabolic risk factors; studies have reported normalisation of body weight and lipid concentrations as well as suppression

of inflammation[5–7]. The diet also lowers the risk of CVD-related mortality[8]. However, differences in food cultures, local resources and ecological aspects may hamper other populations, e.g. Scandinavians, from adopting the Mediterranean diet.

Many foods cultivated in the Nordic countries, for example, apples and berries, rye, rapeseed oil, salmon and dairy products, are considered to have health-enhancing features[9]. A Nordic diet compiled of these foods may, in theory, promote health[10]. Recently, controlled trials of individuals with hypercholesterolaemia or the metabolic syndrome have provided evidence that the healthy Nordic diet improves lipid profiles and reduces inflammation[11,12]. To measure the adherence to the healthy Nordic diet at a population level, a dietary score, called the Baltic Sea Diet Score (BSDS), was developed[13]. The BSDS has been found to be associated with lower abdominal obesity in Finland[14].

In the present study, we aimed to examine the associations between the adherence to the healthy Nordic diet and cardiometabolic risk factors (elevated total cholesterol, LDL-cholesterol (LDL-C), TAG and high-sensitivity C-reactive protein (hs-CRP) concentrations and hypertension, and lowered HDL-cholesterol (HDL-C) concentration) at the population level. We used the BSDS as an indicator of adherence to the healthy Nordic diet and analysed three Finnish health examination studies in a meta-analysis.

Subjects and methods

The present meta-analysis included three cross-sectional Finnish studies: the Dietary, Lifestyle and Genetic Determinants of Obesity and Metabolic Syndrome (DILGOM) study (n 5024); the Health 2000 Survey (n 8028); the clinical part of the Helsinki Birth Cohort Study (HBCS, n 2003). The participants and the methods used in these studies have been described in detail elsewhere[15–18]. In brief, the DILGOM study was implemented in the framework of the National FIN-RISK 2007 Study that includes a representative sample of the Finnish population in five large study areas[16]. Participants who went through the health examination were invited to a more detailed health examination (=DILGOM) concerning obesity and the metabolic syndrome later during the same year[18]. The Health 2000 Survey aimed at determining the health and functional capability of ≥30-year-old Finns, and collected information on the most important health disorders and the associated need for care, rehabilitation and aid[15]. The baseline survey was conducted during the year 2000–2001. A nationally representative sample was drawn from eighty health service districts throughout Finland. The HBCS investigated the effect of early growth on the later risk of non-communicable diseases[17]. The cohort members were born in 1934–1944 at Helsinki University Central Hospital as singletons. Using random number tables, a sample of 2902 participants from this cohort was derived and invited to a clinical examination conducted in 2001–2004.

The DILGOM study, the Health 2000 Survey and the HBCS were conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Ethics Committee of the Helsinki and Uusimaa Hospital District. Written informed consent was obtained from all subjects. Access to personal identification codes was restricted, and data were analysed without personal identification codes.

Dietary habits were assessed using the same semi-quantitative FFQ[19] and its two latest updated versions[20,21]. The updated versions did not differ substantially from each other. Participants recorded their food consumption during the previous year in nine frequency categories. The portion sizes in the FFQ were fixed for each food item and mixed dish in advance (e.g. by the glass or the slice). In the DILGOM study and the HBCS, participants completed the FFQ at the study site, where a trained study nurse reviewed the questionnaire. In the Health 2000 Survey, participants were asked to complete the FFQ at home after the health examination and send it back to the study centre. Researchers calculated the average daily food, nutrient and energy intakes (EI) using the national food composition database (Fineli®) and in-house software[22].

In all three studies, trained study nurses measured height, weight, waist circumference, and systolic and diastolic blood pressure using standard protocols[15,23,24]. All studies computed BMI (kg/m^2). The study nurses drew blood for serum and plasma samples, which were stored at $-70°$C until analysed. Research laboratories used automated clinical chemistry analysers and routine clinical chemistry methods to measure serum lipid fractions (total cholesterol, HDL-C and TAG concentrations) and hs-CRP concentration[25–27]. LDL-C concentrations were calculated using the Friedewald formula[28].

Data handling

The present meta-analysis consisted of participants who returned the FFQ form to the study centre (DILGOM study n 4990, HBCS n 2003 and Health 2000 Survey n 6373). The study was restricted to participants between 25 and 79 years of age, which led to the exclusion of 421 participants older than 79 years in the Health 2000 Survey. After exclusion of missing or incompletely filled FFQ (DILGOM study n 74, HBCS n 2 and Health 2000 Survey n 375), individuals with extremely low or high EI (DILGOM study (n 42) and HBCS (n 20): daily EI cut-offs corresponding to 0·5 % at both ends of the daily EI distributions for men and women; Health 2000 Survey (n 18): daily EI values between <2510 and $>29\,288$ kJ/d (<600 and >7000 kcal/d)), pregnant women (DILGOM study n 27 and Health 2000 Survey n 34), and missing information of response variables (DILGOM study n 71, HBCS n 9 and Health 2000 Survey n 345), the final meta-analysis data comprised 11 928 participants (5494 men and 6434 women; DILGOM study n 4776, HBCS n 1972 and Health 2000 Survey n 5180).

