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Review article

Butter, margarine and serum lipoproteins

Peter L. Zock, Martijn B. Katan *

Department of Human Nutrition, Wageningen Agricultural University, Bomenweg 2, 6703 HD Wageningen, The Netherlands

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Abstract

Intake of *trans* fatty acids unfavorably affects blood lipoproteins. As margarines are a major source of *trans*, claims for the advantages of margarines over butter need to be scrutinized. Here we review dietary trials that directly compared the effects of butter and margarine on blood lipids. We identified 20 studies in which subjects had stable body weights, and margarine and butter were exchanged in the diet at constant energy and fat intake. We calculated the changes in average blood lipid levels between study diets (49 comparisons) as a function of the percentage of calories as margarine substituted for butter. Replacing 10% of calories from butter by hard high-*trans* stick margarines lowered total serum cholesterol by 0.19, LDL by 0.11, and HDL by 0.02 mmol/l, and did not affect the total/HDL cholesterol ratio. Soft low-*trans* tub margarines decreased total cholesterol by 0.25 and LDL by 0.20 mmol/l, did not affect HDL, and decreased the total/HDL cholesterol ratio by 0.20. Based on the total/HDL cholesterol ratio, replacement of 30 g of butter per day by soft tub margarines would theoretically predict a reduction in coronary heart disease risk of 10%, while replacement of butter by hard, high-*trans* margarines would have no effect. Replacing butter by low-*trans* soft margarines favorably affects the blood lipoprotein profile and may reduce the predicted risk of coronary heart disease, but high-*trans* hard margarines probably confer no benefit over butter. © 1997 Elsevier Science Ireland Ltd.

Keywords: Butter; Margarine; Dietary fatty acids; Lipoprotein cholesterol; Humans; Coronary heart disease

1. Introduction

Hypercholesterolemia affects large numbers of people in affluent and increasingly also in developing countries. Diets low in saturated fat have long been the first line of treatment, especially for moderately elevated cholesterol levels. A standard feature of such diets is restricting the intake of butter and milk fat, and partly replacing them by fats of vegetable origin, including margarines. However, new findings on the effects of *trans* fatty acids on blood lipoproteins have thrown doubts on the value of margarines for improving the lipoprotein risk profile. Dietary *trans* fatty acids raise LDL cholesterol and lower HDL cholesterol in humans [1–3]. Some [4–7], but not all [8,9], epidemiologic studies also indicate that high intakes of *trans* fatty acids increase coronary heart disease (CHD) risk. Margarines have long had a 'healthy' image because they are lower in saturated fatty acids and cholesterol than butter. However, some margarines are also rich in *trans* fatty acids. As a result the putative health benefits of margarine need to be reassessed [10–13]. Here we review the effects of butter and margarine on lipoprotein cholesterol concentrations as risk factors for coronary heart disease.

* Corresponding author. Tel.: +31 317 482646 or 2589; fax: +31 317 483342; e-mail: martijn.katan@et3.voed.wau.nl

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2. Methods

2.1. Selection of studies

We screened MEDLINE (1966–1995), Biological Abstracts (1991–1995), and reference lists of pertinent articles and reports for experimental studies of the effects of butter, dairy or milk fat, margarine, or hardened or (partially) hydrogenated fat. Twenty-eight studies directly compared the effects of butter and margarine on blood lipids in humans.

We selected studies in which subjects had stable body weights, at least two-thirds of the intervention consisted of exchanging margarine isocalorically for butter and dairy fats, and in which differences in total fat or carbohydrates between the margarine and the butter diets made up less than 3% of energy intake. This yielded 20 studies [3,14–32] which provided 49 dietary comparisons (Table 1). Twelve were metabolic-ward trials in which all food was provided, and eight employed free-living subjects who were provided with the fats under investigation. Experimental diets were consumed for 8–175 days, and margarine or butter provided between 5 and 45% of total caloric intake.

We classified the margarines as hard (stick or wrapper) or soft (tub). Most studies used commercial margarines, but some also investigated fat blends suitable for margarine production. The majority of the margarines were made of partially hydrogenated or unmodified vegetable oils. The remainder contained lard, tallow, or partially hydrogenated fish or whale oil (Table 1).

Missing information on dietary intervention and the fatty acid composition of the margarines was obtained from the authors [25,28,29] or was estimated from data on commercial margarines that were current at the time of the study in question [17,19,26].

2.2. Data analysis

We calculated the changes in serum or plasma total, LDL, and HDL cholesterol levels, in the ratio of total to HDL cholesterol, and in triglyceride levels as a function of the amount of margarine exchanged for butter (percentage of total caloric intake). Regression analyses were performed using the General Linear Models (GLM) procedure of the SAS package [33]. For cross-over and sequential designs we subtracted the mean level at the end of the margarine period from that at the end of the butter period. For parallel studies, we calculated the difference between the changes on the two treatments. Exchanging margarine for butter comprised on average 97% of calories of the total dietary intervention. For cross-over and parallel studies, the observed changes could be fully attributed to the replacement of butter by margarine, because the study design eliminates drift of variables over time. For sequential designs, spurious changes may be observed because subjects' lipid levels may decrease when they participate in dietary trials, regardless the nature of the dietary intervention. However, of the 13 comparisons with a sequential design (Table 1), seven first supplied the margarine diet and then the butter diet, and the other six first supplied the butter diet. As a result, the effect of drifts of lipid and lipoprotein levels with time on the difference between margarine and butter probably averaged out in the combined estimates. Thus, changes were almost completely attributable to the dietary fats themselves, and zero substitution should produce no change. Therefore, regression lines were forced through the origin.

In analyses of the relation between changes in lipoprotein cholesterol levels and *trans* and saturated fatty acid content, regression lines were not forced through the origin, because other aspects of the margarines, e.g. content of other fatty acids or cholesterol, may vary and affect lipoprotein levels independent of the *trans* or saturated fatty acid content.

