

# Adherence to the World Cancer Research Fund/American Institute for Cancer Research cancer prevention recommendations and breast cancer risk in the Cancer de Màm (CAMA) study

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## Abstract

**Objective:** We investigated the association between adherence to the recommendations of the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) and breast cancer (BC) risk in the Cancer de Màm (CAMA) study in a Mexican population.

**Design:** Population-based case-control study.

**Subjects:** Incident BC cases ( $n$  1000) and controls ( $n$  1074) matched on age, region and health-care system were recruited.

**Setting:** In-person interviews were conducted to assess BC risk factors and habitual diet was assessed with an FFQ. Conformity to the WCRF/AICR recommendations was evaluated through a score incorporating seven WCRF/AICR components (body fatness, physical activity, foods and drinks that promote weight gain, plant foods, animal foods, alcoholic drinks and breast-feeding), with high scores indicating adherence to the WCRF/AICR recommendations.

**Results:** No statistically significant associations between WCRF/AICR score and risk of BC were observed. After excluding BMI from the WCRF/AICR score, the top quartile was associated with a decreased BC risk overall, with  $OR_{Q4-Q1}=0.68$  (95% CI 0.49, 0.92,  $P_{trend}=0.03$ ), and among postmenopausal women, with  $OR_{Q4-Q1}=0.60$  (95% CI 0.39, 0.94,  $P_{trend}=0.03$ ). Inverse associations were observed between BMI and risk of BC overall and among premenopausal women, with  $OR=0.57$  (95% CI 0.42, 0.76,  $P_{trend}<0.01$ ) and 0.48 (95% CI 0.31, 0.73,  $P_{trend}<0.01$ ), respectively. Physical activity level was inversely associated with BC risk.

**Conclusions:** The WCRF/AICR index was not related with BC risk in the CAMA study. A combination of six components excluding BMI showed strong protective associations, particularly in postmenopausal women. Further prospective studies are required to clarify the role of adherence to WCRF/AICR recommendations, particularly with respect to BMI, in the Mexican population.

**Keywords**  
 Breast cancer  
 Diet  
 Physical activity  
 Weight management  
 Mexican women

Breast cancer (BC) is the leading cause of cancer death in women worldwide<sup>(1)</sup>. In Western countries, age-standardized incidence rates range between 56.8 and 109.4 per 100 000 women, while lower rates are observed in Asia, Central America and sub-Saharan Africa<sup>(2)</sup>. Among Mexican women, the age-standardized incidence rate is 26.4 per 100 000 women<sup>(3)</sup>.

Multiple risk factors for BC such as family history, obesity, lactation, adult attained height, and menstrual and reproductive history are well established but are generally difficult to modify<sup>(3–7)</sup>. A substantial amount of research

has explored the influence of modifiable dietary risk factors on BC risk<sup>(8–13)</sup>. Several foods as well as macro- and micronutrients (e.g. vegetables, dietary fibre and vitamins) have been investigated in relation to BC risk<sup>(11,14,15)</sup>, although no consistent and statistically significant associations have been established. One convincing exception is for alcohol consumption<sup>(16)</sup>.

Most epidemiological studies on diet and cancer have largely been on intakes of individual food items or nutrients<sup>(17,18)</sup>. This approach, however, does not fully take into account the complexity of human diets, in terms

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of the large number of foods consumed by individuals, as well as the inter-correlation between those foods<sup>(19)</sup>. There has been an increasing interest towards dietary patterns, rather than individual foods, as a way to investigate the aetiology of BC<sup>(20–22)</sup>. A valuable alternative was constituted by *a priori* scores, defined on dietary guidelines and recommendations. The Healthy Eating Index (HEI), the Diet Quality Index (DQI) and the Recommended Food Score (RFS) are recent examples, but have little or no association with BC risk and/or mortality<sup>(21,23,24)</sup>. More robust evidence with BC risk and mortality was produced by using scores integrating dietary components with other lifestyle factors such as body fatness, physical activity, alcohol consumption and/or smoking habits<sup>(25–27)</sup>.

In 2007, the World Cancer Research Fund (WCRF) in collaboration with the American Institute for Cancer Research (AICR) summarized the existing scientific evidence on the role of foods, nutrition and physical activity in the aetiology of cancer<sup>(4)</sup>. Accordingly, a list of recommendations (eight general and two special) on diet, physical activity and weight management were developed in order to reduce the incidence of cancer in the general population.

In the present study, we evaluated the association between the WCRF/AICR recommendations and the risk of BC in a case–control study of Mexican women within the Cancer de Mâma (CAMA) study, overall and by menopausal status.