The construction of the BSDS has been described in detail elsewhere[13]. In short, the BSDS is based on the healthy Nordic diet[10]. The BSDS included nine dietary components: high intakes of Nordic fruits (apples and berries); Nordic vegetables (tomatoes, cucumbers, leafy vegetables, roots,

cabbages and peas); Nordic cereals (rye, oats and barley); low-fat and fat-free milk; fish (salmon and freshwater fishes); high ratio of PUFA:(SFA + *trans*-fatty acids); low intakes of red and processed meat; total fat (as a percentage of total EI; E%); moderate or low intake of alcohol (ethanol). In each study, the score components were divided using sex-specific quartiles of average daily intakes, and for each dietary component, except alcohol, points from 0 to 3 were assigned according to the predictable impact on health. For alcohol intake, participants received 1 point for moderate or lower intake (≤20 g/d of ethanol for men and ≤10 g/d of ethanol for women) and 0 point if moderate intake was exceeded. The final score ranged from 0 to 25. Higher scores indicate higher adherence to the healthy Nordic diet. The BSDS was divided into quintiles using study-specific quintile cut-offs, and used as the exposure variable.

We used international guidelines to define elevated or lowered values of cardiometabolic risk factors (later referred to as outcome variables). We transformed all the outcome variables to dummy variables, according to the cut-off values defined as follows. Elevated total cholesterol concentration was defined as ≥5·0 mmol/l or use of lipid-lowering medication[1]. Elevated LDL-C concentration was defined as ≥3·0 mmol/l or use of lipid-lowering medication[1]. We used harmonisation criteria of the metabolic syndrome for lowered HDL-C concentration (<1·0 mmol/l for men and <1·3 mmol/l for women)[29]. According to the same criteria, we defined elevated TAG concentration as ≥1·7 mmol/l, and elevated blood pressure as systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or use of blood pressure-lowering medication. Assessment of low-grade inflammation has no univocal recommendation; however, some evidence of higher risk for CVD exists at hs-CRP concentrations ≥3·0 mg/l[30], which we used as the cut-off criteria. Furthermore, concentrations >10 mg/l were excluded from hs-CRP analysis (*n* 415), since they were likely to indicate other than obesity-related inflammation.

All the three studies included questions on the participants' educational attainment, frequency of exercise (times per week) and smoking status. We used these questions to indicate socio-economic status, leisure-time physical activity and smoking status in the present meta-analysis. In the DILGOM study and the HBCS, medication use was obtained from the Social Insurance Institute's register for reimbursements of pharmaceutical expenses. In the Health 2000 Survey, medication use was self-reported.

Statistical analyses

Statistical analyses were performed using SAS version 9.2 (SAS Institute, Inc.) and R Statistical Software version 2.15.1[31]. Since the test for significance of the interaction between sex and the BSDS was $P < 0.05$ for three (out of six) response variables, separate analyses were conducted for men and women. Descriptive data by the BSDS quintiles are reported as means with their standard errors or percentages. For all data, logistic regression was used to calculate OR and two-sided 95% CI for each response variable by the BSDS quintiles in the

three study cohorts. Potential confounding variables were first listed based on the literature. Second, we explored which of these variables were actual confounders in our data, i.e. independently associated with both the outcomes and exposure. This was done using linear regression analysis[32]. For example, women's menopausal age was not associated with exposure; thus, it was not used as a confounding variable in the present study. The following confounding variables were included in modelling: age; leisure-time physical activity; smoking status; education; BMI; Na intake (only for hypertension). Furthermore, to take into account possible misreporting of EI, the ratio of reported EI:predicted BMR was calculated and the participants were classified as either under-reporters (EI:BMR ≤1·14) or plausible reporters (EI:BMR >1·14)[33–35] (26% of the total participants). The final analyses were conducted with and without adjustment for under-reporting.

The random-effects meta-analysis was chosen as the analytic strategy. This two-stage process allows for between-study diversity in study methods (e.g. different laboratories used) and heterogeneity in the associations between the outcome variables and exposure or covariates. In the meta-analysis, the pooled OR and its 95% CI for the mass of data were obtained by combining the study-specific log (OR) and weighing them by the inverse of their variance in a random-effects model[36]. The *P* value for test of trend was obtained from Wald's test of the pooled estimates using the median values of the BSDS quintiles as a continuous variable in the model. Homogeneity among the OR from the original studies was tested using the Q statistic.

In the logistic regression analysis, three main models were used. The first model was adjusted for age (years, continuous); the second model for age, leisure-time physical activity (categorical: <1 time/week, 1–3 times/week and ≥4 times/week), smoking status (categorical: non-smoker, former smoker and current smoker), education (years, continuous) and BMI (kg/m², continuous). When hypertension was used as an outcome variable, Na intake (mg/d, continuous) was also controlled in the second model. In the third model, the associations were examined by excluding the participants who were taking lipid-lowering medication (total cholesterol, LDL-C, HDL-C and TAG concentrations), blood pressure-lowering medication (hypertension) or statin drugs (hs-CRP concentration), adjusting for the variables used in the second model. In interaction analyses, the associations between the outcome variables and the BSDS were examined in separate BMI and waist circumference categories.