The number of subjects varied among the trials. To take this into account, it is usual in meta-analyses to weight each study by the reciprocal of the squared standard error. Most studies did not report the standard error of the differences in lipoprotein levels between subjects on butter and on margarine. We therefore weighted by the square root of the number of subjects, which is inversely proportional to the standard error. This yielded results essentially similar to those obtained by unweighted analysis; therefore we present only unweighted results.

3. Results

Twenty studies comprising 49 comparisons of butter and margarine met our criteria. These were published between 1957 and 1995 (Table 1). Most studies provided one or two dietary comparisons, but de Iongh et al. provided five [22], and Beveridge et al. 16 [20]. Ten studies published between 1980 and 1995 and comprising 15 dietary comparisons provided data on HDL cholesterol.

In 32 comparisons involving a total of 402 subjects hard stick or 'brick' margarine was used; the other 17 comparisons, involving 939 subjects, used soft tub margarines. In five comparisons margarine containing partially hydrogenated fish oils was used. Fig. 1 shows the average composition of butter and of the margarines in the studies reviewed here. Butter contains on average 51 g saturated, 3 g *trans*, 21 g *cis*-monounsaturated, and 2 g of *cis*-polyunsaturated fatty acids per 100g. The margarines on average contained 20 g saturated, 18 g *trans* (range 0–39 g), 22 g *cis*-monounsaturated, and 18 g of *cis*-polyunsaturated fatty acids per 100 g of

Table 1
Overview of studies that compared effects of margarine versus butter on serum lipids in humans

First author and year	*N*	Design and setting[a]	Days	Margarine		Amount (% calories exchanged)	Difference in plasma cholesterol (margarine minus butter, mmol/l)		
				Type[b]	*Trans* content (g/100g)		Total	LDL	HDL
Keys [14] 1957	18	//, controlled, 5–7/arm	11	A: Hard, comm, fish,	13	11	+0.04	+0.12	
				B: Hard, comm, veg	14		−0.09	+0.12	
Horlick [15] 1960	4	Linear, controlled, 2 subjects	8	A: Soft, expt, veg	12	40	−0.91		
				B: Hard, comm, veg	20		−0.26		
Anderson [16] 1961	23	X, controlled	21	Hard, expt, veg	38	31	−0.62		
Wilcox [17] 1961	8	Linear, controlled	15	Hard, comm, veg	24	27	−1.22		
Antonis [18] 1962	36	//, controlled, 18–20/arm	175	Hard, expt, veg	24	25	−0.88	−0.70	
Morse [19] 1962	12	//, controlled, 4/arm	42	A: Hard, comm, veg	20	37	−1.40		
				B: Soft, comm, veg	12		−1.40		
Beveridge [20] 1962 moderate amount of margarine	88	//, controlled, ca. 9/arm	8	A: Soft, comm, veg	17	22.5	−0.35		
				B: Hard, comm, veg	32		−0.48		
				C: Hard, comm, veg	25		−0.51		
				D: Hard, comm, veg	28		−0.39		
				E: Hard, comm, veg	22		−0.60		
				F: Hard, comm, lard	17		−0.35		
				G: Hard, comm, veg	34		−0.59		
				H: Hard, comm, lard	24		−0.58		
Beveridge [20] 1962 high amount of margarine	91	//, controlled, ca. 9/arm	8	A: Soft, comm, veg	17	45	−0.93		
				B: Hard, comm, veg	32		−0.58		
				C: Hard, comm, veg	25		−0.79		
				D: Hard, comm, veg	28		−0.67		
				E: Hard, comm, veg	22		−0.65		
				F: Hard, comm, lard	17		−1.10		
				G: Hard, comm, veg	34		−0.89		
				H: Hard, comm, lard	24		−0.56		
McOsker [21] 1962	22	X, controlled	56	A: Soft, comm, veg	11	39	−1.17		
				B: Hard, comm, veg	16		−0.94		
				C: Hard, expt, lard	6		−0.74		
de Iongh [22] 1965	33	linear, controlled	35	A: Hard, comm	16	30	−0.54		
				B: Hard, exp, fish	16		−0.59		
				C: Hard, exp, veg	39		−0.70		
				D: Hard, exp, fish	28		−0.72		
				E: Soft, exp, fish	5		−0.62		
Dalderup [23] 1969	577	X, free-living	91	Diet, comm, veg 4	24		−0.48		
Vessby [24] 1980	30	Linear, controlled	14	Diet, comm, veg 4	22		−0.90	−0.48	−0.05
Kuusi [25] 1985	78	//, free-living	84	Diet, comm, veg 2	5		−0.26	−0.14	−0.06
Judd [26] 1988	23	X, controlled	42	Soft, comm, veg 12	9		−0.39	−0.39	0
Flynn [27] 1991	71	X, free-living	84	Hard, comm, veg 17	5		−0.23	−0.24	−0.02

Table 1 (continued)

First author and year	*N*	Design and setting[a]	Days	Margarine		Amount (% calories exchanged)	Difference in plasma cholesterol (margarine minus butter, mmol/l)		
				Type[b]	*Trans* content (g/100g)		Total	LDL	HDL
Fumeron [28] 1991	36	X, free-living	21	Diet, comm, veg	4	19	−0.68	−0.48	−0.04
Nestel [29] 1992	27	Linear, free-living	21	A: Soft, expt, veg	5	13	−0.34	−0.31	0
				B: Soft, expt, veg	21		+0.03	+0.05	0
				C: Soft, expt, veg	0		−0.05	−0.05	+0.10
Seppanen [30] 1992	23	Linear, free-living	42	Soft, comm, veg	13	8	−0.08	−0.14	+0.01
Wood [31] 1993	30	X, free-living	42	A: Hard, comm, veg	20	19	−0.18	−0.16	−0.03
				B: Soft, expt, veg	0		−0.05	−0.11	0
Wood [32] 1993	40	X, free-living	42	A: Hard, comm, veg	23	19	−0.34	−0.31	−0.05
				B: Diet, comm, veg	0		−0.62	−0.52	−0.05
Almendingen [3] 1995	31	X, controlled	21	A: Hard, expt, veg	27	19	−0.21	−0.23	0
				B: Hard, expt, fish	32		+0.10	+0.13	−0.07

[a] //, parallel design; X, cross-over design; Linear, sequential design, margarine fed after butter or vice versa.

