

**PJN**

ISSN 1680-5194

PAKISTAN JOURNAL OF  
**NUTRITION**

**ANSI***net*

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## Meat Consumption Is a Risk Factor for Colorectal Cancer: Meta-Analysis of Case-Control Studies

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**Abstract:** Meat has been associated with an increased risk of colorectal cancer in most, but not all, studies. Findings have shown conflicting results and inconclusive with regard to meat consumption in the colorectal cancers. To resolve these inconsistencies, we conducted a meta-analysis of published data on the association between meat and the incidence of colorectal cancer. Meta-analysis method was conducted to estimate the combined odds ratio (OR) between meat consumption and colorectal cancer from case-control studies published between 1989 and 2005. The combined odds ratio (OR) was 1.68 (95% CI; 1.34-2.12) in the 12 published case-control studies. The combined OR varied little by types of meat. Additionally, we evaluated the possible risk factors in meat for colorectal cancer. In conclusion, we found a positive association between meat consumption and colorectal cancer.

**Key words:** Meat, colorectal cancer, red meat

### Introduction

Colorectal cancer is the second most common cancer, next to lung cancer for men and breast cancer for women, in Europe and North America (Boyle and Langman, 2000). Colorectal cancer is the second leading cause of cancer-related death in the United States and accounts for about 11% of all cancer-related deaths (American Cancer Society, 2003). The 5-year relative survival rate is 90% for people whose colorectal cancer is treated in an early stage, but only 37% of cases are found early. Risk does not differ between men and women, but it does increase by age 40, rises sharply at 50-55, and then doubles with each following decade. Colorectal cancer has an incidence rate of 54 per 100,000 and a death rate of 22 per 100,000, but both rates vary by racial/ethnic group (National Cancer Institute, 1996).

Most, but not all, studies show meat eaters have a high risk of colorectal cancer (Giovannucci *et al.*, 1994; Willett *et al.*, 1990; O'Keefe *et al.*, 1999). In some colon cancer studies, the association has been limited to consumption of sausage or other processed meats (Goldbohm *et al.*, 1994; Gaard *et al.*, 1996). A number of studies have found an association between red meat consumption and colorectal cancer (American Cancer Society, 2005; Ries *et al.*, 1998; Sinha *et al.*, 1999).

Taking into account the above discrepancy, we decided to conduct a meta-analysis study on the relationship between meat consumption and colorectal cancer. This article is assessed whether whole meat and red meat are main risk of developing colorectal cancer. Also, whether there is any difference between red meat consumption and whole meat.

### Materials and Methods

We performed a meta-analysis 12 case-control studies that examined the association between meat

consumption and colorectal cancer risk (Benito *et al.*, 1990; Yeh *et al.*, 2003; Tavani *et al.*, 2000; Boutron-Ruault *et al.*, 1999; Levi *et al.*, 1999; Gerhardsson de Verdier, 1995; Neugut *et al.*, 1993; Maureen *et al.*, 2004; Le Marchand *et al.*, 2002; Lee *et al.*, 1989; Deno-Pellegrini *et al.*, 2005; Kulldorff *et al.*, 2000). The outcome of all published studies was regarding the OR of colorectal cancer. The disease was colorectal cancer and did not refer to any stage or classification of cancer. Case-control studies were identified through a Medline search for the period between Feb 1989 and January 2005. The searches were limited to studies published in English. Titles, abstracts, and subject headings in the database were investigated using the keywords colorectal cancer and meat. Over the period of 16 years, 69 articles were found using the keywords colorectal cancer and meat, and 12 articles were found using case control method. In order not to omit relevant articles, the titles, abstracts, and subject headings identified by the keywords colon, rectal, cancer and meat were scanned. The cited references in obtained studies were also reviewed to include all relevant articles.

