

# Consumption of Whole Grains, Refined Cereals, and Legumes and Its Association With Colorectal Cancer Among Jordanians

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## Abstract

**Background.** The role of whole grains, refined cereals, and legumes in preventing or initiating colorectal cancer (CRC) is still uncertain. The aim of this study is to examine the possible association between the consumption of whole grains, refined cereals, and legumes and the risk of developing CRC among Jordanian population. **Methods.** A validated food frequency questionnaire was used to collect dietary data with regard to intake of whole grains, refined cereals, and legumes. A total of 220 diagnosed CRC participants and 281 CRC-free control participants matched by age, gender, occupation, and marital status were recruited. Logistic regression was used to estimate the odds of developing CRC in relation to the consumption of different types of whole grains, refined cereals, and legumes. **Results.** The odds ratio (OR) for developing CRC among cases consumed refined wheat bread at all meals was 3.1 compared with controls (95% CI: 1.2-7.9,  $P_{-Trend} = 0.001$ ); whereas the OR associated with whole wheat bread was 0.44 (95% CI: 0.22-0.92,  $P_{-Trend} = 0.001$ ). The statistical evaluation for daily consumption of rice suggested a direct association with the risk of developing CRC, OR = 3.0 (95% CI: 0.27-33.4,  $P_{-Trend} = 0.020$ ). Weekly consumption of macaroni was associated with CRC with OR of 2.4 (95% CI: 1.1-5.3,  $P_{-Trend} = 0.001$ ). The consumption of corn, bulgur, lentils, and peas suggested a protective trend, although the trend was not statistically significant. **Conclusion.** This study provides additional indicators of the protective role of whole grains and suggests a direct association between consumption of refined grains and higher possibility for developing CRC.

## Keywords

colorectal cancer, whole grains, refined cereals, legumes

## Introduction

Whole grains, refined cereals, and legumes are important components of diets in many areas in the world. Cereals are major sources of energy, proteins, and other nutrients.<sup>1,2</sup> Whole grains, refined cereals, dried peas, and beans differ from each other in their structural and physicochemical properties, and their physiological effects. These differences result from variations in their polysaccharides composition and, more specifically, in the quantity and variety of dietary fibers and starch.<sup>1</sup> In addition, protein content and the amount of phytochemicals, vitamins, minerals, and other bioactive components present play a role in the development of colorectal cancer (CRC).<sup>1</sup> The beneficial effects of whole grains on the prevention and management of chronic diseases (such as coronary heart disease, diabetes, high blood pressure, inflammation, and cancer) were reported in observational and interventional studies.<sup>3,4</sup>

In Jordan, the staple foods are wheat and rice. Khobez, a leavened flat wheat bread (pita bread), is consumed daily with most meals and often used to scoop other foods.<sup>5</sup> The per capita supply of cereals, which consists mainly of wheat and, to a much lesser extent of rice, has remained rather stable since the early 1980s. Within this food group, the supply of rice tends to increase slightly over the period.<sup>5</sup> Boiled rice could be eaten plain, spicy, or with sauces. Also, many vegetables (green beans, okra, cauliflower, eggplants, spinach, etc) are usually cooked or served with rice.<sup>5</sup> Epidemiological,

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clinical, and animal research studies have indicated that polyphenols and fibers (from whole grains and legumes) may exert a protective effect against colon cancer.<sup>6-9</sup>

Cereals (either whole or refined) and legumes are the main components of the Jordanian diet in which wheat is the predominant type of cereals.<sup>5,10</sup> The type of wheat consumed in Jordan and Middle East is the hard red winter wheat.<sup>11</sup> Refined and whole wheat breads are commonly produced from this type of wheat after processing.<sup>11</sup> Unfortunately, the Jordanian population consumption of refined red wheat flour bread was estimated to be about 326 g/d, while the consumption of the whole grain type was about 3 g/d.<sup>10</sup> Therefore, this study aimed to investigate the possible association between whole grains, refined cereals, and legumes intake and the risk of developing CRC in Jordanian population.

