Association Between Western and Mediterranean Dietary Patterns and Mammographic Density

Adela Castelló; Nieves Ascunce; Dolores Salas-Trejo; Carmen Vidal; Carmen Sanchez-Contador; Carmen Santamariña; Carmen Pedraz-Pingarrón; Maria Moreno; Beatriz Pérez-Gómez; Virginia Lope; Nuria Aragonés; Jesús Vioque; Marina Pollán;.

Obstet Gynecol. 2016 Sep;128(3):574-81.

which has been published in final form at
https://doi.org/10.1097/AOG.0000000000001589

Title: Association between Western and Mediterranean dietary patterns and mammographic density.

Authors: Adela Castelló[1,2,3]PhD, Nieves Ascunce[2,4]MD, Dolores Salas-Trejo[5]PhD, Carmen Vidal[6]MD, Carmen Sanchez-Contador[7]MD, Carmen Santamariña[8]MD, Carmen Pedraz-Pingarrón[9]MD, Maria Pilar Moreno[10]MD, Beatriz Pérez-Gómez[1,2,3]PhD, Virginia Lope[1,2,3]PhD, Nuria Aragonés[1,2,3] PhD, Jesús Vioque,[2, 11] PhD, Marina Pollán[1,2,3] PhD on behalf of DDM-Spain research group[†]

1. Cancer Epidemiology Unit. National Center for Epidemiology. Instituto de Salud Carlos III. Madrid, Spain.

2. Consortium for Biomedical Research in Epidemiology & Public Health (CIBERESP). Instituto de Salud Carlos III. Madrid, Spain.

3. Cancer Epidemiology Research Group. Oncology and Hematology Area. IIS Puerta de Hierro (IDIPHIM). Madrid, Spain.

4. Navarre Breast Cancer Screening Program, Public Health Institute. Pamplona, Spain.

5. Valencian Breast Cancer Screening Program, General Directorate of Public Health. Valencia, Spain.

6. Cancer Prevention and Control Unit, Catalonian Institute of Oncology (ICO. Barcelona, Spain.

7. Balearic Islands Breast Cancer Screening Program, Directorate General of Public Health and Participation. Palma de Mallorca, Illes Balears.

8. Galician Breast Cancer Screening Program, Galician Regional Health Authority. A Coruña, Spain.

9. Castile-León Breast Cancer Screening Program, General Directorate of Public Health. Burgos, Spain

10. Aragón Breast Cancer Screening Program. Aragon Health Service. Zaragoza, Spain.

11. Universidad Miguel Hernandez. Sant Joan D'Alacant, Spain.

Membership of the DDM-Spain research group is provided in the Appendix 1

CORRESPONDING AUTHOR:

Dr. Adela Castelló

Cancer Epidemiology Unit, National Center for Epidemiology.

Instituto de Salud Carlos III.

Avenida Monforte de Lemos, 5, 28029, Madrid, Spain.

Phone: +34 91 822 2667.

Fax: +34 91 387 7815.

e-mail: acastello@isciii.es

SOURCES OF SUPPORT

This study was supported by Carlos III Institute of Health FIS (Spanish Public Health Research Fund: PI060386 FIS; PS09/00790 and PI15CIII/0029 research grants); the Spanish Ministry of Health (EC11-273); the Spanish Ministry of Economy and Competitiveness (IJCI-2014-

20900); the Spanish Federation of Breast Cancer Patients (FECMA: EPY 1169-10); and the Association of Women with Breast Cancer from Elche (AMACMEC: EPY 1394/15).

Short title: Dietary patterns and mammographic density

ACKNOWLEDGEMENTS

Authors which to acknowledge the financial support provided by Carlos III Institute of Health (PI060386 FIS;PS09/0790 and PI15CIII/0029), the Spanish Ministry of Economy and Competitiveness (IJCI-2014-20900), the Spanish Federation of Breast Cancer Patients (FECMA EPY 1169-10) and the Association of Women with Breast Cancer from Elche (AMACMEC EPY 1394/15).

Précis

High adherence to the *Western* dietary pattern is associated with higher mammographic density. However, the *Mediterranean* dietary pattern is not associated with mammographic density.