In all of the case-control studies we found, if the study sample was found to overlap or come from the same study project, only the paper with the largest sample size was retained. When colorectal cancer risk was reported separately by different types of meat, whole meat was chosen because it contains all meat substances and thus reflects the true nature of meat. If both hospital and population controls were used for comparison separately, the result of the population control was chosen for the analysis. Two researchers performed data collection and extraction independently. Differences in data extraction were resolved by discussion.

Meta-analysis is a statistical analysis that combines or integrates the results of several studies to provide increased power for the quantitative identification of

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Table 1: Characteristic of case-control studies related to meat consumption and colorectal cancer risk from published studies

Study	Kind of meat	Case (n)	Control (n)	Odds Ratio
Boutron-Ruault, 1999	Whole meat	171	309	1.2
Benito, 1990	Whole meat	286	498	2.85
Gerhardson, 1995	Whole meat	347	505	2.8
Yeh, 2003	Whole meat	727	736	2.44
Lee, 1989	Whole meat	203	425	1.78
Combined	Whole meat	1734	2473	2.13
Tavani, 2000	Red meat	498	7990	1.7
Maureen, 2004	Red meat	952	1205	1.33
Levi, 1999	Red meat	327	491	1.55
Neugut, 1993	Red meat	286	480	1.9
Le Marchand, 2002	Red meat	727	727	8.8
Deneo-Pellegrini, 2005	Red meat	556	1112	3.1
Kulldorff, 2000	Red meat	146	228	1.3
Combined	Red meat	3492	12233	2.2
Combined All	All meat	5226	14706	2.17

Table 2: Effect-equality test for meat consumption and colorectal cancer risk from published studies

Kind of meat	Outcome Measure	Cochran's Q	df	P-value
Whole meat	Odds Ratio	15.0979	4	0.0045
Red meat	Odds Ratio	173.3718	6	0.0000
Combined	Odds Ratio	188.4835	11	0.0000

trends (Egger and Davey Smith, 1997). In the present study, the meta-analysis was performed using NCSS and PASS 2000 Released December 2005.

This software requires the input of the number of cases and controls into a two-by-two table to calculate the combined odds ratio (OR) and 95% confidence interval (CI).

Additional subgroup analyses were carried out to examine the effects of the type of control, the kind of meat.

**Results**

The results of the meta-analysis including number of cases and controls, odds ratios are shown in Table 1. A total of 5226 cases and 14706 controls constitute the subjects of meta-analysis. The principal outcome measured was odds ratio (OR) for the risk of whole meat and red meat consumption related to colorectal cancer.

Table 2 shows the null hypothesis that all effects are equal (homogeneous) versus the alternative that at least one effect has a different effect (heterogeneous). The Table

Shows that the odds ratio for whole meat studies, red meat studies as well as combined studies are statistically different.

Table 3 shows the odds ratio of whole meat consumption related to colorectal cancer is 2.20. As well as, the odds ratio for red meat consumption is 2.13. The upper and lower confidence intervals show there are not any statistical significance between odds ratios

for whole meat and red meat consumption related to colorectal cancer.

Fig. 1 shows odds ratio of case-control studies related to meat consumption and colorectal cancer risk from published studies.

**Discussion**

This study showed that whole meat and red meat were associated with colorectal cancer. Also, there was not any difference between whole meat and red meat related to colorectal cancer.

Meta-analysis is used to improve the statistical efficiency to evaluate the disadvantages of formulated researches, and hypothesis to reach reliable conclusions from the mixed assortment of the potentially relevant studies to determine the most promising directions for future researchers (Chen *et al.*, 2003; Qing *et al.*, 2004).

The risk of colon cancer is greatest in persons who eat diets high in meat and fat and lowest in those who choose high-fiber diets rich in vegetables and fruit (American Institute for Cancer Research, 1997; Potter *et al.*, 1993).