## Materials and methods

### Study population

CAMA recruitment procedures have been described in detail previously<sup>(28)</sup>. In brief, 1000 cases and 1074 controls, pre- and postmenopausal women aged 35–69 years, were recruited between January 2004 and December 2007 from three regions in Mexico and their surrounding metropolitan areas (Mexico City, Monterrey and Veracruz). Participants were resident from one of these regions during at least 5 years prior to recruitment in the study. Cases were identified by trained field staff at twelve hospitals from major health-care institutions in Mexico: the Mexican Institute of Social Security (Instituto Mexicano del Seguro Social (IMSS), six hospitals), the Social Security and Services Institute for State Employees (Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado (ISSSTE), two hospitals) and the Ministry of Health (Secretariade Salud (SS), four hospitals). Inclusion criteria included: (i) patients with a new histologically confirmed diagnosis of BC, regardless of the stage of disease; (ii) patients with no previous treatment such as radiotherapy, chemotherapy or anti-oestrogens such as tamoxifen during the previous 6 months; (iii) patients who were not taking Aromasin<sup>®</sup> (exemestane), Femara<sup>®</sup>

(letrozole), Arimidex<sup>®</sup> (anastrozole) or Megace<sup>®</sup> (megestrol) at the time of the study; and (iv) patients who were not pregnant. Cases known to be HIV-positive ( $n$  1) were excluded from the study. After excluding *in situ* cases ( $n$  20), 980 cases were eligible.

Control subjects were randomly selected by multiple-step random sampling and were frequency-matched to cases according to 5-year age groups, health-care institution and region. The response rate for controls was 87.4% for Mexico City, 90.1% for Monterrey and 97.6% for Veracruz. The study personnel visited the selected households and determined willingness to participate in the study and conducted a face-to-face interview. Finally, an appointment was scheduled for each woman to attend the hospital for anthropometric measurements, mammography and a blood sample. A total of 1074 eligible controls were identified. Natural menopause was defined as twelve consecutive months of amenorrhoea without an obvious cause<sup>(29,30)</sup>.

### Ethics statement

Cases and controls provided written informed consent to participate in the study. The study protocol and data collection instruments were reviewed and approved by the Institutional Review Board at the National Institute of Public Health.

### Data collection and dietary questionnaire

A trained interviewer administered a questionnaire to each selected participant to collect information on her health, physical activity and diet. The health questionnaire collected data on sociodemographic characteristics; reproductive factors (e.g. age at menarche and menopause, number of full-term pregnancies, pregnancy outcomes, breast-feeding, menopausal status); use of oral contraceptives and hormone replacement therapy; family and individual history of chronic diseases (e.g. hypertension, diabetes mellitus, BC); personal history of sexually transmitted diseases; history of body size, smoking, alcohol consumption; and history of X-ray and mammographic studies.

Information on dietary habits was obtained through questions on food consumption during the 12 months preceding the symptoms (for BC cases) or the recruitment (for controls), using a semi-quantitative FFQ adapted from the Nurses' Health Study<sup>(19)</sup> for the Mexican population and validated in Mexico City<sup>(31,32)</sup>. The FFQ included 104 items and ten multiple-choice frequency categories of consumption: '6 or more per day', '4–5 per day', '2–3 per day', '1 per day', '5–6 per week', '2–4 per week', '1 per week', '1–3 per month', 'less than 1 per month' and 'never'. For each food item, the nutrient content per average unit (specified serving size: slice, glass or natural unit) was compiled<sup>(33)</sup> and women were asked how often they had consumed an amount of each food on average over the previous year. Nutrient intakes were computed

by multiplying the frequency response by the nutrient content of specified portion sizes using Microsoft® Office Access 2007. The database for calculating the nutrient intake took advantage of information from the US Department of Agriculture food composition tables<sup>(33)</sup> and it was complemented, when necessary, with a nutrient database developed by the National Institute of Nutrition in Mexico<sup>(34)</sup>.

To assess physical activity within the last 12 months, a semi-structured interview-based questionnaire was used to assess individuals' time spent in physical activity (light-, moderate- and vigorous-intensity, as well as sleep) during a regular week. The questionnaire was based on the 7 d recall questionnaire proposed by Sallis *et al.*<sup>(35)</sup>.

#### **World Cancer Research Fund/American Institute for Cancer Research score composition**

An index score reflecting adherence to the WCRF/AICR recommendations for cancer prevention was constructed; hereafter referred to as the 'WCRF/AICR score'. Out of ten recommendations (components), the following seven were retained to determine the score in women<sup>(36)</sup>: body fatness, physical activity, intake of foods and drinks that promote weight gain, intake of plant foods, intake of animal foods, consumption of alcoholic drinks and breast-feeding in women. Information on the construction of the score is detailed below in Table 2.

The score was designed on recent work evaluating the association between WCRF/AICR guidelines and cancer risk in the European Prospective Investigation into Cancer (EPIC) cohort<sup>(26)</sup>. The score was constructed using quantitative criteria supplied in the WCRF/AICR recommendations. Briefly, for each component, 1 point was assigned when the recommendation was met, 0.5 points when it was partially met and 0 points otherwise. In some cases, arbitrary *a priori* cut-off values were defined for intermediate categories, not based on the distribution of a given variable in our study. For the recommendations including several sub-recommendations (foods and drinks that promote weight gain and plant foods), the final score was the average of each sub-recommendation score. Three recommendations were not implemented in the present work: (i) the recommendation on preservation, processing and preparation of foods because insufficient data were available; (ii) the recommendation on dietary supplements which could not be operationalized in terms of cancer prevention without further assumptions about type or dose of supplementation; and (iii) the special recommendation related to cancer survivors which was outside the scope of the present study. As the WCRF/AICR recommendations were not ranked according to priority, all major recommendations were summed to contribute equally to the total WCRF/AICR score. Therefore, the total WCRF/AICR score ranged from 0 to 7 in the present study, with higher scores indicating greater adherence to the WCRF/AICR recommendations.