[b] Comm, commercial brand; expt, experimental margarine; fish, containing partially hydrogenated fish or whale oil; lard, containing lard or beef tallow; veg, blend of (partially hydrogenated) vegetable oils.

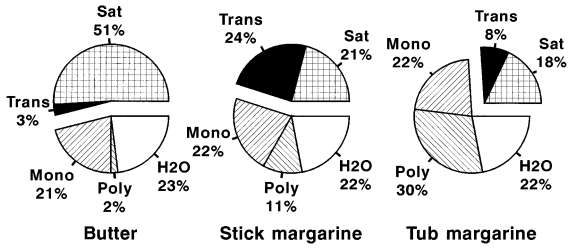

Fig. 1. Composition, in g per 100 g of product, of butter and of the average stick margarines ($N = 32$) and tub margarines ($N = 17$) used in the 20 experiments reviewed. Sat, saturated fatty acids; Trans, *trans* fatty acids; Mono, *cis*-monounsaturated fatty acids; Poly, polyunsaturated fatty acids; and H_20, water plus glycerol and other minor substances. Butter contains about 220 mg, vegetable margarines less than 1 mg, and margarines made with animal fats 70–275 mg cholesterol per 100 g of product.

product. The most abundant saturated fatty acid in both butter and margarine was palmitic acid (C16:0), followed in butter by myristic acid (C14:0) and followed by stearic acid (C18:0) in margarines. Hard stick or 'brick' margarines contained 16 g more *trans* and 19 g less polyunsaturated fatty acids per 100 g than the softer tub margarines (Fig. 1).

3.1. Effects on lipoprotein cholesterol

Substitution of margarine for butter lowered the total cholesterol level in 46 out of 49 comparisons (Fig. 2); for all margarines combined cholesterol decreased on average by 0.21 mmol/l ($P < 0.001$; 95% CI, -0.23 to -0.18 mmol/l) per 10% of daily calories as margarine substituted for butter. Total cholesterol was lowered by 0.19 mmol/l (95% CI; -0.22 to -0.16 mmol/l) on stick and by 0.25 mmol/l (95% CI, -0.30 to -0.20 mmol/l) on tub margarine per 10% of calories exchanged ($P = 0.05$ for difference between stick and tub margarine). Excluding margarines containing partially hydrogenated fish oil did not change these results.

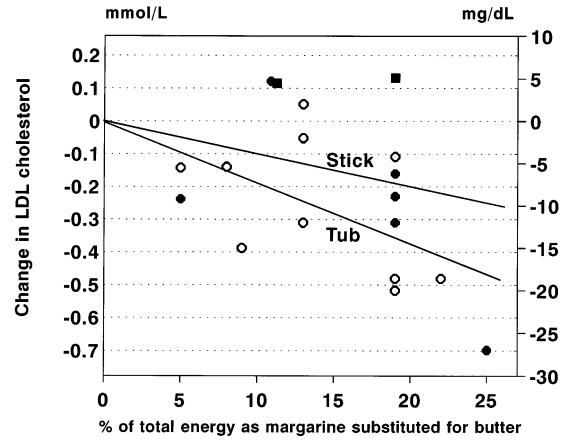

Fig. 3. Changes in LDL cholesterol levels on margarine versus butter diets in 20 studies providing 49 comparisons. (●) Hard stick vegetable margarine; (■) hard stick margarine with partially hydrogenated fish oil; and (○) soft tub margarine.

LDL cholesterol decreased by 0.15 mmol/l for all margarines combined ($N = 18$; $P < 0.001$; 95%CI, -0.22 to -0.08 mmol/l) (Fig. 3). It was lowered by 0.11 mmol/l per 10% of calories on stick ($N = 8$; $P = 0.066$; 95% CI, -0.24 to $+0.01$ mmol/l) and by 0.20 mmol/l on tub margarine ($N = 10$; $P < 0.001$; 95% CI, -0.28 to -0.11 mmol/l; $P = 0.40$ for difference between stick and tub margarine). If margarines with hydrogenated fish oil were excluded, hard margarine lowered LDL cholesterol by 0.17 mmol/l ($N = 6$; $P = 0.021$; 95% CI, -0.29 to -0.03 mmol/l).

Fig. 4 shows the changes in HDL cholesterol and Fig. 5 those in the total/HDL cholesterol ratio. Stick margarine lowered HDL cholesterol by 0.02 mmol/l ($N = 5$; $P = 0.045$; 95% CI, -0.04 to -0.00 mmol/l) and non-significantly raised the total/HDL cholesterol

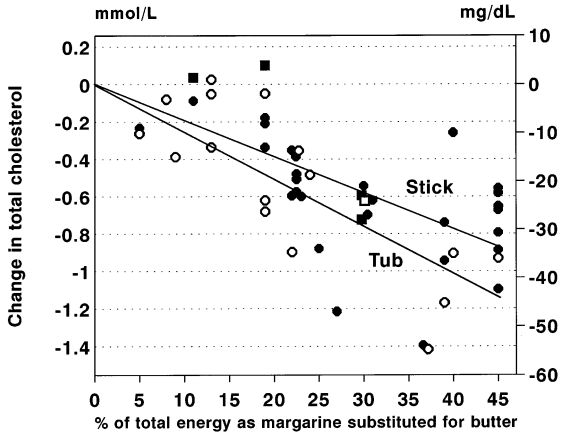

Fig. 2. Changes in total cholesterol levels on margarine versus butter diets in 20 studies providing 49 comparisons. (●) Hard stick vegetable margarine; (■) hard stick margarine with partially hydrogenated fish oil; and (○) soft tub margarine.