Results

Participants with a higher adherence to the Baltic Sea diet were older, more physically active and more educated, less often smokers, had smaller waist circumference and were more likely to use lipid-lowering medication. Total cholesterol concentration decreased due to decreasing HDL-C concentration towards the highest BSDS quintile. No difference in the other lipid fractions was found between the BSDS quintiles, while the hs-CRP concentration tended to decrease

towards the highest BSDS quintile. Of the participants included in the present meta-analysis, 83% had elevated total serum cholesterol concentration or used lipid-lowering medication, 78% had elevated LDL-C concentration or used lipid-lowering medication, 18% of men and 29% of women had low HDL-C concentration, 37% had elevated TAG concentration and 20% had elevated hs-CRP concentration.

The BSDS ranged from 1 to 25 points, and the quintile cut-offs were comparable between the studies (Table 1). The consumption of BSDS components considered healthy increased across the BSDS quintiles, whereas the consumption of components considered unhealthy decreased in all the three studies. In general, the DILGOM study tended to have the highest intakes of all score components, except the intakes of total fat and alcohol, which were highest in the HBCS.

The pooled risk of elevated hs-CRP concentration was lower by 42% in men (model 2; Table 2) and 27% in women (model 2; Table 3) in the highest BSDS quintile compared with the lowest. These associations remained after adjusting for under-reporters (data not shown). In contrast, the risk of lower HDL-C concentration was 40% higher among women (model 2), but not among men, in the highest BSDS quintile compared with the lowest. After adjusting for under-reporters, the association strengthened (data not shown). Among men, a positive trend between the higher BSDS and the risk of elevated LDL-C concentration was found (model 3; P for trend=0·031), even though there was no statistically significant difference between the higher BSDS quintiles compared with the lowest. Adjusting for under-reporters did not affect this association (data not shown). We found no associations between the BSDS and other cardiometabolic risk factors. Furthermore, the associations between the BSDS and cardiometabolic risk factors were not modulated by the participants' BMI and waist circumference (data not shown).

When men using lipid-lowering medication were excluded from the analysis (17% of the total participants), the OR in the fourth and fifth BSDS quintiles attenuated in relation to total cholesterol, LDL-C and TAG concentrations (model 2 v. model 3; Table 2). Among women (19% of the total participants), the OR did not change (model 2 v. model 3; Table 3). In contrast, the OR for the risk of low HDL-C concentration strengthened among the two sexes, but the OR for men remained statistically non-significant. The OR for the risk of hypertension (excluding blood pressure-lowering medication users; 6% of the total participants) and elevated hs-CRP concentration (excluding statin users; 27% of the total participants) were similar among the two sexes. Adjusting for under-reporters did not affect the results (data not shown).

The positive trend across the BSDS quintiles between the higher BSDS and elevated LDL-C concentration disappeared after excluding men using lipid-lowering medication (P=0·40, model 3; Table 2). This result remained after adjusting for under-reporters (data not shown). Furthermore, the trend between the higher BSDS and elevated TAG concentration weakened among men (P=0·34, model 3; Table 2), but strengthened among women (P=0·09, model 3; Table 3), when lipid-lowering medication users were excluded.

Furthermore, when statin users were excluded, the risk for elevated hs-CRP concentration attenuated (P for trend=0·05 for men and P for trend=0·17 for women); however, it became statistically significant again after adjusting for under-reporters in both sexes (data not shown).

To determine whether some of the BSDS components were driving the associations observed, we analysed the associations between individual BSDS components and elevated hs-CRP and lowered HDL-C concentrations. In men, higher intakes of fruits and berries, vegetables, cereals and low-fat milk decreased the risk of elevated hs-CRP concentration (Table 4). In women, higher intakes of fruits and berries, and cereals decreased this risk. In contrast, the risk of lower HDL-C concentration was increased by higher intakes of cereals and low-fat milk, and moderate or lower intake of alcohol, but decreased by the lower intake of total fat (as E%) in women (data not shown).

Discussion

The present meta-analysis is among the first to examine the associations between the healthy Nordic diet, also called the Baltic Sea diet, and cardiometabolic risk factors. In the meta-analysis of three cross-sectional Finnish studies, we found that adherence to the healthy Nordic diet was associated with a lower risk of elevated hs-CRP concentration. This result was independent of the participants' age, leisure-time physical activity, education, smoking status and BMI, and remained significant after excluding statin users. In addition, among women, adherence to the healthy Nordic diet was associated with a higher risk of lower HDL-C concentration. This result strengthened after excluding lipid-lowering medication users. The risk of lower LDL-C concentration increased across the BSDS quintiles among men; however, the trend disappeared after excluding men using lipid-lowering medication. Adjusting for under-reporters did not affect these results.