Abstract

Objective: To examine the association between two dietary patterns (*Western* and *Mediterranean*), previously linked to breast cancer risk, and mammographic density. **Methods:** This cross-sectional study included 3584 women attending population-based breast cancer screening programs and recruited between October 7th, 2007 and July 14th, 2008 (participation rate: 74.5%). Collected data included anthropometric measurements, demographic, obstetric and gynecologic characteristics, family and personal health history, and diet in the preceding year. Mammographic density was blindly assessed by a single radiologist and classified into four categories: <10%, 10–25%, 25–50%, and >50%. The association between adherence to either a *Western* or a *Mediterranean* dietary pattern and mammographic density was explored using multivariable ordinal logistic regression models with random center-specific intercepts. Models were adjusted for age, body mass index, parity, menopause, smoking, family history, hormonal treatment and calorie and alcohol intake. Differences according to women's characteristics were tested including interaction terms.

Results: Women with a higher adherence to the *Western* dietary pattern were more likely to have high mammographic density (n(%)=242(27%)) than women with low adherence (n(%)=169 (19%)) with a fully adjusted odds ratio (aOR_{Q4vsQ1}) of 1.25(95%Confidence Interval (CI)=1.03;1.52)). This association was confined to overweight/obese women (aOR_{Q4vsQ1}(95%CI)= 1.41(1.13;1.76)). No association between *Mediterranean* dietary pattern and mammographic density was observed.

Conclusion:

The Western dietary pattern was associated with increased mammographic density among overweight/obese women. Our results might inform specific dietary recommendations for women with high mammographic density.

Introduction

Breast cancer is the most common malignant tumor among women worldwide and one of the main causes of female mortality in medium and high income countries (1). Early detection and therapeutic advances have improved breast cancer prognosis, but the number of new cases keeps increasing (2) emphasizing the need to prioritize prevention as an indispensable tool to reduce the burden of disease.

High mammographic density is an important risk factor for breast cancer (3). Some results indicate a possible mediating effect of mammographic density in breast cancer risk (4), and this phenotype is currently being used to improve the discrimination of classical predictive models (5). Therefore, it is reasonable to presume that some of the factors associated to breast cancer onset might exert their effect by modifying mammographic density.

We have recently identified two dietary patterns associated with breast cancer risk: a *Western* dietary pattern associated to increased risk (Odds Ratio $(OR)_{\text{high-vs-low-adherence}}$ (95%Confidence Interval (CI))=1.46(1.06;2.01)) and a protective *Mediterranean* pattern ($OR_{\text{high-vs-low-adherence}}$(95%CI)=0.56(0.40;0.79)) (6). The identification of dietary habits associated with mammographic density may inform the design of dietary recommendations for women attending screening who have high mammographic density and, therefore, at higher risk for breast cancer (3). Unfortunately, since a few studies have explored the association between dietary patterns and mammographic density, current evidence remains inconclusive (7, 8). The objective of this study is to explore the association between adherence to the *Western* and *Mediterranean* dietary patterns and mammographic density.

Materials and Methods

In this cross-sectional study ("Determinants of Mammographic Density in Spain") we recruited women aged 45-69 attending breast cancer screening in one of the 7 centers from the population-based public Spanish Breast Cancer Screening network. Women with a previous cancer diagnosis (except non-melanoma skin cancers), attendees unable to respond to the questionnaire or women with a physical limitation preventing the performance of the mammogram were excluded. Among those eligible, women were randomly selected on a daily basis from the list of attendees scheduled for that particular day, taking into account the number of interviews that could be scheduled for the day. These women were invited to participate and, if they accepted, their appointment was re-scheduled to allow enough time for the interview before the mammogram. With an average participation rate of 74.5% (ranged 64.7–84.0% across centers) and a pre-set minimum sample size of 500 women for each of the 7 sites, the recruitment period lasted from October 7th, 2007 through July 14th, 2008, during which, a total of 3,584 women were recruited.

The company Demometrica (http://www.demometrica.com/) provided trained interviewers (one per center) to collect anthropometric, demographic, occupational, physical activity, obstetric and gynecologic data, as well as family and personal history (including weight and height at age 18). Data were entered in a data file in Demometrica headquarters. An internal validation was performed using a random sample of 10% of the questionnaires. In addition, all questionnaires were digitalized to make them easily accessible to researchers for checking for possible inconsistences and unusual values. One hundred and fifty women were re-interviewed to verify their answers. This second interview took place between 2 and 9 months after the first one and results from both interviews were highly concordant.