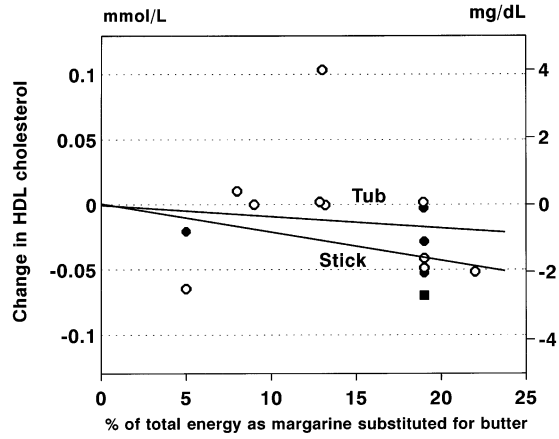

Fig. 4. Changes in HDL cholesterol levels on margarine versus butter diets in 20 studies providing 49 comparisons. (●) Hard stick vegetable margarine; (■) hard stick margarine with partially hydrogenated fish oil; (○) soft tub margarine.

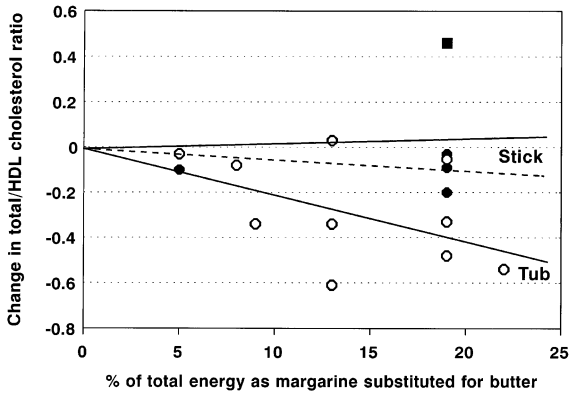

Fig. 5. Changes in the total to HDL cholesterol ratio on margarine versus butter diets in ten studies providing 15 dietary comparisons. (●) Hard stick vegetable margarine; (■) hard stick margarine with partially hydrogenated fish oil; (○) soft tub margarine. The dashed line represents the regression line for vegetable stick margarines.

ratio by 0.01 units ($P = 0.83$) per 10% of calories relative to butter. Soft tub margarines did not significantly affect HDL cholesterol levels (-0.01 mmol/l; $N = 10$; $P = 0.45$) and lowered the total/HDL cholesterol ratio by 0.20 units ($P < 0.002$; 95% CI, -0.29 to -0.10, $P < 0.025$ for difference with stick margarine). For stick margarines, these estimates were based on five comparisons involving 172 subjects. The one comparison using margarine with partially hydrogenated fish oil [3] showed a substantial increase in the total/HDL cholesterol ratio not observed for the other hard margarines. The vegetable stick margarines combined lowered the total/HDL cholesterol ratio non-significantly by 0.06 units per 10% of calories exchanged ($N = 4$; $P = 0.094$; 95% CI, -0.14 to 0.02), which was still significantly smaller than the reduction of 0.20 seen with soft tub margarines.

Forty-six percent of the variance in the change in total cholesterol when margarine replaced butter was explained by the reduction in saturated fatty acids, whereas the change in *trans* fatty acid intake explained only 11%. In contrast, the change in the ratio of total to HDL cholesterol in plasma was significantly predicted only by the change in *trans* fatty acid intake (Fig. 6) ($r^2 = 42\%$, $P = 0.009$), but not by the change in saturated fatty acid intake ($r^2 = 2\%$, $P = 0.62$).

3.2. Other cardiovascular risk factors

Effects on serum triglycerides were minimal. Changes in apolipoprotein A-I and B generally followed changes in HDL and LDL cholesterol [3,24,28,31,32]. Margarines raised lipoprotein(a) levels in two studies [3,29] compared with butter. A high-linoleic acid, low-*trans* margarine was reported to prolong blood clotting time [34].

4. Discussion

4.1. Lipoprotein cholesterol

Replacement of butter by margarine reduced the total and LDL cholesterol concentration, but hard stick margarines also produced somewhat lower HDL cholesterol levels. As a result the total to HDL cholesterol ratio was not significantly changed. Soft tub margarines did significantly reduce the total to HDL cholesterol ratio. This ratio is probably the best blood lipid predictor of coronary heart disease [35], and high values are associated with markedly increased risk [36]. Our data thus suggest that improvement of the lipoprotein risk profile through replacement of butter by margarine is feasible but that it depends on the type, and consequently the fatty acid composition, of the margarine.