Low-grade inflammation, for which elevated hs-CRP concentration is an important marker, is an independent risk factor for CVD[37,38]. Researchers have estimated that the assessment of hs-CRP concentration in individuals at intermediate risk for a cardiovascular event could help to prevent one additional event per 10 years for every 400–500 people screened[39]. Individuals at high risk for CVD could benefit from a hs-CRP concentration <3·0 mmol/l, regardless of their LDL-C concentration[37,38]. Adopting the Baltic Sea diet could therefore have a remarkable effect, since CVD is one of the leading causes of premature death in Finland[16]. However, trials studying the effects of healthy Nordic diet on subjects with hypercholesterolaemia and the metabolic syndrome did not show any decrease in hs-CRP concentration when compared with a control group[11,12]. Further research is thus needed to reveal whether there is a causal relationship between the Baltic Sea diet and hs-CRP concentration. In examining the individual BSDS components, we found that intakes of Nordic fruits and berries, and cereals were associated with a lower risk of elevated hs-CRP concentration. These foods are well known for their anti-inflammatory

Table 1. Age- and sex-adjusted characteristics of the participants in the Dietary, Lifestyle and Genetic Determinants of Obesity and Metabolic Syndrome (DILGOM) study, Health 2000 Survey and Helsinki Birth Cohort Study (HBCS)

(Mean values with their standard errors or percentages)

Characteristics	DILGOM study (n 4776) BSDS quintiles 1 Mean	SEM	3 Mean	SEM	5 Mean	SEM	Health 2000 Survey (n 5180) BSDS quintiles 1 Mean	SEM	3 Mean	SEM	5 Mean	SEM	HBCS (n 1972) BSDS quintiles 1 Mean	SEM	3 Mean	SEM	5 Mean	SEM
BSDS (range)	1–9		12–13		17–25		1–9		12–14		17–25		1–9		12–13		17–24	
Age* (years)	47·0	0·4	53·0	0·4	58·5	0·4	46·8	0·4	50·3	0·4	55·2	0·4	61·1	0·2	61·5	0·2	61·7	0·1
Female† (%)	45		52		58		55		52		56		60		52		55	
Energy under-reporters‡ (%)	35		22		11		43		32		18		43		30		17	
Exercise >4 times/week (%)	20		29		35		18		26		39		22		21		32	
Smokers (%)	27		19		9		37		24		17		42		24		11	
Years of education	12·2	0·1	12·6	0·1	12·9	0·1	11·0	0·1	11·6	0·1	12·1	0·1	11·5	0·2	12·2	0·2	12·7	0·2
Lipid-lowering medication§ (%)	21		21		25		2		4		7		19		24		30	
BMI (kg/m²)	27·2	0·2	26·9	0·2	26·7	0·2	26·8	0·1	27·2	0·2	26·9	0·2	27·7	0·2	27·7	0·3	27·3	0·2
WC (cm)	93·4	0·4	91·5	0·5	89·7	0·4	92·6	0·4	93·3	0·4	91·6	0·4	95·9	0·7	95·6	0·7	93·7	0·6
Body fat percentage	30·2	0·3	30·3	0·3	30·4	0·3	27·9	0·3	27·6	0·3	27·4	0·3	30·2	0·4	28·9	0·5	28·8	0·4
Total cholesterol (mmol/l)	5·3	0·03	5·2	0·03	5·1	0·03	6·0	0·03	6·0	0·03	5·9	0·03	6·0	0·06	6·0	0·06	5·8	0·05
TAG (mmol/)l	1·3	0·03	1·2	0·03	1·2	0·02	1·6	0·03	1·6	0·03	1·6	0·03	1·6	0·05	1·6	0·06	1·4	0·05
HDL-cholesterol (mmol/l)	1·5	0·01	1·5	0·01	1·4	0·01	1·4	0·01	1·3	0·01	1·3	0·01	1·6	0·02	1·6	0·02	1·6	0·02
LDL-cholesterol (mmol/l)	3·2	0·03	3·2	0·03	3·2	0·03	3·8	0·04	3·9	0·04	3·7	0·04	3·7	0·05	3·7	0·05	3·5	0·04
Systolic blood pressure (mmHg)	135	1	133	1	135	1	134	1	134	1	134	1	146	1	145	1	144	1
Diastolic blood pressure (mmHg)	80	0·4	79	0·4	79	0·4	83	1·0	83	1·0	82	1·0	89	1·0	89	1·0	88	1·0
hs-CRP (mg/l)	2·8	0·2	2·1	0·2	1·7	0·2	2·5	0·2	2·2	0·2	1·5	0·2	3·8	0·3	3·7	0·3	2·9	0·3
Fruits and berries (g/d)	70	4	115	4	225	4	60	3	100	3	180	3	60	7	120	7	230	7
Vegetables (g/d)	190	6	280	6	410	6	150	5	230	5	350	5	170	8	250	8	370	8
Cereals (g/d)	56	1	78	1	113	1	42	1	61	1	88	1	33	2	55	2	84	2
Low-fat milk (g/d)	190	10	270	10	390	9	180	8	260	8	340	8	160	13	205	13	280	12
Fish (g/d)	33	2	45	2	63	2	27	1	37	1	51	1	32	2	45	2	61	2
Red meat (g/d)	180	2	140	2	90	2	165	2	130	2	90	2	162	4	115	4	69	3
Total fat (E%)	35·3	0·1	31·5	0·1	26·8	0·1	40·2	0·1	36·1	0·1	32·3	0·1	37·1	0·2	32·7	0·2	28·6	0·2
Fat ratio	0·4	<0·1	0·5	<0·1	0·6	<0·1	0·3	<0·1	0·4	<0·1	0·5	<0·1	0·35	<0·1	0·4	<0·1	0·5	<0·1
Alcohol (g/d)	9·4	0·4	7·6	0·4	5·6	0·4	6·5	0·3	5·4	0·3	4·3	0·3	10·5	0·7	9·2	0·7	8·0	0·7

BSDS, Baltic Sea Diet Score; WC, waist circumference; hs-CRP, high-sensitivity C-reactive protein; E%, percentage of total energy intake.
* Adjusted only for sex.
† Adjusted only for age.
‡ Energy under-reporters were defined based on the Goldberg cut-off and the WHO definition as the ratio of reported energy intake:predicted BMR[32–34].
§ Lipid-lowering medication included in Anatomical Therapeutic Chemical Classification System code C10A.