## Subjects and Methods

### Study Population and Methods

A total of 501 volunteers participated in the study, 248 males and 253 females. Of those 220 were diagnosed CRC cases, and 281 were healthy disease-free controls. Participants were enrolled in the study from January 2010 to December 2012. Those diagnosed with CRC were recruited from 5 large Jordanian hospitals (King Hussein Cancer Center, King Abdullah University Hospital, Prince Hamzeh Hospital, Jordan University Hospital, and Al-Basheer Hospital) with oncology services. For inclusion in the diagnosed CRC cancer group, subjects must have obtained their diagnosis less than 1 year prior to the time of the first interview in addition of being Jordanian aged 18 years or older. Cases were excluded if they had a critical illness, if they were currently hospitalized, or if they complained of diabetes mellitus, liver disease, and rheumatoid arthritis. To be included in the study as a control, volunteers had to be Jordanian aged 18 years or older, apparently healthy, able to communicate clearly and verbally, free of CRC, diabetes mellitus, liver disease, and rheumatoid arthritis. Because it was very difficult to enroll anyone outside the hospital setting, most of the controls were selected using convenience sampling from visitors and accompanying individuals (friends, relatives, or neighbors) who were not first- or second-degree relative or spouse of the CRC cases. In addition, outpatients and hospital administrative staff were recruited. The control group was matched as closely as possible for age, gender, occupation, and marital status. The ratio for cases against controls was 1:1.

The ethical committees of all 5 hospitals approved the study protocol, and written informed consent was obtained from all participants prior to starting the study. The study protocol was approved by the King Hussein Cancer Center

Institutional Review Board Committee (09 King Hussein Cancer Center 10; May 2009), and other hospitals gave their approval accordingly.

### Data Collection

Trained research assistants collected the data through a structured questionnaire and carried out the anthropometric measurements. During the interview, different valid questionnaires were used to collect personal and family histories, diet history, and physical activity levels. Participants were asked specifically if any of their family members were ever diagnosed with CRC or any other type of cancer. The anthropometric measurements, including body weight and height and calculating body mass index (BMI), were carried out according to Lee and Nieman<sup>12</sup> by the trained research assistants.

### Food Frequency Questionnaire

A validated Food Frequency Questionnaire (FFQ) in Arabic was used to assess the diets of the volunteers. The FFQ was modified from the Diet History Questionnaire I of the US National Cancer Institute. It was validated for use in the Jordanian setting.<sup>13</sup>

For the CRC group, participants were asked about their food intake before being diagnosed and during the past 12 months. For each food type, the participants were asked whether they consumed each food item separately (eg, rice, bulgur, cornflakes, white beans, etc). An answer in the affirmative resulted in additional questions related to frequency and amount of food consumed. If the participants' diet did not include a food type, then related questions were skipped. Participants were asked how frequently, on average during the past year, they consumed 1 standard serving of a specific food item in 9 different categories (<1 per month, 2-3 per month, 1-2 per week, 3-4 per week, 5-6 per week, 1 per day, 2-3 per day, 4-5 per day, or 6 per day). Food models and standard measuring tools were used to help participants estimate the portion size they consumed. Responses on consumption frequency of a specified serving size for each food item were converted into average daily intake rates.<sup>13</sup> Dietary intakes were also analyzed using dietary analysis software (ESHA Food Processor SQL version 10.1.1; ESHA, Salem, OR) with additional data on foods consumed in Jordan.<sup>14</sup>

### The 7-Day Physical Activity Recall

The 7-day Physical Activity Recall (PAR) was originally developed by Sallis et al<sup>15</sup> and was used in this study to measure physical activity level.<sup>16</sup> The PAR interview focuses on collecting data on intensity, time or duration, and type of activity. The number of hours spent in different

activity levels were obtained and converted into metabolic equivalents (METs). PAR covers different levels of physical activity and intensity such as aerobic exercise, work-related activities, gardening, walking, recreation, and leisure-time activities. Average METs for walking = 3.3 METs, for moderate activity = 4.0 METs, for vigorous activity = 8.0 METs. The score expressed as MET-min per week was calculated as (MET level × minutes of activity/day × days per week). Total Physical Activity MET-minutes/week is obtained by METs summation and categorized as inactive below 600 MET min/wk, minimally active and Health Enhancing Physical Activity (HEPA) active.<sup>15</sup>