4.2. Fatty acid composition of margarines

Some margarines are an important source of dietary *trans* fatty acids, while butter is high in saturated fatty acids but contains only a low proportion of *trans*. *Trans* fatty acids and saturates produce similarly high levels of LDL cholesterol in plasma, but *trans* fatty acids also lower HDL cholesterol [37]. One might therefore expect that substitution of margarines for butter would increase the ratio of total to HDL cholesterol in plasma, or at best leave it unchanged. However, we found that soft margarines decreased the ratio of total to HDL cholesterol as compared with butter, whereas hard margarines did not. The explanation of these findings probably lies in the absolute amounts of *trans* and saturated fatty acids in butter in comparison with margarines. As illustrated in Fig. 1, the combined amount of saturated plus *trans* fatty acids in the studies reviewed was about 54/100 g for butter, 45/100 g for hard stick margarines and about 26/100 g for softer tub margarines, the remainder being *cis*-unsaturated fatty acids. Analysis of food fats sold nowadays in the US and Europe [38,39] also shows that the saturated plus *trans* fatty acid content is commonly highest in butter, intermediate in stick, and lowest in tub margarines. Replacement of butter by margarine thus involves replacing saturated fat by a mix of *trans* and *cis* unsaturated fat. If the proportion of *trans* is high, as it is in stick margarines, the effect on the total to HDL cholesterol ratio in plasma will be nil. If butter is replaced by a margarine low in *trans* and high in *cis*-unsaturated fat the total/HDL cholesterol ratio in plasma will fall [40]. Hard margarines with partially hydrogenated fish oil may contain higher amounts of saturated plus *trans* fatty acids than butter; the study by Almendingen et al. [3] shows that such margarines may increase the total/HDL cholesterol ratio compared with butter and with

hard margarines containing partially hydrogenated vegetable oils (Fig. 5).

European soft margarines nowadays contain less *trans* than the products reviewed here (Fig. 1) or sold in the US [39,41]. Such soft margarines are low in saturated and free of *trans* fatty acids, and are thus expected to produce somewhat lower total/HDL ratios than the soft margarines reviewed here.

Until recently, stick margarines in both Europe and the US contained 15–25 g *trans* per 100 g product [39,42]. Outside the US, hard margarines are increasingly made with tropical oils instead of partially hydrogenated oils, both because of price and because of the negative publicity about *trans* fatty acids. This confers a health benefit if the sum of *trans* plus saturated fatty acids in the product is lowered, but not if a decrease in *trans* fatty acids is bought at the expense of a larger increase in lauric, myristic, or palmitic acid, which will raise LDL cholesterol [43]. For optimal effects on the lipoprotein profile, the sum of *trans* plus saturated fat in margarines should be as low as possible.

Replacement of butter by vegetable margarines also reduces cholesterol intake, and this accounts for about 30% of the fall in total cholesterol observed here (Fig. 2) [44,45]. However, the reduction in dietary cholesterol also lowers HDL cholesterol [46–49]; therefore the observed changes in the total to HDL cholesterol ratio are probably due to changes in fatty acid rather than cholesterol intake.

4.3. Methodological issues

The number of subjects varied widely between studies. However, weighting each comparison by the square root of the number of subjects yielded results virtually identical to those obtained by unweighted regression. Stratification of the dietary comparisons according to study design (cross-over, parallel, or sequential) or according to study setting (metabolic ward versus free-living) also did not affect outcomes. However, the effects of study setting could not be separated from the effect of the type of margarine used (Table 1); soft margarines were predominantly tested in free-living settings, where the amount of margarine consumed may have been less then prescribed. The effects of soft margarines could thus have been underestimated. Excluding one study [20] which provided 16 comparisons for total cholesterol did not affect outcomes. Thus, our findings changed little when different analytical approaches were used.

4.4. Labelling of food fats

Our data suggest that knowledge of the saturated fat content of dietary fats is not sufficient to predict their effect on coronary heart disease risk. Changes in saturated fat intake predicted 46% of the variance of the change in total cholesterol but none of that in the total to HDL cholesterol ratio, which is a better predictor of coronary heart disease than the level of total cholesterol [36]. In contrast, the change in *trans* fat predicted 42% of the change in the total/HDL cholesterol ratio. Fig. 6 illustrates that the total/HDL cholesterol ratio was favourably affected in those experiments in which margarine supplied about the same amount of *trans* fatty acids as butter (zero change), and was less affected or increased with margarines supplying larger amounts of *trans* fat. This is consistent with the unfavourable effect of *trans* fatty acids on the total/HDL cholesterol ratio observed in recent trials [50]. Food labelling regulations in most countries require declaration of the saturated fat content but not of the *trans* content. Nearly half of the margarines sold nowadays in the US are of the more traditional stick type, which contain substantial amounts of *trans* fatty acids [51]. Adding the *trans* contents on labels would help patients with moderate hypercholesterolemia to select foods that lower their total to HDL cholesterol ratio in blood.

4.5. Predicted consequences for CHD risk

Each 0.6 mmol/l decrease in total or LDL cholesterol reduces coronary heart disease risk by 50% at age 40 [52]. Based on these figures, substituting 10% of calories or 30 g of margarine for butter (25 g of triglycerides) in a 2200 kcal diet would reduce CHD risk by 9–16% for stick and by 17–21% for tub margarine. However, such an approach ignores changes in HDL cholesterol induced by margarines. There is evidence that HDL is causally involved in atherosclerosis [53–57] and thus a more prudent approach should take changes in plasma HDL into account. We therefore based calculations of heart disease risk on the ratio of total to HDL choles-

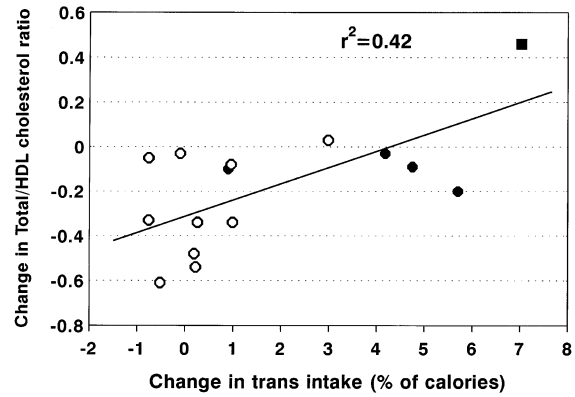

Fig. 6. Changes in the ratio of total to HDL cholesterol in 15 dietary comparisons as a function of the change in *trans* fatty acid intake accompanying the replacement of butter with margarine. (●) Hard stick vegetable margarine; (■) hard stick margarine with partially hydrogenated fish oil; (○) soft tub margarine.

terol, which is a superior measure compared with either total or LDL cholesterol [36].