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Table 2. Pooled risk of cardiometabolic risk factors by the Baltic Sea Diet Score (BSDS) in a Finnish meta-analysis of men

(Pooled odds ratios and 95 % confidence intervals)

| | BSDS quintiles | | | | | | | | | | |
| | 1 (n 1146) | 2 (n 1119) | | 3 (n 1022) | | 4 (n 1127) | | 5 (n 1080) | | | |
Models	Reference	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	P*	P†
Cholesterol concentration ≥5·0 mmol/l or lipid-lowering medication (n)	905	889		828		892		902			
Model 1‡	1·00	0·85	0·65, 1·12	0·94	0·74, 1·17	0·88	0·66, 1·16	0·95	0·68, 1·34	0·68	0·23
Model 2§	1·00	0·87	0·62, 1·22	0·98	0·77, 1·24	0·94	0·65, 1·37	1·04	0·72, 1·50	0·80	0·18
Without medication users (n)	666	617		544		543		511			
Model 3‖	1·00	0·80	0·57, 1·12	0·92	0·72, 1·18	0·80	0·63, 1·02	0·87	0·65, 1·17	0·25	0·42
LDL-C concentration ≥3 mmol/l or lipid-lowering medication (n)	878	893		840		923		909			
Model 1	1·00	1·05	0·86, 1·30	1·21	0·97, 1·52	1·17	0·94, 1·45	1·15	0·92, 1·44	0·10	0·71
Model 2	1·00	1·07	0·86, 1·32	1·24	0·97, 1·58	1·21	0·97, 1·52	1·23	0·97, 1·56	0·031	0·61
Without medication users (n)	645	626		559		579		516			
Model 3	1·00	1·05	0·83, 1·31	1·16	0·91, 1·48	1·18	0·83, 1·67	1·07	0·81, 1·40	0·40	0·20
HDL-C concentration <1·0 mmol/l (n)	210	218		173		195		204			
Model 1	1·00	0·99	0·72, 1·35	0·92	0·73, 1·16	1·01	0·74, 1·38	0·99	0·69, 1·43	0·95	0·17
Model 2	1·00	1·00	0·69, 1·44	0·93	0·73, 1·18	1·08	0·81, 1·46	1·14	0·77, 1·69	0·41	0·19
Without medication users (n)	171	181		129		142		131			
Model 3	1·00	1·15	0·89, 1·48	0·92	0·70, 1·22	1·15	0·86, 1·54	1·21	0·90, 1·61	0·43	0·30
TAG concentration ≥1·7 mmol/l (n)	465	489		444		491		532			
Model 1	1·00	1·06	0·89, 1·26	1·00	0·84, 1·19	0·97	0·82, 1·16	1·14	0·94, 1·37	0·34	0·44
Model 2	1·00	1·05	0·87, 1·27	1·02	0·85, 1·23	1·04	0·87, 1·26	1·29	0·98, 1·71	0·11	0·15
Without medication users (n)	285	289		218		203		203			
Model 3	1·00	1·03	0·83, 1·29	0·89	0·70, 1·31	0·85	0·67, 1·09	0·96	0·75, 1·24	0·34	0·88
Hypertension¶ (n)	804	797		720		832		807			
Model 1	1·00	0·96	0·71, 1·30	0·85	0·70, 1·03	0·97	0·75, 1·24	0·90	0·67, 1·20	0·54	0·07
Model 2	1·00	0·97	0·67, 1·37	0·85	0·69, 1·05	1·00	0·72, 1·38	0·92	0·73, 1·16	0·67	0·14
Without medication users (n)	591	548		483		541		473			
Model 3	1·00	0·96	0·66, 1·39	0·84	0·68, 1·04	0·99	0·72, 1·34	0·91	0·68, 1·22	0·65	0·11
hs-CRP concentration ≥3·0 mg/l (n)	243	211		190		208		154			
Model 1	1·00	0·78	0·63, 0·98	0·74	0·60, 0·92	0·70	0·56, 0·87	0·46	0·32, 0·67	<0·001	0·10
Model 2	1·00	0·83	0·66, 1·04	0·81	0·64, 1·02	0·83	0·62, 1·10	0·58	0·43, 0·78	0·004	0·15
Without statin users (n)	159	137		106		104		81			
Model 3	1·00	0·85	0·64, 1·12	0·76	0·57, 1·01	0·68	0·50, 0·91	0·59	0·36, 0·97	0·05	0·53

LDL-C, LDL-cholesterol; HDL-C, HDL-cholesterol; hs-CRP, high-sensitivity C-reactive protein.