Smoking status was defined as "current smoker" for those women who smoke at the time of mammography or quit less than 6 months before; and as "nonsmoker" otherwise. Dietary intake during the preceding year was collected using a 117-items food frequency questionnaire (Appendix 2) similar to Willett questionnaire (9) and suitably adapted to and validated in Spanish adult populations (10, 11). Post-menopausal status was defined as self-reported absence of menstruation in the last 12 months. Weight, height, waist and hip circumferences were measured twice using the same protocol and identical balance scales, stadiometers and measuring tapes. A third measure was taken when the first two were not similar.

Mammographic density was blindly assessed by a single radiologist, unaware of the survey data. He read the craniocaudal mammogram of the left breast using a visual semiquantitative score with six categories proposed by Boyd (12) based on percentage of dense tissue in the breast, i.e., categories A (0%), B (0-10%), C (10–25%), D (25–50%), E (50–75%) and F (>75%). This scale has been associated with subsequent development of sporadic and familial breast cancer (3, 13) . Given the small percentage of women in categories A (4%) and F (5%), the two lowest and two highest categories were grouped together, creating the definitive outcome variable categorized as: <10%, 10–25%, 25–50%, and >50%.

Here we examined two dietary patterns identified in a previous case-control study (6) as being associated with breast cancer risk: a) *Western* dietary pattern, characterized by a high intake of high-fat dairy products, processed meat, refined grains, sweets, caloric drinks, convenience food and sauces and by low intakes of low-fat dairy products and whole grain, was associated with increased risk of breast cancer; and b) the *Mediterranean* dietary pattern characterized by high intake of fish, vegetables, legumes, boiled potatoes, fruits, olives and vegetable oil, and a

low intake of juices, was associated with a reduced risk of breast cancer . These two dietary patterns were identified applying principal components analysis without rotation of the variance-covariance matrix over 26 inter-correlated food groups (14). This method reports a set of weights (pattern loadings) associated with each food group that represents the correlation between food consumption and the component/pattern scores that can be used to reproduce such patterns in other samples as explained in detail in Castelló et al.(15). Briefly, we grouped 95 of the 117 items of the food frequency questionnaire (excluding non-caloric and alcoholic beverages) into 26 food groups (**Table 1**), and calculated the level of adherence scores for the *Western* and *Mediterranean* dietary patterns as a linear combination of the weights for each food group and pattern published in Castelló et al. (6) and the food group consumption reported the participants in the current study

Regarding the statistical analysis, first, we calculated basic descriptive statistics of the anthropometric, sociodemographic and lifestyle characteristics for all women, and by categories of mammographic density. Normally distributed continuous variables were described using the mean±standard deviation. Differences across categories of mammographic density were tested with ANOVA tests. Non-normally distributed continuous variables were described using the median (interquartile interval) and differences by mammographic density were tested with non-parametric Kruskal-Wallis tests. Categorical variables were described using the number of cases and corresponding percentages, and differences by mammographic density were tested with chi-square tests.

Associations between adherence to either dietary pattern and mammographic density were evaluated using ordinal logistic regression models with random center-specific intercepts including center as a random effect. As fixed-effects terms, age, body mass index (BMI), parity, menopausal and smoking status, family history of breast cancer, use of hormonal replacement

therapy and calorie and alcohol intake were considered as potential confounders. Three mixed models were adjusted in order to explore the confounding effect of different sets of variables. Model 1 was only adjusted by age and BMI (additionally to the random effects term); Model 2 also included parity, menopausal and smoking status, family history of breast cancer, and use of hormonal replacement therapy. Finally, calorie and alcohol intake were added to Model 3. Both, categorical (grouping the scores of adherence into quartiles) and continuous (1-standard deviation increase) associations with the scores were examined with all three models. For Model 3, nonlinear associations between the adherence to each pattern and mammographic density were assessed by fitting fractional polynomials.

With regards to the sample size, 22.8% of women had a mammographic density of over 50%. Therefore, our data allowed us to detect differences of 8% or more in the percentage of women classified in this category between extreme quartiles of adherence to each dietary pattern with a power of 80%.

Finally, when significant associations were found, separate analyses were performed by categories of all potential confounders above mentioned and represented in forest plots . Heterogeneity of effects was tested in model 3 by including an interaction term between the score of adherence and the corresponding variable.

Analyses were performed using STATA/MP (version 14.0, 2015, StataCorp LP) and statistical significance was set at 2-sided $p < 0.05$.