#### **Statistical analyses**

The *t* test was used to assess differences between cases and controls for continuous variables, i.e. height, weight, waist circumference, waist-to-hip ratio, BMI, age at menarche, age at first pregnancy, number of births, energy intake, breast-feeding, alcohol consumption and physical activity. A  $\chi^2$  test was used to test for differences between cases and controls for categorical variables, including socio-economic status, family history of BC, history of fibrocystic disease, use of oral contraceptives, use of hormone therapy, education, smoking and marital status. To estimate the association between the WCRF/AICR score and the risk of BC, conditional logistic regression models were used to compute odds ratios and associated 95% confidence intervals.

Matching accounted for age category, health-care system and region (model 1). Confounding factors were then included in the model (model 2), i.e. family history of BC (yes/no), age at menarche, age at first pregnancy, parity (number of children born alive), socio-economic status (lower, middle and upper), hormone replacement therapy (yes/no) and total energy consumption (kcal/d). Smoking status and use of oral contraceptive were not included in the different models because their inclusion in the statistical model did not change the results. Analyses were carried out for all women, and separately among pre- and postmenopausal women.

The score was categorized into quartiles based on the distribution of controls. The lowest quartile (from 0 to 3.25 points) was considered as the reference.

Also, the association of each component of the WCRF/AICR recommendations was evaluated in models mutually adjusted for all other components of the score. Tests for trends were computed using a continuous variable with values from 0 to 7 and *P* values were determined (*P*<sub>trend</sub>). Throughout the work, *P* < 0.05 was considered statistically significant. All analyses were conducted using the statistical software package SAS version 9.2.

#### **Results**

Postmenopausal women represented 59% and 56% of cases and controls, respectively, as displayed in Table 1. The response rate in control women was high in the three regions (87%, 90% and 97% in Mexico City, Monterrey and Veracruz, respectively). Cases and controls were similar with respect to the frequency of ever smoking, ever use of oral contraceptives and age at menarche. Compared with controls, cases displayed lower BMI values (29.3 kg/m<sup>2</sup> *v.* 30.5 kg/m<sup>2</sup>, *P* < 0.01), were more likely to have a family history of BC (6% *v.* 4%, *P* = 0.01), had on average fewer children and were more likely to have children later in life.

The different components of the WCRF/AICR score are described in Table 2. Compared with controls, cases

**Table 1** Clinical characteristics of the study participants: women aged 35–69 years, incident BC cases and controls matched on age, region and health-care system, CAMA study, Mexico, January 2004–December 2007

Categorical variables	Cases (n 980)		Controls (n 1074)		P value*
	n	%	n	%	
Menopausal status					0.19
Premenopausal	405	41	476	44	
Postmenopausal	575	59	598	56	
Socio-economic level					<0.01
Lower	304	31	359	34	
Middle	253	26	357	33	
Upper	423	43	358	33	
Education					0.49
Neither	65	7	90	9	
Primary	70	7	75	7	
Secondary	581	59	615	57	
>Secondary	263	27	294	27	
Marital status					<0.01
Married/living with a partner	613	61	732	68	
Separated or divorced	154	15	125	12	
Widow	107	11	125	12	
Single	126	13	92	8	
Parity					<0.01
Nulliparous	113	12	67	6	
1–2 children	331	34	304	28	
3–4 children	344	35	384	36	
≥5 children	186	19	316	30	
Smoking status					0.03
Ever	242	25	226	21	
Never	732	75	843	79	
Family history of BC					<0.01
No	920	94	1034	96	
Yes	60	6	40	4	
History of fibrocystic disease					<0.01
No	820	84	980	91	
Yes	148	15	83	8	
Unknown	12	1	11	1	
Ever use of oral contraceptives					0.98
No	539	55	594	55	
Yes	438	45	480	45	
Ever use of hormone therapy					<0.01
No	822	85	965	90	
Yes	149	15	106	10	
Alcohol intake†					<0.01
Drinker	322	33	254	24	
Non-drinker	648	67	819	76	
Continuous variables	Mean	P10–P90	Mean	P10–P90	P value*
Age (years)	52	39.1–65.8	51	39.2–65.3	0.01
BMI (kg/m <sup>2</sup> )	29.3	23.5–36.0	30.5	24.5–37.5	<0.01
Waist-to-hip ratio	0.90	0.82–0.98	0.91	0.83–0.99	0.02
Waist circumference	96.3	82–111	99.4	85–116	<0.01
Age at menarche (years)	12.8	11.0–15.0	12.8	11.0–15.0	0.31
Age at first pregnancy (years)	22.9	17.0–22.0	21.3	16.0–20.0	<0.01
Cumulative lactation (months)‡	25.1	0–66	31.8	0–70	<0.01
Energy intake (kJ/d)	9244	5807–13 239	8110	5066–11 702	<0.01
Energy intake (kcal/d)	2208	1387–3162	1937	1210–2795	<0.01
Physical activity (MET h/week)§	107.9	96.0–119.0	106.2	95.0–118.0	<0.01

BC, breast cancer; CAMA, Cancer de M ama; MET, metabolic equivalent of task; P10–P90, 10th–90th percentile.

\*From  $\chi^2$  test for categorical variables and *t* test for continuous variables.

†Median (interquartile range) among drinkers (330 cases and 254 controls).

‡Among parous women.