### Statistical Analyses

Descriptive analyses were conducted to examine the frequency of different variables. The consumption of whole grains (bread and bulgur), refined cereals (bread, rice, cornflakes, and macaroni), and legumes (lentils, green beans, and peas) were computed in 2 ways. The first computation was based on the frequency of consumption of each food type (daily, weekly, monthly, and rarely). The second category was based on the time that food usually consumed (never, 1/4 the meals, 1/2 the meals, and all the meals). Additionally, consumption was grouped into 2 separate categories based on the number of servings consumed daily: ≤1.0 serving per day and ≥2 servings per day. In all categories, the referent group had the lowest intake. Logistic regression was used to calculate odds ratio (OR), CI, linear regression, and *P* value for trend with age (continuous), sex, BMI (continuous), physical activity level (continuous), total energy intake (continuous), red meat consumption, occupation, education level, marital status, and family history for the CRC participants were evaluated as potential confounders.<sup>17</sup> Chi-square was used to detect the differences among categorical variables. The significance level was set at *P* < .05. All statistical analyses were conducted in SPSS version 19.0 (IBM SPSS Statistics for Windows, IBM Corporation).

### Results

Table 1 shows the distribution of risk factors for the study participants. Colorectal cancer and control subjects were matched for several parameters, including age, sex, occupation, and marital status. Table 2 shows the adjusted odds ratio (AOR) and 95% CIs for whole grains and legumes. The results obtained indicate that the risk for developing CRC is significantly associated with consuming whole grain versus refined breads at all meals. The OR for developing CRC among cases consuming refined wheat bread at all meals was 3.1 compared with controls (95% CI: 1.2-7.9, *P*<sub>-Trend</sub> = 0.001); whereas the OR associated with whole wheat bread was 0.44 (95% CI: 0.22-0.92, *P*<sub>-Trend</sub> = 0.001).

**Table 1.** Selected Characteristics of the Participants Studied.<sup>a</sup>

	Control (n = 281)	Case (n = 220)
Age, years (mean ± SD)	51.25 ± 11.12	52.89 ± 11.67
Sex, n (%)		
Male	132 (47)	116 (52.7)
Female	149 (53)	104 (47.3)
BMI, kg/m <sup>2</sup> (mean ± SD)	29.06 ± 5.6	27.71 ± 6.15
BMI (kg/m <sup>2</sup> ) category		
Underweight (<18.5)	2 (0.7)	5 (2.5)
Normal (18.5-24.9)	52 (18.8)	57 (27.9)
Overweight (25-29.9)	122 (44.2)	83 (40.7)
Obese ≥30	100 (36.2)	59 (28.9)
Marital status, n (%)		
Married	248 (88.3)	199 (90.5)
Single	17 (6)	5 (2.3)
Divorced	1 (0.4)	3 (1.4)
Widowed	15 (5.3)	13 (5.9)
Occupation, n (%)		
Yes	100 (35.6)	69 (31.4)
No	181 (64.4)	151 (68.6)
Smoking, n (%)		
Smoker	53 (18.9)	37 (16.8)
Nonsmoker	227 (81.1)	173 (78.6)
Family history of CRC, n (%)		
Yes	101 (36.5)	84 (38.5)
No	176 (63.5)	134 (61.5)
Other health problem, n (%)		
Yes	119 (42.7)	83 (37.7)
No	160 (57.3)	136 (61.8)
Education, n (%)		
Illiterate	11 (3.9)	17 (7.7)
Primary and secondary	137 (49.1)	107 (56.4)
Diploma and BSc	113 (40.5)	86 (39.1)
MSc and PhD	18 (6.5)	10 (4.5)
MET, n (%)		
Inactive <sup>b</sup>	131 (52.2)	121 (56.3)
Minimally active <sup>c</sup>	53 (21.1)	37 (17.2)
HEPA active <sup>d</sup>	67 (26.7)	57 (26.5)

Abbreviations: BMI, body mass index; HEPA, health enhancing physical activity; CRC, colorectal cancer; MET, metabolic equivalent.

<sup>a</sup>Significance is at *P* ≤ .05.

<sup>b</sup>Inactive: not fitting in “minimally active” or “HEPA active.”

<sup>c</sup>Minimally active: at least 600 MET per week.