The protocol study “Determinants of Mammographic Density in Spain” was formally approved by the bioethics and animal welfare committee at the Carlos III Institute of Health and all participants signed an informed consent, including permission to publish the results from the research.

RESULTS

Thirty-six participants were excluded from analyses: 10 women who developed breast cancer within 6 months of study entry and mammography, 16 did not have mammographic density assessment, 2 did not have BMI information, and 8 participants reported a daily kcal intake under 750 Kcal or above 4500 Kcal. Therefore, analyses included data from 3548 women for whom we had complete information regarding all the variables of interest. As expected, pre/perimenopausal women showed a higher percentage of dense tissue (higher mammographic density). An elevated mammographic density was also associated with family history of breast cancer, tobacco use, high calorie and alcohol intake, younger age and lower BMI and parity (**Table 2**).

Crude associations summarized in **Table 2** showed that, compared to women in the lowest quartile of adherence to the Western dietary pattern, a higher proportion of those in the highest quartile had a mammographic density of over 50% (19% (n=169) vs. 27% (n=242), respectively). This association was not observed for the *Mediterranean* dietary pattern, 21% (n=187) of women in the lowest quartile of adherence and 24% (n=211) of those in the highest quartile of adherence had mammographic density of over 50%.

Multivariable analyses supported these findings confirming that, while breast density did not differ by level of adherence to the *Mediterranean* dietary pattern (aOR_{Q4vsQ1}(95%CI)= 0.99(0.81-1.21) and $aOR_{1\text{-standard deviation increase}}$ (95%CI)= 1.02(0.95-1.09)), those with a high adherence to the *Western* dietary pattern had higher mammographic density (aOR_{Q4vsQ1}(95%CI)= 1.25(1.03;1.52) and $aOR_{1\text{-standard deviationincrease}}$ (95%CI)= 1.09(1.02;1.18)) (**Table 3**). No statistically significant departure from linearity was observed in this association when the analysis with fractional polynomials was performed (data not shown).

Stratified analysis by subgroups revealed that, the effect of the *Western* dietary pattern on mammographic density was confined to women with a BMI over 25 (aOR_{Q4vsQ1}(95%CI)= 1.41(1.13;1.76), heterogeneity p-value=0.068). Our results also suggested some differences according to parity, calorie intake and tobacco consumption, but none of the interaction terms reached statistical significance (**Figure 1**).

DISCUSSION

Our results suggest that, whereas the Mediterranean diet was not related to mammographic density, a higher adherence to the Western dietary pattern was associated with higher mammographic density. Subgroup analyses suggest that this effect may be confined to overweight/obese women, and to be stronger among parous, non-smokers, and women with elevated calorie intake. However, our tests for heterogeneity approached significance at best, probably for lack of power. Thus, larger studies are needed to confirm these potential differential effects of diet on mammographic density.

Taking into account that high mammographic density is considered one of the key risk factors for breast cancer (3) , we expected to identify associations between dietary patterns and mammographic density similar in direction to those found for dietary patterns and breast cancer by Castelló et al. (6). However, while we found a positive association for the *Western* dietary pattern, mammographic density was not influenced by adherence to the *Mediterranean* dietary pattern.

Our findings support previous studies exploring the association between mammographic density and specific nutrients or foods included in the *Western* dietary pattern that reported positive associations with total energy, (16) high density foods (17), total,

saturated, and cholesterol fats (18, 19), proteins (18) and meat (20). Not surprisingly, a Western-type diet contrasts with the recommendations issued by the World Cancer Research Fund and the American Association for Cancer Research to reduce cancer burden. Adherence to these recommendations has been positively associated with a reduction of breast cancer risk (21) and mammographic density (17) in our context.

On the other hand, a weak inverse association with the *Mediterranean* dietary pattern (8) or with some of its main components such as olive oil (16),vegetables and fiber (22)has been previously reported. Others have found an absence or even a positive association of some of these items with mammographic density (19, 23, 24). . These inconclusive findings suggest that a reduction in mammographic density may not be one of the key mechanisms through which the Mediterranean diet lowers breast cancer risk. A possible explanation for the contradictory effect of a *Mediterranean* diet on mammographic density and breast cancer, is that this diet could be influencing the fat deposit of the breast without altering the percentage of dense tissue. Obesity, a condition inversely associated with mammographic density, increases breast cancer risk via several mechanisms, including the inflammatory effect of adipokines (25), while the *Mediterranean* diet seems to counteract an inflammatory state (26).