§Estimated from 7 d activity diary that queried all activities (working and leisure).

displayed a lower frequency of high physical activity (43 % *v.* 61 %) and of breast-feeding for longer than 6 months (64 % *v.* 74 %), but higher frequency of ‘fruits and vegetables’ intake larger than 600 g/d (63 % *v.* 48 %) and of ‘dietary fibre’ intake larger than 25 g/d (62 % *v.* 45 %).

After controlling for confounding factors, the WCRF/AICR score was not associated with risk of BC overall or by menopausal status, with OR comparing the score in the top *v.* bottom quartile (OR<sub>Q4–Q1</sub>) equal to 1.17 (95 % CI 0.75, 1.82, *P*<sub>trend</sub> = 0.26) and 0.97 (95 % CI 0.64, 1.46,

**Table 2** WCRF/AICR recommendations for cancer prevention and operationalization of the WCRF/AICR score in the CAMA study

WCRF/AICR recommendations	Personal recommendations	Operationalization†	Scoring	Cases (n 980)		Controls (n 1074)		Overall (n 2054)	
				n	%	n	%	n	%
1. Body fatness: Be as lean as possible without becoming underweight	1a. Ensure that body weight through childhood and adolescent growth projects towards the lower end of the normal BMI range at age 21 1b. Maintain body weight within the normal range from age 21 1c. Avoid weight gain and increases in waist circumference throughout adulthood	Insufficient data available	NA	181	19	144	13	325	16
				411	43	413	39	824	41
				363	38	505	48	868	43
2. Physical activity: Be physically active as part of your everyday life*	2a. Be moderately physically active, equivalent to brisk walking, for at least 30 min every day 2b. As fitness improves, aim for 60 min or more of moderate PA or for 30 min or more of vigorous PA every day 2c. Limit sedentary habits such as watching television	Insufficient data available	NA	419	43	652	61	1071	52
				208	21	119	11	327	16
				352	36	303	28	655	32
3. Foods and drinks that promote weight gain: Limit consumption of ED foods, avoid sugary drinks†	3a. Consume ED foods sparingly 3b. Avoid sugary drinks 3c. Consume fast foods sparingly, if at all	Moderate PA: ≥ 35 (MET h/week) Moderate PA: 17.5–34.9 (MET h/week) Moderate PA: 0–17.4 (MET h/week) Insufficient data available	NA	18	2	5	1	23	1
				476	49	443	41	919	45
				472	49	623	58	1095	54
4. Plants foods: Eat mostly foods of plant origin†	4a. Eat at least five portions/servings (at least 600 g) of a variety of non-starchy V&F every day 4b. Eat relatively unprocessed cereals (grains) and/or pulses (legumes) with every meal 4c. Limit refined starchy foods 4d. People who consume starchy roots or tubers as staples should also ensure sufficient intake of non-starchy vegetables, fruits and pulses (legumes)	V&F intake: ≥600 g/d V&F intake: 200–599 g/d V&F intake: <200 g/d Dietary fibre intake: ≥25 g/d Dietary fibre intake: 12.5–24.9 g/d Dietary fibre intake: 0–12.4 g/d Insufficient data available Not applicable to this population	1 0.5 0 1 0.5 0 NA NA	606	63	507	48	1113	54
				315	32	499	46	814	40
				49	5	67	6	116	6
5. Animal foods: Limit intake of RM and avoid PM	5a. People who eat RM to consume less than 500 g/week, very little if any to be processed RM & PM <500 g/week and PM <3 g/d RM & PM <500 g/week and PM 3 to <50 g/d RM & PM >500 g/week and PM ≥50 g/d	RM & PM <500 g/week and PM <3 g/d RM & PM <500 g/week and PM 3 to <50 g/d RM & PM >500 g/week and PM ≥50 g/d	1 0.5 0	217	22	194	18	411	20
				639	66	749	70	1388	68
				114	12	130	12	244	12

Table 2 Continued

WCRF/AICR recommendations	Personal recommendations	Operationalization†	Scoring	Cases (n 980)		Controls (n 1074)		Overall (n 2054)	
				n	%	n	%	n	%
6. Alcoholic drinks: Limit alcoholic drinks	6a. If alcoholic drinks are consumed, limit consumption to no more than two drinks a day for men and one drink a day for women	Alcohol intake: 0–10 g/d Alcohol intake: 10.1–20 g/d Alcohol intake: >20 g/d	1 0.5 0	939 17 14	97 2 1	1060 7 6	98 1 1	1999 24 20	98 1 1
7. Preservation, processing, preparation: Limit consumption of salt. Avoid mouldy cereals (grains) or pulses (legumes)	7a. Avoid salt-preserved, salted or salty foods; preserve foods without using salt 7b. Limit consumption of processed foods with added salt to ensure an intake of less than 6 g (2.4 g Na)/d 7c. Do not eat mouldy cereals (grains) or pulses (legumes)	Insufficient data available Insufficient data available Insufficient data available	NA NA NA						
8. Dietary supplements: Aim to meet nutritional needs through diet alone	8a. Dietary supplements are not recommended for cancer prevention	Not applicable to this population	NA						
WCRF/AICR special recommendations									
S1. Breast-feeding: Mothers to breast-feed; children need to be breast-fed	S1a. Aim to breast-feed infants exclusively up to 6 months and continue with complementary feeding thereafter	Cumulative breast-feeding: ≥6 months Cumulative breast-feeding: <6 months Cumulative breast-feeding: 0 months	1 0.5 0	629 119 232	64 12 24	796 109 169	74 10 16	1425 228 401	69 11 20
S2. Cancer survivors: Follow the recommendations for cancer prevention	S2a. All cancer survivors to receive nutritional care from an appropriately trained professional S2b. If able to do so, and unless otherwise advised, aim to follow the recommendations for diet, healthy weight and physical activity	Not applicable to this population Not applicable to this population							

WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research; CAMA, Cancer de Mãma; ED, energy-dense; RM, red meat; PM, processed meat; PA, physical activity; V&F, vegetables and fruits; MET, metabolic equivalent of task; NA, not available.