<sup>d</sup>HEPA active: more than 3000 MET per week.

Even though no significant association was observed between refined bread consumption at any level and the risk of having CRC, the trend of consumption was significant in male participants (*P*<sub>-Trend</sub> = 0.030). A significant negative association between CRC and the consumption of whole wheat bread at all meals was observed in males with OR in males at 0.37 (95% CI: 0.14-1.0, *P*<sub>-Trend</sub> = 0.004) as shown in Table 3. This association was also observed in female

**Table 2.** Adjusted Odds Ratio (AOR)<sup>a</sup> for the Consumption of Cereals and Legumes and Colorectal Cancer (CRC) Risk.

Item	Category of Consumption				P for Trend
	≤1 Daily	≥2 Daily			
<b>Bread</b>					
No. of cases	7	213			.1
No. of controls	18	263			
AOR (95% CI)	1	8.9 (1.1-70.8)			
Item	Category of Consumption				P for trend
	Never	1/4 of the Meals	1/2 of the Meals	≥3/4 of the Meals	
<b>Refined bread</b>					
No. of cases	16	8	12	184	.001
No. of controls	42	16	13	210	
AOR (95% CI)	1	3.0 (0.77-11.9)	2.1 (0.45-10.13)	3.1 (1.2-7.9)	
<b>Whole wheat bread</b>					
No. of cases	151	33	12	24	.001
No. of controls	152	58	13	58	
AOR (95% CI)	1	0.52 (0.26-1.0)	0.61 (0.172-2.169)	0.44 (0.22-0.92)	
Item	Category of Consumption				P for trend
	Rarely <sup>b</sup>	Monthly	Weekly	Daily	
<b>Rice</b>					
No. of cases	4	6	117	93	.021
No. of controls	6	8	183	84	
AOR (95% CI)	1	5.3 (0.34-81.9)	1.0 (0.21-20.6)	3.0 (0.27-33.4)	
<b>Bulgur</b>					
No. of cases	73	127	20	—	.460
No. of controls	101	151	28	1	
AOR (95% CI)	1	0.94 (0.62-1.6)	0.74 (0.30-1.5)	—	
<b>Cornflakes</b>					
No. of cases	193	9	12	6	.128
No. of controls	255	17	3	6	
AOR (95% CI)	1	0.87 (0.33-2.5)	5.3 (0.67-48.0)	1.0 (0.23-4.3)	
<b>Lentils</b>					
No. of cases	112	54	53	1	.512
No. of controls	127	92	60	2	
AOR (95% CI)	1	0.84 (0.58-1.4)	1.3 (0.72-2.4)	0.36 (0.01-8.6)	
<b>White beans</b>					
No. of cases	138	72	10	—	.053
No. of controls	157	107	17	—	
AOR (95% CI)	1	1.0 (0.61-1.7)	0.86 (0.37-2.1)	—	
<b>Green beans</b>					
No. of cases	35	149	36	—	.210
No. of controls	58	184	39	—	
AOR (95% CI)	1	1.1 (0.64-2.0)	1.0 (0.57-2.2)	—	
<b>Pea</b>					
No. of cases	43	135	40	2	.174
No. of controls	57	180	44	—	
AOR (95% CI)	1	0.89 (0.46-1.4)	1.0 (0.44-2.0)	—	
<b>Corn</b>					
No. of cases	114	68	33	5	.135
No. of controls	133	80	53	15	
AOR (95% CI)	1	0.86 (0.55-1.4)	0.53 (0.38-1.1)	0.2 (0.06-0.92)	

(continued)

Table 2. (continued)

Item	Category of Consumption				P for trend
	Rarely <sup>b</sup>	Monthly	Weekly	Daily	
Macaroni					
No. of cases	63	112	45	—	.001
No. of controls	99	157	24	1	
AOR (95% CI)	1	1.0 (0.68-1.7)	2.4 (1.1-5.3)	—	

<sup>a</sup>Adjusted odds ratio: Adjusted for age, gender, total energy, red meat consumption, physical activity, smoking, education level, marital status, work, income, other health problems and CRC history.

<sup>b</sup>Reference group.

participants (but nonsignificant) with OR = 0.39 (95% CI: 0.10-1.5,  $P_{-Trend} = 0.029$ ).