Our estimate of the effect of hard stick margarine on total/HDL cholesterol was based on five data points (Fig. 5), but these comprised a total of 172 subjects studied in properly controlled trials in three locations over periods of 3–12 weeks. Elimination of the one outlying comparison did not materially affect the estimate. We therefore regard our estimate as the best figure currently available for the effect of hard stick margarine on the total/HDL cholesterol ratio. Every reduction of 0.01 in this ratio reduces the risk of myocardial infarction by approximately 0.5% [35]. This would imply that replacing 30 g of butter with stick margarine would not affect CHD risk, while replacing butter with soft tub margarine would reduce the risk by 10%. A still larger risk reduction might be achieved by replacing butter and other hard fats with modern low-saturated zero-*trans* margarines, which have a fatty acid composition approximating that of liquid oils [58].

Our risk predictions agree with the outcomes of the Finnish Mental Hospital Study [59,60], in which replacement of butter and dairy fats by a soft margarine low in *trans* and high in *cis*-polyunsaturated fatty acids lowered CHD incidence by 45% in the men ($P = 0.008$) and by 36% in the women ($P = 0.07$) during 6 years of treatment. As for other risk factors, *trans* fatty acids raise lipoprotein(a) levels [3,29,61]; this might cause some additional increase in CHD risk when large amounts of hard *trans*-rich margarines are consumed. Blood pressure is probably not affected by exchanging butter and margarine [62–65]. The effects of different fatty acids on blood clotting tendency and fibrinolysis are poorly understood, but some studies tend to favour *cis*-unsaturated over saturated fatty acids [34,66,67]. Cholesterol in butter probably does not affect the total to HDL cholesterol ratio, but it has been argued that dietary cholesterol is atherogenic-independent of its effect on lipoprotein cholesterol [68]. This would imply that reducing cholesterol intake by substituting margarine for butter would add to the CHD risk reduction caused by changes in fatty acid intake.

In US Nurses, consumption of margarines and of *trans* fatty acids from vegetable fats was associated with a significant increase in CHD risk [5]. In Framingham, consumption of margarine—but not butter—at entry was associated with CHD incidence in men in the next 20 years [69]. The Nurses recorded their diets in 1980 and the Framingham men in 1966–69, and it is likely that the margarines and shortenings consumed in the US at that time were mainly hard, high-*trans* products [70]. In the Iowa Women's Health Study, consumption of margarine was negatively associated with CHD mortality [71]. This association weakened after adjustment for vitamin E intake, suggesting that it could be partly attributed to protection by vitamin E. However, vitamin-E-rich margarines are generally also rich in polyunsaturated fatty acids, and they also tend to be lower in *trans* [42]. Thus, vitamin E content may be a marker for the type of margarine, and the data from the Iowa women [71] are compatible with a protective effect of soft tub margarines.

5. Conclusion

Our findings support recent FAO/WHO recommendations that consumers should replace hard fats with liquid oils and soft fats to reduce the intake of both saturated and *trans* fatty acids [72]. However, consumers can make optimal choices only if *trans* contents are reported on the labels of food fats.

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References

[1] Mensink RP, Katan MB. Effect of dietary trans fatty acids on high-density and low-density lipoprotein cholesterol levels in healthy subjects. N Engl J Med 1990;323:439.
[2] Zock PL, Katan MB. Hydrogenation alternatives: effects of trans fatty acids and stearic acid versus linoleic acid on serum lipids and lipoproteins in humans. J Lipid Res 1992;33:399.
[3] Almendingen K, Jordal O, Kierulf P, Sandstad B, Pedersen JI. Effects of partially hydrogenated fish oil, partially hydrogenated soybean oil and butter on serum lipoproteins and Lp[a] in men. J Lipid Res 1995;36:1370.
[4] Thomas LH, Winter JA, Scott RG. Concentration of 18:1 and 16:1 *trans* unsaturated fatty acids in the adipose body tissue of decedents dying of ischaemic heart disease compared with controls: analysis by gas liquid chromatography. J Epidemiol Community Health 1983;37:16.
[5] Willett WC, Stampfer MJ, Manson JE, et al. Intake of *trans* fatty acids and risk of coronary heart disease among women. Lancet 1993;341:581.
[6] Ascherio A, Hennekens CH, Buring JE, Master C, Stampfer MJ, Willett WC. Trans-fatty acids intake and risk of myocardial infarction. Circulation 1994;89:94.
[7] Ascherio A, Rimm EB, Giovannucci EL, Spiegelman D, Stampfer M, Willett WC. Dietary fat and risk of coronary heart disease in men: cohort follow up study in the United States. Br Med J 1996;313:84.
[8] Aro A, Kardinaal AFM, Salminen I, et al. Adipose tissue isomeric *trans* fatty acids and risk of myocardial infarction in nine countries: the EURAMIC study. Lancet 1995;345:273.
[9] Roberts TL, Wood DA, Riemersma RA, Gallagher PJ, Lampe FC. *Trans* isomers of oleic and linoleic acids in adipose tissue and sudden cardiac death. Lancet 1995;345:278.
[10] Grundy SM. Trans monounsaturated fatty acids and serum cholesterol levels. N Engl J Med 1990;323:480.
[11] Willett WC, Ascherio A. *Trans* fatty acids: are the effects only marginal? Am J Public Health 1994;84:722.