†Using the moderate physical activity (MET h/week) that combines recreational and occupational activities.

‡The score for recommendations 3 and 4 was the result of averaging the scores of each sub-recommendation (3a and 3b; 4a and 4b).

§ED food was calculated as energy (kcal; 1 kcal = 4.1868 kJ) from foods (solids foods and semi-solid or liquid foods such as soups) divided by the weight (g) of these foods. Drinks (including water, tea, coffee, juice, soft drinks, alcoholic drinks and milk) were not included in the calculation<sup>(27)</sup>. Sugary drinks included both soft drinks and fruit and vegetable juices.

**Table 3** Multivariate-adjusted odds ratios and 95 % confidence intervals between WCRF/AICR score and BC risk, overall and by menopausal status, among women aged 35–69 years, incident BC cases and controls matched on age, region and health-care system, CAMA study, Mexico, January 2004–December 2007

	Cases		Controls		Overall (n 936/1047)*		Premenopausal (n 387/468)*		Postmenopausal (n 549/579)*	
	n	%	n	%	OR	95 % CI	OR	95 % CI	OR	95 % CI
<b>Model 1†</b>										
Quartile 1	264	27	266	25	1.00	Reference	1.00	Reference	1.00	Reference
Quartile 2	315	33	354	33	0.87	0.69, 1.11	1.11	0.73, 1.66	0.81	0.59, 1.11
Quartile 3	200	20	233	22	0.80	0.61, 1.04	1.06	0.70, 1.59	0.63	0.45, 0.90
Quartile 4	199	20	221	20	0.84	0.65, 1.10	1.05	0.90, 1.24	0.72	0.50, 1.03
$P_{\text{trend}}$						0.03		0.52		0.003
<b>Model 2‡</b>										
Quartile 1	264	27	266	25	1.00	Reference	1.00	Reference	1.00	Reference
Quartile 2	315	33	354	33	1.04	0.81, 1.35	1.14	0.77, 1.68	0.99	0.69, 1.42
Quartile 3	200	20	233	22	1.05	0.78, 1.40	1.32	0.84, 2.06	0.91	0.61, 1.36
Quartile 4	199	20	221	20	1.04	0.78, 1.41	1.17	0.75, 1.82	0.97	0.64, 1.46
$P_{\text{trend}}$						0.96		0.26		0.39

WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research; BC, breast cancer; CAMA, Cancer de Mâma.

\*Frequencies of case and control participants, only includes participants from informative case sets.

†Assessed by analysing BC cases and their individual matched controls by conditional logistic regression, conditioning for matching factors (age, region and health-care institution).

‡Further adjusted for age at first pregnancy, number of full-term pregnancies, energy intake, socio-economic status, age at menarche, hormone therapy and family history of BC (no/yes).

$P_{\text{trend}}=0.39$ ) in pre- and postmenopausal women, respectively (Table 3).

Sensitivity analyses were carried out by excluding, in turn, each component of the WCRF/AICR recommendations (Table 4) from the overall score. Notably, the exclusion of the BMI component resulted in a marked reduction of BC risk overall, with  $OR_{Q4-Q1}=0.68$  (95 % CI 0.49, 0.92,  $P_{\text{trend}}=0.03$ ), and among postmenopausal women, with  $OR_{Q4-Q1}=0.60$  (95 % CI 0.39, 0.94,  $P_{\text{trend}}=0.03$ ). Two individual components were significantly associated with BC risk, as shown in Table 5. An inverse association was observed between BMI and risk of BC, with OR comparing obese *v.* normal-weight women equal to 0.57 (95 % CI 0.42, 0.76,  $P_{\text{trend}}<0.01$ ) and 0.48 (95 % CI 0.31, 0.73,  $P_{\text{trend}}<0.01$ ) overall and among premenopausal women, respectively. Women with high physical activity levels ( $\geq 35$  MET h/week) compared with low physical activity ( $\leq 17.5$  MET h/week; MET = metabolic equivalent of task) displayed OR equal to 0.61 (95 % CI 0.49, 0.76,  $P_{\text{trend}}<0.01$ ) and 0.42 (95 % CI 0.31, 0.59,  $P_{\text{trend}}<0.01$ ) overall and among postmenopausal women, respectively.

## Discussion

In a case-control study conducted in Mexico we observed that an index of adherence to the WCRF/AICR cancer prevention recommendations was not associated with the risk of BC. However, after excluding BMI, the WCRF/AICR score index was inversely associated with BC risk overall and among postmenopausal women, while a marginal effect was observed among premenopausal women.