Some studies showed, frequent consumption of meat, particularly red meat, is associated with an increased risk of colon cancer (Singh and Fraser, 1998; Giovannucci *et al.*, 1994). Statistics show meat-eaters develop colon cancer at triple the rate vegetarians do. Total fat and saturated fat, which tend to be substantially higher in animal products than in plant-derived foods, and refined sugar, all heighten colon cancer risks. Researchers zeroed in on red meat, finding that

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Table 3: Odds ratio and confidence interval for meat consumption and colorectal cancer risk from published studies

Type of meat	Odds Ratio	95% Upper Confidence interval	95% Lower Confidence interval
Whole meat	2.13	1.57	2.90
Red meat	2.20	1.86	4.08
Combined	2.17	1.49	3.16

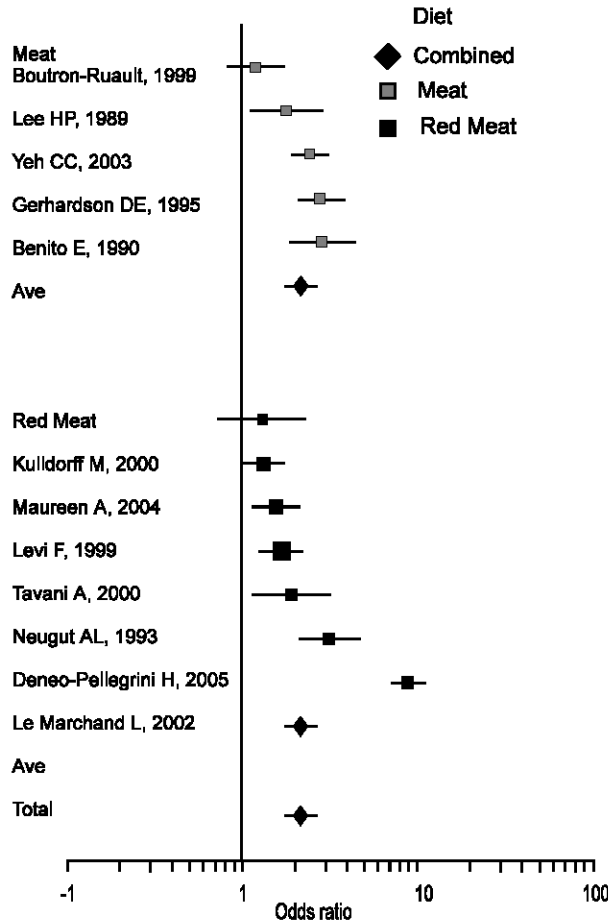


Fig. 1: Odds Ratio of case-control studies related to meat consumption and colorectal cancer risk from published studies

individuals eating beef, pork, or lamb daily have approximately three times the colon cancer risk, compared to people who generally avoid these products (Willett *et al.*, 1990; Giovannucci *et al.*, 1994). A recent review of 32 case-control and 13 cohort studies concluded that meat consumption is associated with an increase in colorectal cancer risk, with the association being more consistently found with red meat and processed meat (Giovannucci *et al.*, 1994). According to the results of our study, whole meat and red meat were associated with a significant increase in risk for colorectal cancer. These findings are in accordance with most of the previous case- controls studies (Norat and Riboli, 2001; Manousos *et al.*, 1983; Chao *et al.*, 2005;

Gerhardsson *et al.*, 1991; Bailar and Mosteller, 1992). The strength of our study was the ability to compare red meat and whole meat, as risk factors for colorectal cancer using meta analysis. Although, combined OR for red meat was more than whole meat but the differences was not statistically significant. Since, other risk factors like cigarette smoking, physical activity and processed meat may influence on colorectal cancer. Processed meat includes foods preserved by salting, or the addition of nitrites or nitrates, and high consumption of these foods can increase exposure to nitrosamines and their precursors. The amount of these substances in processed meat likely varied by region and over time but we had no information to assess the impact of these differences in our study results.

Our study had several limitations. We had no information on meat cooking methods to estimate exposure to heterocyclic amines or other specific carcinogens produced from pyrolysis of meat; because our study was meta-analysis of conducted case-control studies. Also, we had no information on family history of colorectal cancer from the studies. In conclusion, our findings strongly support a relationship between meat consumption and increased risk of colorectal cancer.

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