The results for those consuming rice daily also showed an association with the risk of developing CRC, OR = 3.0 (95% CI: 0.27-33.4,  $P_{-Trend} = 0.021$ ). Weekly consumption of macaroni was associated with the risk of developing CRC, OR = 2.4 (95% CI: 1.1-5.3,  $P_{-Trend} = 0.001$ ). This observation was true among females, OR = 6.1 (95% CI: 1.4-26.5,  $P_{-Trend} = 0.003$ ), but not in males (Table 3). In contrast, higher consumption of corn, bulgur, lentils, and peas showed a protective trend against CRC development.

## Discussion

The present study targeted the possible association between cereals and legumes and risk of CRC development. Results of this study indicated that higher consumption of refined cereals and white bread is associated with higher CRC risk. The current study also showed that higher intake of whole grains and legumes is associated with lower risk for developing CRC. These findings are in agreement with observations reported in previous studies conducted in Europe, South America, and Asia<sup>18-22</sup> in which researchers reported that the risk for developing CRC was higher among individuals who consumed their carbohydrates as rice, white bread, and pasta as compared with individuals who consumed their carbohydrates as whole grain cereals.<sup>18-22</sup> In a case-control study conducted in northern Italy involving 339 cases of colon cancer, 236 cases of rectal cancer, and 778 controls, a positive association was observed with frequent consumption of starchy food (pasta or rice) with relative risk of 3 for colon cancer and 1.8 for rectal cancers in highest versus lowest tertiles.<sup>23</sup> Another case-control study was conducted in Italy in that regard involving 1953 cases (1125 men and 828 women) with histologically confirmed incidences of cancer of the colon or rectum and 4154 controls subjects (2073 men and 2081 women).<sup>24</sup> Results showed a direct association with the glycemic load (OR = 1.8; 95% CI: 1.5-2.2), and glycemic index (OR = 1.7; 95% CI: 1.4-2.0) in highest versus lowest quintiles. Researchers interpreted their results through the detrimental effect of refined carbohydrates in the etiology of

the CRC.<sup>24</sup> In 1999, Chatenoud et al<sup>25</sup> reported that consumption of refined cereals was associated with higher risk of cancers of the large bowel with ORs for the highest tertile of refined cereal intakes 1.5 for colon cancer and 1.3 for cancer of the rectum.<sup>25</sup> A systematic review and dose-response meta-analysis of prospective studies done by Aune et al<sup>26</sup> showed that the summary relative risk of developing CRC from consuming 10 g daily of total dietary fiber (n = 16 studies) was 0.90 (95% CI: 0.86-0.94), for legume fiber (n = 4 studies) was 0.62 (95% CI: 0.27-1.42), for cereal fiber (n = 8 studies) was 0.90 (95% CI: 0.83-0.97), and the relative risk for an additional 3 servings daily of whole grains (n = 6 studies) was 0.83 (95% CI: 0.78-0.89).<sup>26</sup>

The protective effect of whole grains against risk of developing CRC could be attributed to nutrients and phytochemicals content of whole grains including dietary fibers, resistant starch, oligosaccharides escaping from digestion in the small intestine and then being fermented in the gut to produce short-chain fatty acids. Furthermore, whole grains are rich in antioxidants, including trace minerals and phenolic compounds. These phenolic compounds may exert a preventive effect in the disease process. Additionally, whole grains may mediate insulin and glucose responses.<sup>27,28</sup> Thus, refined grains and white bread are classified as high glycemic index foods. Consuming foods with high glycemic index may lead to chronic hyperglycemia and obesity-induced insulin resistance resulting in hyperinsulinemia. Hyperinsulinemia may stimulate proliferation and promote metastasis of malignant colonic epithelial cells by increasing the bioactivity of insulin-like growth factor 1 (IGF-1).<sup>29-31</sup> In contrast, results from a cohort study involving Chinese women suggest that no association exist between a diet characterized by high glycemic index, glycemic load, or by a high intake of carbohydrates with the risk of developing CRC.<sup>32</sup>

In an earlier study by Slattery et al,<sup>33</sup> it was reported that refined grain products were associated with higher risk of 40% overall, with a *P* value chi-square test for the threshold effect of 0.01.<sup>33</sup> There was also a significant interaction between sex and refined grain intake ( $P < 0.05$ ). While the consumption of refined grains in men and women was found

**Table 3.** Adjusted Odds Ratio (AOR)<sup>a</sup> for Rice, Macaroni, and Bread Consumption Among Male and Female Participants and the Risk of Colorectal Cancer (CRC).