It is worth mentioning that the effect of the *Western* dietary pattern on mammographic density was only observed among overweight/obese women. Adipocytes are potent endocrine cells that produce hormones and growth factors; obesity strongly influences this endocrine millieu (27). Our results may reflect a synergic effect of this dietary pattern and the local adipose tissue on the fibro glandular component of the breast.

For its kind, this is a fairly large and carefully-conducted study on risk factors and mammographic density; however, it presents some limitations. First, the sample size was insufficient to detect significant interactions even when some differences by subgroups are

observed. Second, the representativeness of the selected sample might be slightly biased since healthy screening participants might be more concerned about their health than non-participants. However, participation rates in Spanish breast cancer screening programs are high (28) and women in our study are very similar to the women in the Spanish National Health Survey in terms of age range, socioeconomic level, prevalence of smoking and physical activity (29). Third, the visual assessment of breast density by a single radiologist, may imply a degree of subjectivity. However, the radiologist had very high intra-observer concordance (30), and we have confirmed that the visual scale used here is a predictor of subsequent breast cancer development risk (3). Additionally, the collection of data with different mammographic devices and interviewers in different centers might introduce some heterogeneity. These unmeasured sources of variability were taken into account by including random center-specific intercepts in our regression models. Finally, it should be noted that the cross-sectional design of the current study precludes the establishment of causal relationships between adherence to dietary patterns and mammographic density. However, it is hard to think that this association is acting in the other direction since information on diet was collected before the mammographic exploration.

REFERENCES

1. WHO. Global health risks: mortality and burden of disease attributable to selected major risks. Geneva, World Health Organization, 2009. 2009.
2. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JW, Comber H, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. European journal of cancer (Oxford, England : 1990). 2013;49(6):1374-403.
3. Pollan M, Ascunce N, Ederra M, Murillo A, Erdozain N, Ales-Martinez J, et al. Mammographic density and risk of breast cancer according to tumor characteristics and mode of detection: a Spanish population-based case-control study. Breast cancer research : BCR. 2013;15(1):R9.
4. Li J, Humphreys K, Eriksson L, Edgren G, Czene K, Hall P. Mammographic density reduction is a prognostic marker of response to adjuvant tamoxifen therapy in postmenopausal patients with breast cancer. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2013;31(18):2249-56.

5. Tice JA, Cummings SR, Smith-Bindman R, Ichikawa L, Barlow WE, Kerlikowske K. Using clinical factors and mammographic breast density to estimate breast cancer risk: development and validation of a new predictive model. Annals of internal medicine. 2008;148(5):337-47.
6. Castello A, Pollan M, Buijsse B, Ruiz A, Casas AM, Baena-Canada JM, et al. Spanish Mediterranean diet and other dietary patterns and breast cancer risk: case-control EpiGEICAM study. British journal of cancer. 2014;111(7):1454-62.
7. Takata Y, Maskarinec G, Park SY, Murphy SP, Wilkens LR, Kolonel LN. Mammographic density and dietary patterns: the multiethnic cohort. European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP). 2007;16(5):409-14.
8. Voevodina O, Billich C, Arand B, Nagel G. Association of Mediterranean diet, dietary supplements and alcohol consumption with breast density among women in South Germany: a cross-sectional study. BMC public health. 2013;13:203.
9. Willett WC, Sampson L, Stampfer MJ, Rosner B, Bain C, Witschi J, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am J Epidemiol. 1985;122(1):51-65.
10. Vioque J, Navarrete-Munoz EM, Gimenez-Monzo D, Garcia-de-la-Hera M, Granado F, Young IS, et al. Reproducibility and validity of a food frequency questionnaire among pregnant women in a Mediterranean area. Nutrition journal. 2013;12:26.
11. Vioque J, Weinbrenner T, Asensio L, Castello A, Young IS, Fletcher A. Plasma concentrations of carotenoids and vitamin C are better correlated with dietary intake in normal weight than overweight and obese elderly subjects. The British journal of nutrition. 2007;97(5):977-86.
12. Boyd NF, Byng JW, Jong RA, Fishell EK, Little LE, Miller AB, et al. Quantitative classification of mammographic densities and breast cancer risk: results from the Canadian National Breast Screening Study. