



Whole grain intake and cardiovascular disease: A meta-analysis

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Abstract *Background and aims:* Whole grain food sources have been associated with lowered risk of cardiovascular disease (CVD). Studies in recent years have strengthened this observation and elucidated potential mechanisms for this association. This study sought to quantitate the available observational evidence on whole grain intake and clinical cardiovascular events.

Methods and results: Seven prospective cohort studies with quantitative measures of dietary whole grains and clinical cardiovascular outcomes were identified from MEDLINE searches and a review of the literature. Based on event estimates adjusted for cardiovascular risk factors, greater whole grain intake (pooled average 2.5 servings/d vs. 0.2 servings/d) was associated with a 21% lower risk of CVD events [OR 0.79 (95% CI: 0.73–0.85)]. Similar estimates were noted for different CVD outcomes (heart disease, stroke, fatal CVD) and in sex-specific analyses. Conversely, refined grain intake was not associated with incident CVD events [1.07 (0.94–1.22)].

Conclusions: There is a consistent, inverse association between dietary whole grains and incident cardiovascular disease in epidemiological cohort studies. In light of this evidence, policy-makers, scientists, and clinicians should redouble efforts to incorporate clear messages on the beneficial effects of whole grains into public health and clinical practice endeavors.

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Introduction

Cardiovascular disease (CVD) accounts for one-third of deaths worldwide, and the World Health

Organization estimates that, over the next two decades, developing countries will bear the brunt of the increasing burden of CVD [1]. Over thirty years ago, Dr. Trowell noted that sub-Saharan Africa had a lower prevalence of ischemic heart disease than industrialized European and American populations, hypothesizing that observed differences were attributable to the relative intake of refined versus whole plant food sources [2]. This came to be known as the “fiber hypothesis”, which related fiber intake from cereal and plant sources to chronic heart and gastrointestinal diseases. The first prospective evaluation of the “fiber hypothesis” with respect to heart disease came from the United Kingdom [3]. Morris et al. found that cereal fiber (but not vegetable fiber) was negatively associated with incident ischemic heart disease. The first study to prospectively associate *whole grain* consumption with cardiovascular events was the Seventh Day Adventists’ study, in which individuals who consumed wheat bread had a 55% lower risk of non-fatal MI than those who ate white bread [4]. In 2003, Dr. Anderson synthesized data from thirteen studies evaluating intake of whole grains, fruits, vegetables, and fiber with respect to risk for clinical cardiovascular disease [5]. Of five studies prospectively evaluating whole grain intake and cardiovascular risk, higher intake of whole grains was associated with a 29% lower risk for cardiovascular events (adjusted RR 0.71, 95% CI 0.48–0.94). However, since this analysis, multiple observational studies have replicated this association and important causal pathways have been elucidated, including effects on glucose homeostasis, serum lipids, and endothelial function. We sought to quantitate the available observational evidence on whole grain intake and clinical cardiovascular events and review the potential mechanisms of this association.

Methods

We identified observational studies that evaluated the association between whole grain intake and clinical cardiovascular events using the following inclusion criteria: 1. the studies were performed using self-reported quantitative measures of whole grain intake (e.g. servings/day); 2. cardiovascular events were ascertained prospectively; and 3. the studies provided adequate data to generate adjusted event rates. Studies were identified from a MEDLINE search for ‘whole grain’ and ‘cardiovascular disease’ from 1966 to April 2006. Additional studies were drawn from reference lists of relevant manuscripts. Data were extracted by two independent investigators, and inconsistencies were

resolved by mutual agreement. For within-study comparisons, individuals in the highest quantile of whole grain intake were compared to individuals with the lowest whole grain intake. Covariate-adjusted event rates were derived from published event rates and adjusted relative risk estimates. For studies that reported risk estimates for multiple cardiovascular endpoints, the most comprehensive cardiovascular disease endpoint was utilized for the primary analysis. For studies that evaluated this association in multiple models, we evaluated estimates based on demographic-adjusted models and more fully-adjusted models (i.e. including cardiovascular risk factors) separately. Secondary analyses evaluated specific endpoints (coronary heart disease (CHD)/CHD mortality, ischemic stroke/stroke mortality) and subgroups (men, women) based on risk-factor adjusted estimates. Additionally, the relationship between refined grain intake and cardiovascular events was assessed using studies that provided this information.

We identified eight publications from seven cohorts with both quantitative whole grain estimates and clinical cardiovascular event rates that included sufficient data for analysis (Table 1). Other reports of interest were excluded for the following reasons: retrospective study design [6], use of qualitative rather than quantitative whole grain measures (i.e. “What type of bread do you use?”) [4], and presentation of data subsequently updated [7]. Studies that met entry criteria and provided sufficient data were included in the analyses, with study weights based on the inverse variance. For the main and secondary analyses, we evaluated the Mantel-Haentzel test for heterogeneity. As there was no evidence of significant heterogeneity ($Q = 0.04$ – 8.17 , $p = 0.07$ – 0.83), fixed-effects models were used. Publication bias was evaluated using funnel plots and the Egger test [8], and sensitivity analyses corrected for bias using the trim-and-fill method [9]. All analyses were performed using MIX v. 1.2 (Kitasato University, 2006; <http://www.mix-for-meta-analysis.info/index.html>).

Results

Six studies provided information for demographic-adjusted analyses [10–15], and seven included information for risk-factor-adjusted analyses [10–16] (Table 2). Among these cohorts, the pooled average intake of those with high intake was 2.5 servings/d, while consumption in the comparison group averaged 0.2 servings/day. High intake of whole grains was associated with a 37% lower risk of incident cardiovascular disease in the analyses

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