Two prospective studies assessing the impact of the WCRF/AICR recommendations on BC have been published to date<sup>(26,37)</sup>. Within the EPIC cohort, women within the highest WCRF/AICR score were 16 % less likely to develop BC compared with those in the first category of the score (with a similar operationalization to our score) with hazard ratio equal to 0.84 (95 % CI 0.78, 0.90)<sup>(26)</sup>. The VITamins And Lifestyle (VITAL) study cohort found that postmenopausal women meeting at least five of the WCRF/AICR recommendations had 60 % lower BC risk (hazard ratio = 0.40; 95 % CI 0.25, 0.65) compared with women not meeting any recommendation<sup>(37)</sup>. A possible explanation is that in our study BMI was differentially associated with BC risk compared with the EPIC and VITAL cohorts. No major change in BC risk was observed in both EPIC and VITAL studies after excluding BMI from their respective index scores, indicating that BMI played only a partial role in the observed associations. Moreover, when physical activity was removed from the index, the WCRF/AICR score was associated with an increase in BC risk. We believe that the observed association might be due to the major role that BMI plays in the WCRF/AICR score related to BC risk.

In our study, when BMI was excluded from the WCRF/AICR score, a statistically significant inverse association between the WCRF/AICR score and BC risk was observed overall and among postmenopausal women. BMI was inversely associated with BC risk overall and among premenopausal women. A weak non-statistically significant decrease in BC risk was also observed among postmenopausal women. These findings are in contrast with positive relationships between BMI and BC risk consistently observed among postmenopausal women<sup>(38–41)</sup>

**Table 4** Odds ratios and 95 % confidence intervals for BC risk according to WCRF/AICR score and after alternate subtraction of each of its components, overall and by menopausal status, among women aged 35–69 years, incident BC cases and controls matched on age, region and health-care system, CAMA study, Mexico, January 2004–December 2007

	Cases		Controls		Overall* (n 936/1047)†		Premenopausal* (n 387/468)†		Postmenopausal* (n 549/579)†	
	n	%	n	%	OR	95 % CI	OR	95 % CI	OR	95 % CI
<b>WCRF/AICR‡</b>										
Quartile 1	264	27	266	25	1.00	Reference	1.00	Reference	1.00	Reference
Quartile 2	315	33	354	33	1.04	0.81, 1.35	1.14	0.77, 1.68	0.99	0.69, 1.42
Quartile 3	200	20	233	22	1.05	0.78, 1.40	1.32	0.84, 2.06	0.91	0.61, 1.36
Quartile 4	199	20	221	20	1.04	0.78, 1.41	1.17	0.75, 1.82	0.97	0.64, 1.46
<i>P</i> <sub>trend</sub>					0.96		0.26		0.39	
<b>WCRF/AICR – BMI§,  </b>										
Quartile 1	312	32	273	26	1.00	Reference	1.00	Reference	1.00	Reference
Quartile 2	321	33	379	35	0.85	0.66, 1.10	0.82	0.56, 1.21	0.84	0.58, 1.20
Quartile 3	217	22	249	23	0.84	0.63, 1.12	0.87	0.57, 1.33	0.77	0.52, 1.14
Quartile 4	121	13	173	16	0.68	0.49, 0.92	0.85	0.50, 1.44	0.60	0.39, 0.94
<i>P</i> <sub>trend</sub>					0.03		0.51		0.03	
<b>WCRF/AICR – Physical activity¶,  </b>										
Quartile 1	253	26	296	28	1.00	Reference	1.00	Reference	1.00	Reference
Quartile 2	208	21	307	29	0.92	0.70, 1.21	0.86	0.57, 1.29	0.98	0.66, 1.45
Quartile 3	251	26	263	24	1.27	0.96, 1.69	1.10	0.72, 1.69	1.46	0.98, 2.18
Quartile 4	267	27	208	19	1.74	1.29, 2.35	1.61	1.03, 2.53	1.97	1.29, 3.02
<i>P</i> <sub>trend</sub>					<0.01		0.03		<0.01	
<b>WCRF/AICR – Foods that promote weight gain§</b>										
Quartile 1	234	24	212	20	1.00	Reference	1.00	Reference	1.00	Reference
Quartile 2	255	36	402	37	0.93	0.71, 1.21	1.23	0.81, 1.86	0.78	0.54, 1.13
Quartile 3	205	21	251	23	0.92	0.68, 1.24	1.31	0.81, 2.11	0.73	0.49, 1.10
Quartile 4	186	19	209	20	0.92	0.67, 1.27	1.29	0.79, 2.10	0.71	0.46, 1.10
<i>P</i> <sub>trend</sub>					0.67		0.21		0.09	
<b>WCRF/AICR – Plant foods§</b>										
Quartile 1	254	26	245	23	1.00	Reference	1.00	Reference	1.00	Reference
Quartile 2	336	34	364	34	1.26	0.97, 1.64	1.68	1.12, 2.54	1.09	0.76, 1.57
Quartile 3	215	22	229	21	1.27	0.94, 1.71	1.72	1.09, 2.73	1.06	0.71, 1.58
Quartile 4	175	18	236	22	0.99	0.72, 1.35	1.12	0.69, 1.82	0.93	0.61, 1.43
<i>P</i> <sub>trend</sub>					0.57		0.51		0.20	
<b>WCRF/AICR – Meat§</b>										
Quartile 1	265	27	262	24	1.00	Reference	1.00	Reference	1.00	Reference
Quartile 2	331	34	369	34	1.06	0.82, 1.36	1.18	0.79, 1.75	1.02	0.72, 1.44
Quartile 3	213	22	265	25	0.90	0.68, 1.20	1.10	0.71, 1.72	0.81	0.55, 1.19
Quartile 4	171	17	178	17	1.02	0.75, 1.40	1.27	0.80, 2.03	0.86	0.56, 1.33
<i>P</i> <sub>trend</sub>					0.34		0.51		0.08	
<b>WCRF/AICR – Alcohol§</b>										
Quartile 1	253	26	262	25	1.00	Reference	1.00	Reference	1.00	Reference
Quartile 2	321	33	355	33	1.09	0.84, 1.41	1.21	0.82, 1.80	1.01	0.70, 1.45
Quartile 3	200	20	231	21	1.11	0.83, 1.49	1.38	0.88, 2.17	0.95	0.63, 1.42
Quartile 4	204	21	226	21	1.08	0.80, 1.46	1.30	0.83, 2.05	0.94	0.63, 1.43
<i>P</i> <sub>trend</sub>					0.48		0.07		0.48	
<b>WCRF/AICR – Breast-feeding§, **</b>										
Quartile 1	214	22	252	24	1.00	Reference	1.00	Reference	1.00	Reference
Quartile 2	224	23	273	25	1.01	0.76, 1.34	1.25	0.81, 1.92	0.87	0.60, 1.28
Quartile 3	270	27	277	26	1.17	0.89, 1.54	1.81	1.18, 2.78	0.84	0.58, 1.22
Quartile 4	271	28	272	25	1.15	0.87, 1.51	1.56	0.96, 2.41	0.94	0.65, 1.37
<i>P</i> <sub>trend</sub>					0.49		0.11		0.52	

WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research; BC, breast cancer; CAMA, Cancer de Mâma.

\*Assessed by analysing BC cases and their individual matched controls by conditional logistic regression, conditioning for matching factors (age, region and health-care institution) and adjusted for age at first pregnancy, number of full-term pregnancies, energy intake, socio-economic status, age at menarche, hormone therapy and family history of BC (no/yes).

†Frequencies of case and control participants, only includes participants from informative case sets.

‡Total WCRF/AICR score range: 0–7.

§The WCRF/AICR score minus one component ranged from 0 to 6.

||Statistical model was further adjusted for BMI.

¶Statistical model was further adjusted for physical activity.

\*\*Statistical model was further adjusted for breast-feeding.

and with inverse relationships among premenopausal women in Caucasian populations<sup>(39,42–44)</sup>. Few studies have investigated the association of BMI and BC risk in women from Hispanic origin and results have been

conflicting<sup>(45–47)</sup>. While, in a case–control study, delays in ascertainment of cancer onset may possibly lead to an underestimation of habitual weight among cases, this is unlikely to explain our results given that BC does not



**Table 5** Mutually adjusted odds ratios and 95 % confidence intervals for BC risk associated with the components of the WCRF/AICR score, overall and by menopausal status, among women aged 35–69 years, incident BC cases and controls matched on age, region and health-care system, CAMA study, Mexico, January 2004–December 2007

WCRF/AICR score	Case/control participants	Overall* (n 936/1047)†		Premenopausal* (n 387/468)†		Postmenopausal* (n 549/579)†	
		OR	95 % CI	OR	95 % CI	OR	95 % CI
<b>BMI</b>							
1	181/144	1.00	Reference	1.00	Reference	1.00	Reference
0.5	411/413	0.82	0.61, 1.09	0.75	0.50, 1.11	0.86	0.56, 1.31
0	363/505	0.57	0.42, 0.76	0.48	0.31, 0.73	0.67	0.42, 1.02
$P_{\text{trend}}$		<0.01		<0.01		0.10	
<b>Physical activity</b>							
1	419/652	0.61	0.49, 0.76	0.84	0.64, 1.17	0.42	0.31, 0.59
0.5	208/119	1.18	0.92, 1.66	1.47	0.98, 2.24	1.08	0.70, 1.59
0	352/303	1.00	Reference	1.00	Reference	1.00	Reference
$P_{\text{trend}}$		<0.01		0.01		<0.01	
<b>Foods that promote weight gain</b>							
1	0/0	–	–	–	–	–	–
0.75	15/7	3.16	1.12, 8.76	2.59	0.51, 13.21	3.98	1.02, 13.63
0.5	156/140	1.32	0.92, 1.99	1.27	0.73, 2.21	1.34	0.89, 2.34
0.25	466/476	1.17	0.89, 1.56	1.08	0.78, 1.51	1.24	0.87, 1.92
0	333/450	1.00	Reference	1.00	Reference	1.00	Reference
$P_{\text{trend}}$		0.10		0.24		0.03	
<b>Plant foods</b>							
1	506/386	1.00	Reference	1.00	Reference	1.00	Reference
0.75	184/220	0.80	0.60, 1.05	0.80	0.53, 1.22	0.77	0.53, 1.13
0.5	208/372	0.75	0.53, 1.02	0.74	0.48, 1.12	0.69	0.47, 1.04
0.25	46/68	1.01	0.60, 1.68	0.75	0.33, 1.68	1.21	0.60, 2.44
0	26/27	1.37	0.67, 2.78	1.34	0.44, 4.04	1.64	0.62, 4.36
$P_{\text{trend}}$		0.25		0.33		0.69	
<b>Red and processed meat</b>							
1	217/194	1.00	Reference	1.00	Reference	1.00	Reference
0.5	639/749	0.67	0.52, 0.87	0.63	0.39, 1.01	0.68	0.50, 0.94
0	114/130	0.57	0.38, 0.85	0.54	0.29, 1.00	0.58	0.33, 1.02
$P_{\text{trend}}$		0.40		0.57		0.35	
<b>Alcohol intake</b>							
1	939/1060	1.00	Reference	1.00	Reference	1.00	Reference
0.5	17/7	1.18	0.46, 3.01	1.24	0.27, 5.63	1.17	0.34, 4.03
0	14/6	1.33	0.44, 4.01	4.45	0.5, 39.89	0.63	0.16, 2.42
$P_{\text{trend}}$		0.16		0.10		0.99	
<b>Breast-feeding</b>							
1	629/796	1.00	Reference	1.00	Reference	1.00	Reference
0.5	119/109	1.16	0.84, 1.61	1.43	0.90, 2.27	0.96	0.6, 1.53
0	232/169	1.12	0.8, 1.57	1.14	0.68, 1.92	1.06	0.66, 1.7
$P_{\text{trend}}$		0.27		0.67		0.35	

WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research; BC, breast cancer; CAMA, Cancer de Măma.

\*Assessed by analysing BC cases and their individual matched controls by conditional logistic regression, conditioning for matching factors (age, region and health-care institution) and adjusted for age at first pregnancy, number of full-term pregnancies, energy intake, socio-economic status, age at menarche, hormone therapy, family history of BC (no/yes) and all the other WCRF/AICR components simultaneously.

†Frequencies of case and control participants, only includes participants from informative case sets.

usually lead to loss of weight and that only incident cases were included in the study. The lack of positive association between BMI and BC among postmenopausal women, which has been observed in many studies conducted among Caucasian populations, might be explained by the different fat distribution of Hispanic women<sup>(48)</sup>.

Studies in the USA show that American women of African or Hispanic origin are more likely to be obese than Caucasian women<sup>(49)</sup>. In our Mexican study population, 85 % of women were overweight or obese, whereas in the EPIC and VITAL cohorts, the frequencies were 61 % and 52 %, respectively<sup>(26,37)</sup>. This observation may suggest that the thresholds of BMI customarily used to identify normal-weight, overweight and obese individuals may not adapt

to populations other than in Europe and North America<sup>(50,51)</sup>. A WHO expert consultation addressed this issue in Asian populations and considered whether population-specific cut-off points for BMI were necessary<sup>(52)</sup>. To the best of our knowledge, there is no similar debate around Latin American populations. Therefore, adaptation of the WCRF/AICR recommendations outside Caucasian populations may need to consider other markers of adiposity or weight gain.

Several studies have shown that regular physical activity is beneficial to control weight and may also decrease the risk of some types of cancer, including BC<sup>(53–56)</sup>. Recently, moderate-intensity physical activity for 3 h/week was associated with a lower risk of BC in both pre- and

postmenopausal women, also suggesting differential associations with respect to menopausal status<sup>(57)</sup>. Other recent epidemiological studies have shown that BC risk reduction in relation to physical activity was greater in post- than in premenopausal women<sup>(55,57–60)</sup>. In our study, high physical activity was heterogeneously associated with BC risk compared with low physical activity level, with a 16% and 58% BC risk reduction among pre- and postmenopausal women, respectively. These results call for further investigation on the role of lack of physical activity as a risk factor in Latin American populations, possibly using prospective cohort studies.

Several limitations of the present study should be considered in interpreting our findings. Recall bias is a source of misclassification in case–control studies assessing diet through self-reported questionnaire measurements, possibly differentially expressed among cases and controls. However, interviewing women close to the time of diagnosis may have reduced the impact of potential changes in dietary and other lifestyle habits, likely to occur in cancer patients. The fact that in Mexico there is limited awareness about lifestyle risk factors related with BC may have attenuated the extent of differential classification. FFQ in general are subject to measurement error and this may have limited our ability to accurately measure relevant dietary components. The questionnaire measurements were validated and shown to perform reasonably well<sup>(31)</sup>. Not all WCRF/AICR recommendations were included in our score, either because of a lack of available data or because they were not applicable to the study population. This refers mostly to processing and preservation of foods, salt intake and vitamin supplementation. In addition, while epidemiological studies showed that abdominal adiposity such as waist circumference may be a better predictor of some cancer types, such as colorectal or pancreatic<sup>(61,62)</sup>, waist circumference was not part of the WCRF/AICR recommendations. However, additional analyses including waist circumference in the WCRF/AICR score instead of BMI produced very similar results.

In conclusion, adherence to the WCRF/AICR recommendations was not related to the risk of BC in the CAMA study. However, after exclusion of BMI from the original index, a statistically significant inverse association between the WCRF/AICR score and BC risk was observed. Further large prospective studies are required to clarify the role and relevance of adherence to the WCRF/AICR recommendations, and the role of adiposity, on BC risk in the Mexican population.

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