* Two-sided P value (Wald's test) for linear trend across the BSDS quintiles was tested, using the median values of the BSDS quintiles as continuous variables.

† Two-sided P value for heterogeneity between the studies.

‡ Adjusted for age.

§ Adjusted for age, physical activity, smoking status, education and BMI.

‖ Model 3 is model 2 excluding lipid-lowering medication (total cholesterol, LDL-C, HDL-C and TAG concentrations), blood pressure-lowering medication (hypertension) or statin (hs-CRP concentration) users.

¶ Hypertension was defined as systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or use of blood pressure-lowering medication. For hypertension, model 2 was also adjusted for Na intake (mg/d, continuous).

Table 3. Pooled risk of cardiometabolic risk factors by the Baltic Sea Diet Score (BSDS) in a Finnish meta-analysis of women

(Pooled odds ratios and 95 % confidence intervals)

	1 (*n* 1260)	2 (*n* 1165)		3 (*n* 1110)		4 (*n* 1520)		5 (*n* 1379)			
Models	Reference	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	*P**	*P*†
Cholesterol concentration ≥5·0 mmol/l or lipid-lowering medication (*n*)	920	832		852		1167		1149			
Model 1‡	1·00	0·85	0·70, 1·05	0·91	0·74, 1·12	0·84	0·69, 1·02	0·94	0·75, 1·19	0·45	0·67
Model 2§	1·00	0·87	0·71, 10·7	0·93	0·75, 1·16	0·86	0·70, 1·06	1·01	0·80, 1·26	0·77	0·80
Without medication users (*n*)	752	655		653		851		797			
Model 3‖	1·00	0·89	0·71, 1·10	0·92	0·74, 1·15	0·84	0·68, 1·03	0·93	0·70, 1·23	0·36	0·48
LDL-C concentration ≥3 mmol/l or lipid-lowering medication (*n*)	903	804		835		1167		1122			
Model 1	1·00	0·84	0·69, 1·03	0·94	0·77, 1·15	0·95	0·79, 1·16	0·91	0·62, 1·33	0·84	0·09
Model 2	1·00	0·88	0·71, 1·07	0·98	0·80, 1·22	0·99	0·81, 1·21	1·04	0·75, 1·44	0·51	0·23
Without medication users (*n*)	736	628		641		853		775			
Model 3	1·00	0·89	0·71, 1·09	0·99	0·80, 1·24	0·97	0·79, 1·20	0·97	0·68, 1·40	0·94	0·14
HDL-C concentration <1·3 mmol/l (*n*)	342	331		301		451		410			
Model 1	1·00	1·13	0·94, 1·36	1·03	0·80, 1·33	1·15	0·97, 1·36	1·15	0·94, 1·41	0·11	0·38
Model 2	1·00	1·22	1·00, 1·48	1·11	0·91, 1·36	1·29	1·07, 1·55	1·40	1·07, 1·83	0·006	0·25
Without medication users (*n*)	300	278		255		356		328			
Model 3	1·00	1·20	0·97, 1·48	1·16	0·93, 1·44	1·29	1·06, 1·58	1·67	1·12, 2·48	0·007	0·14
TAG concentration ≥1·7 mmol/l (*n*)	323	326		335		498		428			
Model 1	1·00	0·96	0·79, 1·17	0·96	0·79, 1·17	1·03	0·86, 1·23	0·90	0·74, 1·08	0·49	0·72
Model 2	1·00	1·01	0·83, 1·24	1·06	0·81, 1·38	1·14	0·89, 1·47	1·08	0·89, 1·32	0·20	0·89
Without medication users (*n*)	200	177		165		225		170			
Model 3	1·00	1·04	0·81, 1·34	0·99	0·77, 1·28	1·05	0·75, 1·47	0·68	0·43, 1·06	0·08	0·54
Hypertension¶ (*n*)	649	629		641		912		919			
Model 1	1·00	0·95	0·79, 1·14	0·98	0·81, 1·18	1·05	0·80, 1·39	1·04	0·87, 1·25	0·44	0·97
Model 2	1·00	0·95	0·78, 1·15	0·96	0·79, 1·17	1·05	0·82, 1·33	1·07	0·88, 1·31	0·37	0·97
Without medication users (*n*)	512	491		489		667		641			
Model 3	1·00	0·97	0·80, 1·18	0·99	0·81, 1·20	1·04	0·82, 1·32	1·08	0·89, 1·31	0·39	0·79
hs-CRP concentration ≥3·0 mg/l (*n*)	300	269		240		306		251			
Model 1	1·00	0·93	0·76, 1·12	0·84	0·69, 1·03	0·76	0·63, 0·92	0·65	0·53, 0·79	<0·001	0·48
Model 2	1·00	0·98	0·79, 1·21	0·91	0·73, 1·13	0·81	0·66, 1·00	0·73	0·58, 0·91	0·001	0·83
Without statin users (*n*)	208	171		158		201		140			
Model 3	1·00	0·94	0·73, 1·21	0·93	0·72, 1·20	0·92	0·69, 1·22	0·69	0·53, 0·91	0·17	0·92

LDL-C, LDL-cholesterol; HDL-C, HDL-cholesterol; hs-CRP, high-sensitivity C-reactive protein.
* Two-sided *P* value (Wald's test) for linear trend across the BSDS quintiles was tested, using the median values of the BSDS quintiles as continuous variables.
† Two-sided *P* value for heterogeneity between the studies.
‡ Adjusted for age.
§ Adjusted for age, physical activity, smoking status, education and BMI.
‖ Model 3 is model 2 excluding lipid-lowering medication (total cholesterol, LDL-C, HDL-C and TAG concentrations), blood pressure-lowering medication (hypertension) or statin (hs-CRP concentration) users.
¶ Hypertension was defined as systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or use of blood pressure-lowering medication. For hypertension, model 2 was also adjusted for Na intake (mg/d, continuous).

properties, which may be the mechanism behind the lower risk[40–42].