Item	Category of Consumption				P for Trend
	Never	1/4 the Meals	1/2 the Meals	≥3/4 of the Meals	
<b>Refined bread</b>					
<b>Male</b>					
No. of cases	6	5	5	100	.030
No. of controls	17	7	7	101	
AOR (95% CI)	1	2.2 (0.34-14.42)	1.7 (0.20-14.9)	3.5 (0.88-14.3)	
<b>Female</b>					
No. of cases	10	3	7	84	.167
No. of controls	25	9	6	109	
AOR (95% CI)	1	2.6 (0.20-33.12)	3.7 (0.24-59.6)	2.8 (0.56-13.9)	
<b>Whole wheat bread</b>					
<b>Male</b>					
No. of cases	89	11	5	11	.004
No. of controls	79	22	7	24	
AOR (95% CI)	1	0.50 (0.18-1.4)	0.43 (0.08-2.4)	0.37 (0.14-1.0)	
<b>Female</b>					
No. of cases	62	22	7	13	.029
No. of controls	73	36	6	34	
AOR (95% CI)	1	0.45 (0.15-1.4)	1.0 (0.11-9.3)	0.39 (0.10-1.5)	
<b>Category of Consumption</b>					
Item	Rarely <sup>b</sup>	Monthly	Weekly	Daily	P for trend
<b>Rice</b>					
<b>Male</b>					
No. of cases	3	4	56	53	.610
No. of controls	2	2	77	51	
AOR (95% CI)	1	9.0 (0.36-305.8)	1.0 (0.14-13.0)	1.5 (0.16-19.2)	
<b>Female</b>					
No. of cases	—	2	61	40	—
No. of controls	4	6	106	33	
AOR (95% CI)	1	—	—	—	
<b>Macaroni</b>					
<b>Male</b>					
No. of cases	36	61	19	—	.101
No. of controls	48	71	12	1	
AOR (95% CI)	1	1.2 (0.65-2.5)	2.8 (1.0-8.3)	—	
<b>Female</b>					
No. of cases	27	51	26	—	.003
No. of controls	51	86	12	—	
AOR (95% CI)	1	0.82 (0.35-1.8)	6.1 (1.4-26.5)	—	

<sup>a</sup>Adjusted odds ratio: Adjusted for age, gender, total energy, red meat consumption, physical activity, smoking, education level, marital status, work, income, other health problems and CRC history.

<sup>b</sup>Reference group.

to be associated with the risk of developing CRC (OR = 1.32, CI: 0.89-1.97 for men and OR = 1.58, CI: 0.96-2.58 for women), the risk for CRC decreases with consumption of whole grains OR = 0.67 (CI: 0.46-0.98) for men and OR = 0.74 (CI: 0.43-1.27) for women.<sup>33</sup> Intake of whole grain products was associated with a 30% reduced risk of rectal

cancer for both men and women combined; the intake of whole grain products and sex was not significant ( $P < 0.27$ ), and the  $P$  value for the threshold effect was 0.03.<sup>33</sup> These results are in agreement with our results in which consuming refined bread frequently was found to be associated significantly with higher CRC risk (approximately 170%), while

consuming macaroni weekly was shown to be associated with higher risk for CRC development significantly, 6 fold in females (OR = 6.1). Egeberg et al<sup>34</sup> conducted a cohort study to investigate the association between consumption of whole grain products and colon and rectal cancer.<sup>34</sup> This association was prospectively examined using data on 461 incident cases of colon cancer and 283 incident cases of rectal cancer that developed during 10.6 years of follow-up among 26630 men and 29189 women taking part in the Diet, Cancer, and Health cohort. Incidence rate ratios (IRRs) of colon and rectal cancer related to total or individual whole grain product intake were calculated using Cox regression.<sup>34</sup> The results of the study revealed that higher whole grain product intake was associated with lower risk of colon cancer and rectal cancer in men. The adjusted IRR (95% CI) was 0.85 (0.77-0.94) for colon cancer and 0.90 (0.80-1.01) for rectal cancer per daily 50-g increment in intake. For colon cancer, the association was confined to intake of whole grain bread, in particular. No consistent associations between total or individual whole grain product consumption and colon or rectal cancer risk were observed in women.<sup>34</sup>

