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Saturated Fats Compared With Unsaturated Fats and Sources of Carbohydrates in Relation to Risk of Coronary Heart Disease

A Prospective Cohort Study

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ABSTRACT

BACKGROUND The associations between dietary saturated fats and the risk of coronary heart disease (CHD) remain controversial, but few studies have compared saturated with unsaturated fats and sources of carbohydrates in relation to CHD risk.

OBJECTIVES This study sought to investigate associations of saturated fats compared with unsaturated fats and different sources of carbohydrates in relation to CHD risk.

METHODS We followed 84,628 women (Nurses' Health Study, 1980 to 2010), and 42,908 men (Health Professionals Follow-up Study, 1986 to 2010) who were free of diabetes, cardiovascular disease, and cancer at baseline. Diet was assessed by a semiquantitative food frequency questionnaire every 4 years.

RESULTS During 24 to 30 years of follow-up, we documented 7,667 incident cases of CHD. Higher intakes of polyunsaturated fatty acids (PUFAs) and carbohydrates from whole grains were significantly associated with a lower risk of CHD comparing the highest with lowest quintile for PUFAs (hazard ratio [HR]: 0.80, 95% confidence interval [CI]: 0.73 to 0.88; p trend <0.0001) and for carbohydrates from whole grains (HR: 0.90, 95% CI: 0.83 to 0.98; p trend $= 0.003$). In contrast, carbohydrates from refined starches/added sugars were positively associated with a risk of CHD (HR: 1.10, 95% CI: 1.00 to 1.21; p trend $= 0.04$). Replacing 5% of energy intake from saturated fats with equivalent energy intake from PUFAs, monounsaturated fatty acids, or carbohydrates from whole grains was associated with a 25%, 15%, and 9% lower risk of CHD, respectively (PUFAs, HR: 0.75, 95% CI: 0.67 to 0.84; $p < 0.0001$; monounsaturated fatty acids, HR: 0.85, 95% CI: 0.74 to 0.97; $p = 0.02$; carbohydrates from whole grains, HR: 0.91, 95% CI: 0.85 to 0.98; $p = 0.01$). Replacing saturated fats with carbohydrates from refined starches/added sugars was not significantly associated with CHD risk ($p > 0.10$).

CONCLUSIONS Our findings indicate that unsaturated fats, especially PUFAs, and/or high-quality carbohydrates can be used to replace saturated fats to reduce CHD risk. (J Am Coll Cardiol 2015;66:1538–48) © 2015 by the American College of Cardiology Foundation.

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A recent systematic review and meta-analysis reported no significant association between the consumption of saturated fatty acids (SFAs) and the risk of coronary heart disease (CHD) (1), but the study failed to specify the replacement macronutrient for saturated fat. Another meta-analysis observed that substituting SFAs with overall carbohydrates was not associated with the risk of CHD (2). Consistent with this analysis, a low-carbohydrate diet score (a higher score being indicative of higher protein and fat intake and lower intake of carbohydrates) was not associated with an increased CHD risk in women (3). None of these studies, however, discriminated between different sources of dietary carbohydrates.

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Carbohydrates, traditionally classified as simple versus complex, depending on the number of chained sugar moieties, are also frequently classified according to their effect on blood sugar levels, as quantified by the glycemic index (GI). Carbohydrate classification by the GI has been shown to be more strongly associated with cardiometabolic disease than total carbohydrates. For example, whereas no association was observed between overall carbohydrate intake and the risk of CHD (4,5), diets with a low GI were associated with a lower risk of CHD (4,5) and type 2 diabetes (6) compared with high-GI diets. Therefore, it is not surprising that null associations between SFAs and coronary risk were observed in studies that did not distinguish between the quality of carbohydrates that were being substituted for SFAs.

Only a few studies have considered the quality of the carbohydrates substituting for SFAs in CHD (7,8). One study (7) observed that substituting SFAs with carbohydrates was associated with a nonsignificantly lower risk of myocardial infarction (MI) among participants who consumed a low-GI diet, but with a significantly increased risk among participants who consumed a high-GI diet. However, this association was not replicated in another study (8). To address uncertainties about the associations between dietary fats, carbohydrate quality, and CHD, we aimed to investigate the predicted effects of isocaloric substitutions of carbohydrates for fats, with an a priori hypothesis that the effects of different types of fats on the risk of CHD depend on the carbohydrate quality of the replacement. Two well-established cohorts of U.S. women and men: the NHS (Nurses' Health Study) (9) and the HPFS (Health Professionals Follow-up Study) (10) were the basis for this study. This analysis may have important public health implications for guiding people toward healthy dietary choices as they work to reduce their SFA intake.

PARTICIPANTS AND METHODS

STUDY POPULATION. In 1976, 121,701 female nurses in the United States 30 to 55 years of age enrolled in the NHS (9). In 1980, 98,047 of these women completed an extensive food frequency questionnaire (FFQ). In 1986, 51,529 U.S. men, 40 to 75 years of age, were enrolled in the HPFS and returned questionnaires about diet and medical history (10). Participants from both cohorts provided information on diet and lifestyle factors, medical history, and newly diagnosed diseases through self-administered mailed questionnaires at baseline and every 2 to 4 years thereafter.

For the present analysis, we excluded women and men (n = 7,615) with implausible FFQ data (<800 or >4,200 kcal/day for men, <600 or >3,500 kcal/day for women, or >70 food items missing). We also excluded participants with previously diagnosed cancer (n = 5,676), cardiovascular disease (n = 5,609), or diabetes (n = 3,137) at baseline, or loss of follow-up after baseline (n = 3). The final analysis sample size was 84,628 women and 42,908 men.

The study protocol was approved by the institutional review boards of Brigham and Women's Hospital and the Harvard T.H. Chan School of Public Health. Return of the self-administered questionnaires was considered informed consent.

ASCERTAINMENT OF CHD. We included nonfatal MI and CHD death as our primary endpoint of total CHD, which was identified primarily through a review of medical records, as previously described (11). Participants (or next of kin for deceased participants) reporting a primary endpoint were asked for permission to have their medical records reviewed by physicians who were blinded to the participant's risk factor status. MI was confirmed if the World Health Organization criteria were met (12). MIs that required hospital admission and for which confirmatory information was obtained by phone interview or letter, but for which no medical records were available, were classified as probable. We included all confirmed and probable cases because results were similar in both previous (9) and present analyses when probable cases were excluded.

Deaths were identified by reports from next of kin, the U.S. postal system, or using certificates obtained from state vital statistics departments and the National Death Index. Follow-up for deaths was >98% complete (13). Cases of fatal CHD specifically were

ABBREVIATIONS AND ACRONYMS

CHD = coronary heart disease
CI = confidence interval
FFQ = food frequency questionnaire
GI = glycemic index
HR = hazard ratio
MI = myocardial infarction
MUFA = monounsaturated fatty acid
PUFA = polyunsaturated fatty acid
SFA = saturated fatty acid