In contrast to the findings on hs-CRP, the present results showed that adherence to the Baltic Sea diet was associated with a higher risk of lower HDL-C concentration, especially in women. A moderate or low intake of alcohol seemed to be the most important factor driving this association. Moderate alcohol consumption has long been known to increase HDL-C concentrations[43]. High intakes of cereals and low-fat milk were associated with lower HDL-C concentration, which may relate to the high content of added sugars in some frequently used products (confectioneries and yogurts); however, the evidence is inconsistent[44]. A low-fat diet may decrease HDL-C concentration; however, this hypothesis also remains speculative[45–47]. In the present study, participants in the highest BSDS quintile had a mean total fat intake of 29·5 E%, which fits the Nordic nutrition recommendations[48]. Changes in HDL-C concentration observed in Nordic diet trials with comparable total fat estimates (E%) in the intervention group have also produced inconsistent results[11,12].

We hypothesised that there would be inverse associations between the BSDS and the risk of elevated total cholesterol, LDL-C and TAG concentrations. In contrast, the risk of high LDL-C concentration increased across the BSDS quintiles,

and no difference in the risk of elevated total cholesterol and TAG concentrations between the BSDS quintiles appeared. This finding may partly relate to medication use. Since diet plays a crucial role alongside medication in the treatment of dyslipidaemia[49], it is highly likely that health professionals have advised individuals with lipid-lowering medication to change their diet. In cross-sectional settings, this may evoke a positive association between a healthy diet and a cardiometabolic risk factor. Regarding total cholesterol, LDL-C and TAG, our sensitivity analysis supports this hypothesis, but then again, the analysis does not support this hypothesis for HDL-C. Thus, we cannot rule out the possibility that the diet may actually increase the risks. However, our evidence suggests that medication users are following a healthier diet that may have resulted from receiving dietary counselling. Furthermore, there may be some factors that we were not able to take into account in the present meta-analysis, for example genetic variation in apoE that may confound or modulate the risks of adverse cholesterol concentrations.

We found no association between the BSDS and hypertension. The use of blood pressure-lowering medication did not seem to modulate the result. However, this is, in fact, a positive finding since we earlier observed that adherence to the diet was associated with higher Na intake, the most important

Table 4. Elevated high-sensitivity C-reactive protein (hs-CRP) concentrations by Baltic Sea Diet Score (BSDS) components in a Finnish meta-analysis*†

(Pooled odds ratios and 95 % confidence intervals)

| | BSDS component quartile | | | | | | | |
| | 1 | 2 | | 3 | | 4 | | | |
BSDS components‡	1 (Reference)	OR	95 % CI	OR	95 % CI	OR	95 % CI	P§	P‖
Men (*n* 5494)									
Fruits and berries	1·00	0·89	0·73, 1·09	0·74	0·60, 0·91	0·71	0·56, 0·89	0·019	0·28
Vegetables	1·00	0·86	0·70, 1·06	0·82	0·66, 1·01	0·73	0·59, 0·89	0·029	0·10
Cereals	1·00	0·90	0·73, 1·10	0·84	0·68, 1·03	0·81	0·65, 1·00	0·031	0·51
Low-fat milk¶	1·00	0·89	0·73, 1·09	0·81	0·66, 0·99	0·80	0·65, 0·98	0·027	0·78
Fish	1·00	0·82	0·66, 1·01	0·85	0·70, 1·06	0·89	0·72, 1·10	0·78	0·78
Meat products	1·00	1·07	0·86, 1·32	1·25	0·97, 1·62	1·00	0·80, 1·23	0·66	0·83
Fat ratio**	1·00	0·97	0·69, 1·37	1·10	0·89, 1·35	0·92	0·66, 1·28	0·20	0·35
Total fat (E%)	1·00	1·06	0·76, 1·49	0·96	0·78, 1·19	1·18	0·96, 1·45	0·36	0·74
Alcohol	1·00††	1·07	0·86, 1·33					0·85	0·89
Women (*n* 6434)									
Fruits and berries	1·00	0·93	0·77, 1·11	0·78	0·65, 0·95	0·80	0·65, 0·96	0·07	0·76
Vegetables	1·00	1·11	0·73, 1·68	0·96	0·80, 1·16	1·01	0·74, 1·38	0·32	0·32
Cereals	1·00	1·00	0·83, 1·21	0·90	0·74, 1·09	0·81	0·66, 0·98	0·028	0·77
Low-fat milk¶	1·00	0·92	0·76, 1·11	0·95	0·79, 1·14	0·99	0·83, 1·20	0·59	0·99
Fish	1·00	1·04	0·85, 1·27	0·87	0·68, 1·11	0·90	0·70, 1·56	0·44	0·09
Meat products	1·00	1·05	0·86, 1·27	1·14	0·94, 1·39	1·15	0·94, 1·39	0·11	0·77
Fat ratio**	1·00	1·07	0·78, 1·45	1·16	0·81, 1·66	1·02	0·74, 1·40	0·11	0·12
Total fat (E%)	1·00	1·19	0·99, 1·44	1·16	0·96, 1·40	1·14	0·94, 1·38	0·98	0·34
Alcohol	1·00††	1·03	0·77, 1·36					0·99	0·25

E%, percentage of total energy intake.
* Model was adjusted for age, physical activity, smoking status and BMI.
† Elevated hs-CRP concentration defined as ≥3·0 mmol/l.
‡ Study- and sex-specific cut-off quartiles were used. Participants in the higher quartiles of the presumably beneficial effect were assigned higher points than those in the lowest quartiles. In contrast, participants in the lower quartiles of the presumably detrimental effects were assigned higher points than those in the highest quartiles.
§ Two-sided P value was obtained from Wald's test, using intake of each component as a continuous variable in the model.
‖ Two-sided P value for heterogeneity between the studies.
¶ Fat-free milk and milk with <2 % fat.
** Ratio of PUFA:(SFA + *trans*-fatty acids).
†† Men who consumed ≤20 g/d of alcohol and women who consumed ≤10 g/d of alcohol received 1 point, otherwise a 0 point was given. Thus, for alcohol, point 0 was assigned to the reference group and point 1 assigned to the adherence to the Baltic Sea diet.

dietary risk factor for hypertension[13]. In other words, the result suggests that despite slightly higher Na intake, there is no evidence that participants adhering to the diet had a higher risk of hypertension. Furthermore, the BSDS does not include any specific measure for Na intake, which may hamper the detection of its association with hypertension.

The strengths of the present meta-analysis were its high power and the population-based approach in the DILGOM study and the Health 2000 Survey. Validated and standardised questionnaires and measurements, as well as robust and careful statistical testing, were the other strengths of the present study. All the three studies used the same FFQ, which is considered to be a standard method for assessing long-term dietary intakes in large epidemiological studies[50]. The FFQ has been validated for food and nutrient intakes and reproducibility against food diaries[19–21]. Some studies have shown that dietary scores provide a valid estimate of diet quality when they are based on the FFQ method[51]. We used a cut-off of ≥3·0 mg/l for defining elevated hs-CRP concentration[30]. In preliminary analyses, we tested several cut-offs (e.g. >1·0, >2·0 and >3·0 mg/l) that produced similar results, indicating that the association is not dependent on the cut-off chosen (data not shown). The statistically significant trend test also supports this conclusion.

The present study also has some limitations. As discussed earlier, the cross-sectional design limits the conclusions that can be drawn. Overestimation of healthy and underestimation of unhealthy food consumption could have led to some misclassifications in the BSDS quintiles or weakened the associations observed[52]. However, we aimed to control this by excluding participants with extreme EI, and adjusting the analyses for energy under-reporting. A recent study focusing on methodological aspects in relation to HDL-C concentration analyses in Finland showed that various direct HDL-C assays may have led to unexpected misclassifications of some participants[53]. This may have affected the HDL-C association observed to some extent. Furthermore, HDL-C subfraction (HDL2- and HDL3-cholesterol) concentrations were not measured. Even though the role of these subfractions in the aetiology of atherosclerosis or thrombosis is not well understood, the majority of published reports have linked the cardioprotective properties of HDL-C with HDL2[54,55]. Analysing the associations between the BSDS and these subfractions would have eased the interpretation of the present results.

The dietary score method has its strengths and limitations. Dietary scores have the advantage to take into account the cumulative effects and interactions between several foods and nutrients. The score cut-off method may have led to participants in the highest quintile having different dietary profiles. For example, within the third BSDS quintile, some participants may have received only 1 point by consuming Nordic cereals while some participants obtained 3 points. The cut-off for the highest BSDS quintile was 17 points in each study. This high cut-off requires higher consumption than the population median for most of the components; in case of unhealthy components, this requires lower consumption than the population median. Furthermore, the results

from the DILGOM study showed that participants within the highest quintile (cut-off 17 points) had similar nutrient intake profiles, for example similar intakes of fibre, vitamins C and D, total fat and alcohol[13]. In addition, the consumption of BSDS components was fairly similar between the studies in the present meta-analysis.

In conclusion, high adherence to the Baltic Sea diet may lower the risk of low-grade inflammation among Finns, which may decrease the risk of chronic diseases among the average population. Nevertheless, high adherence to the diet may set women at a higher risk of lower HDL-C concentration. The health consequences of these finding are controversial, since, for example, the cardioprotective properties of HDL-C subfractions[54,55], the causal relationship between HDL-C concentration and CVD risk[56] and the reliability of HDL-C assays remain uncertain[53]. Further longitudinal studies are needed to verify the associations between the Baltic Sea diet and the risk of CVD.

Acknowledgements

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