[12] Mann GV. Metabolic consequences of dietary trans fatty acids. Lancet 1994;343:1268.
[13] Longnecker MP. Do trans fatty acids in margarine and other foods increase the risk of coronary heart disease? Epidemiology 1993;4:492.
[14] Keys A, Kimura N, Kusukawa A, Yoshitomi M. Serum cholesterol in Japanese coal miners. A dietary experiment. Am J Clin Nutr 1957;5:245.
[15] Horlick L. The effect of artificial modification of food on the serum cholesterol level. Can Med Assoc J 1960;83:1186.
[16] Anderson JT, Grande F, Keys A. Hydrogenated fats in the diet and lipids in the serum of man. J Nutr 1961;75:388.
[17] Wilcox EB, Galloway LS. Serum cholesterol and different dietary fats. J Am Diet Assoc 1961;38:227.
[18] Antonis A, Bersohn I. The influence of diet on serum lipids in South African White and Bantu prisoners. Am J Clin Nutr 1962;10:484.
[19] Morse EH, Bicknell E, Lewis EP, Merrow SB, Newhall CA. Relation of dietary fats to blood lipids in young men. J Am Diet Assoc 1962;41:323.
[20] Beveridge JMR, Connell WF. The effect of commercial margarines on plasma cholesterol levels in man. Am J Clin Nutr 1962;10:391.
[21] McOsker DE, Mattson FH, Sweringen HB, Cincinnati BCE, Kligman AM. The influence of partially hydrogenated dietary fats on serum cholesterol levels. J Am Med Assoc 1962;180:380.
[22] de Iongh H, Beerthuis RK, den Hartog C, Dalderup LM, van der Spek PAF. The influence of some dietary fats on serum lipids in man. Bibl Nutr Dieta 1965;7:137.
[23] Dalderup LM, Doornbos R, den Hartog C, Van Haard WB, De Vries JE, Keller GHM. A practical method for decreasing the serum cholesterol level in man. Am J Clin Nutr 1969;22:1521.
[24] Vessby B, Gustafsson I-B, Boberg J, Karlström B, Lithell H, Werner I. Substituting polyunsaturated for saturated fat as a single change in a Swedish diet: effects on serum lipoprotein metabolism and glucose tolerance in patients with hyperlipoproteinaemia. Eur J Clin Invest 1980;10:193.
[25] Kuusi T, Ehnholm C, Huttunen JK, et al. Concentration and composition of serum lipoproteins during a low-fat diet at two levels of polyunsaturated fat. J Lipid Res 1985;26:360.
[26] Judd JT, Oh SY, Henning B, Dupont J, Marshall MW. Effects of low fat diets differing in degree of fat unsaturation on plasma lipids, lipoproteins, and apolipoproteins in adult men. J Am Coll Nutr 1988;7:223.
[27] Flynn MA, Nolph GB, Sun GY, Navidi M, Krause G. Effects of cholesterol and fat modification of self-selected diets on serum lipids and their specific fatty acids in normocholesterolemic and hypercholesterolemic humans. J Am Coll Nutr 1991;10:93.
[28] Fumeron F, Brigant L, Parra H-J, Bard J-M, Fruchart J-C, Apfelbaum M. Lowering of HDL_2-cholesterol and lipoprotein A-I particle levels by increasing the ratio of polyunsaturated to saturated fatty acids. Am J Clin Nutr 1991;53:655.
[29] Nestel P, Noakes M, Belling B, et al. Plasma lipoprotein lipid and Lp(a) changes with substitution of elaidic acid for oleic acid in the diet. J Lipid Res 1992;33:1029.
[30] Seppänen-Laakso T, Vanhanen H, Laakso I, Kohtamäki H, Viikari J. Replacement of butter on bread by rapeseed oil and rapeseed oil-containing margarine: effects on plasma fatty acid composition and serum cholesterol. Br J Nutr 1992;68:639.
[31] Wood R, Kubena K, Tseng S, Martin G, Crook R. Effect of palm oil, margarine, butter, and sunflower oil on the serum lipids and lipoproteins of normocholesterolemic middle-aged men. J Nutr Biochem 1993;4:286.
[32] Wood R, Kubena K, O'Brien B, Tseng S, Martin G. Effect of butter, mono- and polyunsaturated fatty acid-enriched butter, *trans* fatty acid margarine, and zero *trans* fatty acid margarine on serum lipids and lipoproteins in healthy men. J Lipid Res 1993;34:1.
[33] SAS Institute. SAS/STAT User's Guide, Version 6, 4th edn., Volume 2. Cary, NC: SAS Institute, 1989.
[34] O'Brien JR, Etherington MD, Jamieson S. Acute platelet changes after large meals of saturated and unsaturated fats. Lancet 1976;i:878.
[35] Stampfer MJ, Sacks FM, Salvani S, Willett WC, Hennekens CH. A prospective study of cholesterol, apolipoproteins, and the risk of myocardial infarction. N Engl J Med 1991;325:373.
[36] Kinosian B, Glick H, Garland G. Cholesterol and coronary heart disease: predicting risks by levels and ratios. Ann Intern Med 1994;121:641.
[37] Zock PL, Mensink RP, Katan MB. Dietary trans fatty acids and lipoprotein cholesterol (Letter). Am J Clin Nutr 1995;61:617.
[38] Michels K, Sacks F. Trans fatty acids in European margarines (Letter). N Engl J Med 1995;332:541.
[39] Exler J, Lemar L, Smith J. USDA Food Composition Data: Fat and fatty acid content of selected foods containing trans-fatty acids. Special purpose table no. 1. at http://www.nal.USDA.gov/fnic/foodcomp/data/
[40] Mensink RP, Katan MB. Effect of dietary fatty acids on serum lipids and lipoproteins: a meta-analysis of 27 trials. Arterioscler Thromb 1992;12:911.
[41] Katan MB. Exit *trans* fatty acids (Commentary). Lancet 1995;346:1245.
[42] Hulshof PJM, van de Bovenkamp P, Boogerd L, et al. Food analyses of the Department of Human Nutrition. Part 11: Edible Fats and Oils (In Dutch). Wageningen: Department of Human Nutrition, Agricultural University, 1991.
[43] Zock PL, de Vries JHM, Katan MB. Impact of myristic acid versus palmitic acid on serum lipid and lipoprotein levels in healthy women and men. Arterioscler Thromb 1994;14:567.
[44] Keys A, Anderson JT, Grande F. Serum cholesterol response to changes in the diet. II. The effect of cholesterol in the diet. Metabolism 1965;14:759.
[45] Hegsted DM. Serum-cholesterol response to dietary cholesterol: a re-evaluation. Am J Clin Nutr 1986;44:299.
[46] Katan MB, Berns MAM, Glatz JFC, Knuiman JT, Nobels A, Vries JHM. Congruence of individual responsiveness to dietary cholesterol and to saturated fat in humans. J Lipid Res 1988;29:883.
[47] Brown SA, Morrisett J, Patsch JR, Reeves R, Gotto AM, Jr., Patsch W. Influence of short term dietary cholesterol and fat on human plasma Lp(a) and LDL levels. J Lipid Res 1991;32:1281.
[48] Hegsted DM, Ausman LM, Johnson JA, Dallal GE. Dietary fat and serum lipids—an evaluation of the experimental data. Am J Clin Nutr 1993;57:875.
[49] Ginsberg HN, Karmally W, Siddiqui M, et al. Increases in dietary cholesterol are associated with modest increases in both LDL and HDL cholesterol in healthy young women. Arterioscler Thromb Vasc Biol 1995;15:169.
[50] Willett WC, Ascherio A. Response to the International Life Sciences Institute report on *trans* fatty acids. Am J Clin Nutr 1995;62:524.
[51] Expert Panel on Trans Fatty Acids and Coronary Heart Disease. Trans fatty acids and coronary heart disease risk. Kris-Etherton PM (ed). Am J Clin Nutr 1995;62:655S.
[52] Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? Br Med J 1994;308:367.
[53] NIH Consensus Development Panel. Triglyceride, high-density lipoprotein, and coronary heart disease. J Am Med Assoc 1993;269:505.
[54] Kitamura A, Iso H, Naito Y, et al. High-density lipoprotein cholesterol and premature coronary heart disease in urban Japanese men. Circulation 1994;89:2533.
[55] Johansson J, Olsson AG, Bergstrand L, et al. Lowering of HDL2b by probucol partly explains the failure of the drug to

affect femoral atherosclerosis in subjects with hypercholesterolemia. A Probucol Quantitative Regression Swedish Trial (PQRST) report. Arterioscler Thromb Vasc Biol 1995;15:1049.
[56] Serfaty-Lacrosniere C, Civeira F, Lanzberg A, et al. Homozygous Tangier disease and cardiovascular disease. Atherosclerosis 1994;107:85.
[57] Tall AR. Plasma cholesteryl ester transfer protein and high-density lipoproteins: new insights from molecular genetics studies. J Intern Med 1995;237:5.
[58] Katan MB. European researcher calls for reconsideration of trans fatty acids (Letter). J Am Diet Assoc 1994;94:1097.
[59] Turpeinen O, Karvonen MJ, Pekkarinen M, Miettinen M, Elosuo R, Paavilainen E. Dietary prevention of coronary heart disease: the Finnish Mental Hospital Study. Int J Epidemiol 1979;8:99.
[60] Miettinen M, Turpeinen O, Karvonen MJ, Pekkarinen M, Paavilainen E, Elosuo R. Dietary prevention of coronary heart disease in women: the Finnish Mental Hospital Study. Int J Epidemiol 1983;12:17.
[61] Mensink RP, Zock PL, Katan MB, Hornstra G. Effect of dietary cis and trans fatty acids on serum lipoprotein(a) levels in humans. J Lipid Res 1992;33:1493.
[62] Margetts BM, Beilin LJ, Armstrong BK, et al. Blood pressure and dietary polyunsaturated and saturated fats: a controlled trial. Clin Sci 1985;69:165.
[63] Sacks FM, Stampfer MJ, Munoz A, McManus K, Canessa M, Kass EH. Effect of linoleic and oleic acids on blood pressure, blood viscosity, and erythrocyte cation transport. J Am Coll Nutr 1987;6:179.
[64] Mensink RP, de Louw MHJ, Katan MB. Effects of dietary trans fatty acids on blood pressure in normotensive subjects. Eur J Clin Nutr 1991;45:375.
[65] Zock PL, Blijlevens RAMT, de Vries JHM, Katan MB. Effects of stearic acid and trans fatty acids verus linoleic acid on blood pressure in normotensive women and men. Eur J Clin Nutr 1993;47:437.
[66] Renaud S, Godsey F, Dumont E, Thevenon C, Ortchanian E, Martin JL. Influence of long-term diet modification on platelet function and composition in Moselle farmers. Am J Clin Nutr 1986;43:136.
[67] Tholstrup T, Marckmann P, Jespersen J, Vessby B, Jart A, Sandström B. Effect on blood lipids, coaggulation, and fibrinolysis of a fat high in myristic acid and a fat high in palmitic acid. Am J Clin Nutr 1994;60:919.
[68] Stamler J, Shekelle R. Dietary cholesterol and human coronary heart disease. Arch Pathol Lab Med 1988;112:1032.
[69] Gillman MW, Cupples LA, Gagnon D, Posner BM, Ellison C, Castelli WP. Margarine intake and subsequent heart disease (Abstract). Circulation 1995;91:925.
[70] Sommerfeld M. Trans unsaturated fatty acids in natural products and processed foods. Prog Lipid Res 1983;22:221.
[71] Kushi LH, Folsom AR, Prineas RJ, Mink PJ, Wu Y, Bostick RM. Dietary antioxidant vitamins and death from coronary heart disease in postmenopausal women. N Engl J Med 1996;334:1156.
[72] Joint Experts. Fats and oils in human nutrition. Report of a joint expert consultation. Rome: FAO/WHO, 1994.