A large population-based Scandinavian cohort study consisting of 108000 Danish, Swedish, and Norwegian persons, of whom 1123 developed CRC during a median of 11 years of follow-up was conducted to trace the association between the daily intake of whole grain products (wheat, rye, and oats) and the incidence of CRC using Cox proportional hazards models.<sup>35</sup> Intake of whole grain products was found to be associated with a lower incidence of CRC per 50-g increment (IRR, 0.94; 95% CI: 0.89-0.99), and the same tendency was found for total whole grain intake (IRR, 25-g increment, 0.94; 95% CI: 0.88-1.01). Intake of whole grain wheat was associated with a lower incidence of CRC (IRR for highest vs lowest quartile of intake, 0.66; 95% CI: 0.51-0.85), but no statistical significant linear trend was observed ( $P_{-Trend} = 0.18$ ). On the other hand, no significant association was found for whole grain rye or oats.<sup>35</sup> Contrary to the previous studies, 1 recent study revealed that wheat class (red vs white) and not the state of refinement (whole vs refined), appears to influence colon cancer risk, with hard red wheat protective relative to soft white wheat.<sup>36</sup> Thus, epidemiological associations of reduced colon cancer risk with whole grain consumption may actually reflect different wheat classes.<sup>36</sup> However, the only available and consumed type of wheat in Jordan is red hard winter wheat but still the incidence of CRC is increasing. One of the suggested underlying mechanisms of action for the protective effect of whole grains against CRC is the effects of fibers on reducing glycemic load and improving insulin resistance, influenced by IGF-1.<sup>37</sup> IGF-1 is known to stimulate cell proliferation; increase production of vascular endothelial growth factor, an angiogenic factor, which supports tumor growth; and inhibit apoptosis in healthy and cancerous colon epithelial cells as well.<sup>38</sup>

## Study Limitations

Dietary recall data in cases may be different from controls as data was collected after diagnosis of the disease. Measuring dietary intakes using FFQ is vulnerable to memory errors. However, using a validated FFQ may decrease these possible errors. Nevertheless, the impact of cooking on bioavailability of different nutrients was not counted for. As with the other case control studies, selection and recall biases may have affected the study results. Selection bias may have affected the results as controls were selected by convenience sampling from hospital personnel, outpatients, visitors, and accompanying persons and not from the general population. Finally, the sample size is rather small, although the CRC cases were recruited from 5 different large hospitals between January 2010 and December 2012. And since Jordan is a small country with an estimated population in 2009 that reached 5980000, it was difficult to recruit more cases given that the overall age-standardized incidence CRC was found to be 17.3/100000 in 2009.

## Conclusions

In conclusion, results of this study suggest that whole grains and legumes may exert a protective effect against CRC development. Because of the globalization and changes in dietary patterns toward the western dietary pattern, whole grains were replaced by refined cereals in Middle Eastern countries. The present study shows how the type of cereal consumed in Jordan and Middle Eastern countries could be associated with developing CRC. These results may serve as an additional encouragement in the development of health promotional programs involving dietary factors as an aid to reduce the risk of developing CRC in our Jordanian population. Further studies are recommended to investigate the findings of the current study.

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## Author Contributions

Conception and design: RF Tayyem and H Bawadi. Acquisition of data: IN Shehadah, L Agraib. Analysis and interpretation of data: RF Tayyem, L Agraib, D Heath, and N Al-Awwad. Writing, reviewing, and/or revising the manuscript: RF Tayyem, D Heath, IN Shehadah, K Bani-Hani, H Bawadi, and N Al-Awwad. Administrative, technical, or material support: RF Tayyem and H Bawadi. Study supervision: RF Tayyem, L Agraib, and IN Shehadah.

## Declaration of Conflicting Interests

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