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# No evidence of decreased risk of colorectal adenomas with white meat, poultry, and fish intake: a meta-analysis of observational studies

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#### ABSTRACT

*Purpose*: Observational studies on the association between white meat (including fish and poultry) intake and the risk of colorectal adenoma (CRA), the precursor of colorectal cancer, have reported mixed results. To provide a quantitative assessment of this association, we summarized the evidence from observational studies.

Methods: Relevant studies published on or before April 30, 2012 were identified from MEDLINE and EMBASE. Summary effect size estimates with 95% confidence intervals (CIs) were calculated with a random-effects model. Between-study heterogeneity was assessed using the Cochran Q and I² statistics. Results: A total of 23 publications from 21 independent studies (16 case—control and 5 cohort studies) were included in this meta-analysis. Based on high versus low analysis, the summary effect size estimate of CRA was 0.96 (95% CI, 0.84—1.09) for white meat intake, 0.98 (95% CI, 0.80—1.19) for fish intake, and 0.98 (95% CI, 0.80—1.18) for poultry intake. Subgroup analyses revealed that the null associations of CRA with intake of white meat (fish/poultry) were independent of geographic locations, study design, type of food frequency questionnaire, number of cases, and adjustments for confounders, such as body mass index, use of nonsteroidal anti-inflammatory drugs, dietary energy intake, smoking, and physical activity. Conclusions: Intake of white meat (fish/poultry) is not associated with the risk of CRA.

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#### Introduction

Every year, more than 1 million new cases of colorectal cancer (CRC) are diagnosed and 655,000 deaths resulting from this disease are observed [1,2]. Because food residues and metabolites come into direct contact with the large intestinal mucosa, diet has long been thought to be an important factor in the etiology of CRC. In 2007, the World Cancer Research Fund/American Institute for Cancer Research drew a conclusion that high consumption of red and processed meat convincingly increases the risk of CRC [3]. Over the last four decades, poultry consumption has surpassed beef consumption in the United States [4], but fish consumption has remained low. However, with regard to the association between the intake of fish and poultry (referred to as white meat, which has a different composition than red meat) and the risk of CRC, the American Institute for Cancer Research panel has suggested that the evidence for poultry intake and CRC risk was too limited to draw

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any conclusions, whereas the evidence for fish intake was limited to suggestive that eating fish protects against CRC [3].

Colorectal adenomas (CRAs) are generally considered to be precursor lesions for most cases of CRC, by a process referred to as the adenoma—carcinoma sequence [5]. Better understanding of the etiology of adenomas might permit more rational development of intervention studies with adenomas as end points [6]. However, little is known about the risk factors for CRAs, except for age, family history, smoking [7], obesity [8], physical inactivity [9], and a diet high in red and processed meat. An early quantitative review that was published in 2000 and based on the four studies found that fish and poultry consumption probably had no effect on the risk of colorectal polyps [10]. Importantly, this quantitative review did not report the association specific for fish and poultry, respectively. Since then, many epidemiologic studies have evaluated this association, with mixed results [11-27]. Some studies have reported inverse associations [26,27], whereas several others have observed null associations [17,21-25].

To better characterize this issue, we conducted a comprehensive meta-analysis of the current epidemiologic literature by using our own methods and criteria in the selection of studies, presentation of data, and in our conclusions and interpretation of the evidence.

There are no potential conflicts of interest among all the authors.

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#### Methods

#### Data sources and searches

Two independent investigators (B.X. and J.S.) conducted a computerized literature search in MEDLINE (from 1966) and EMBASE (from 1974) for articles published until April 30, 2012. We searched the databases for studies containing the following text word and/or Medical Subject Heading terms: (1) white meat OR fish OR shellfish OR poultry OR chicken OR guinea fowl OR turkey OR duck AND (2) adenoma OR polyps, AND (3) colorectal OR colon OR rectal OR large bowel. Furthermore, we reviewed the reference lists of the relevant articles to identify additional studies. Only articles written in English were included. This meta-analysis followed the Meta-analysis of Observational Studies in Epidemiology guidelines [28].

#### Study selection

Studies were included in this meta-analysis if they were published as an original article; used a case—control, nested case—control, or cohort design; and reported associations in the form of effect size estimates with the 95% confidence intervals (CIs) for white meat (including fish and/or poultry), at least adjusted or matched for age. Non—peer-reviewed articles, ecologic assessments, experimental studies, and mechanistic studies were excluded. Studies were excluded if only data concerning recurrence or growth of adenomatous polyps were reported [29—31]. If data were duplicated in more than one study, the most recent study was included.

#### Data extraction

Two researchers (B.X. and J.S.) independently extracted the following data from each included study: the first author's last

name, year of publication, geographic location(s), number of cases, methods of ascertainment of dietary variables, duration of follow-up in cohort studies, covariate adjustments, and effect size estimates with corresponding 95% CIs for the highest versus lowest level. From each study, we extracted the risk estimates that reflected the greatest degree of control for potential confounders. For one study that reported effect size estimates for both healthy and hospital controls, we only extracted the risk estimates for the healthy controls [32].

#### Definition of exposure

In the current meta-analysis, white meat was defined as the sum of all fish and poultry. Poultry included chicken, guinea fowl, turkey, and duck as well as the processed poultry components of turkey or chicken. Total fish intake included all types of finfish and shellfish as well as canned tuna.

#### Statistical methods

We used the random-effects model to calculate summary effect size estimates and 95% CIs of CRA for the highest versus lowest level of white meat (fish and/or poultry) intake. This model, developed by DerSimonian and Laird [33], accounts for heterogeneity among studies. When sex-specific risk estimates were available, respectively, we first analyzed all estimates for CRA together by means of a fixed-effects model and then separately analyzed the estimates for males and females. For one study [19] that reported CRA risk for fresh processed fish as well as fresh and preserved seafood, respectively, we combined effect size estimates for the four variables as effect size estimate for "total fish" using a fixed-effects model.

All statistical analyses were performed using STATA, version 11.0 (STATA, College Station, TX) and R-package statistical software (version 2.11.0 beta, R Development Core Team). A two-tailed P < .05 was considered to be significant.

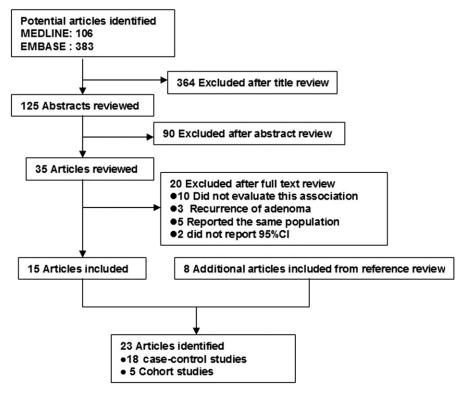


Fig. 1. Flow diagram of systematic literature search.

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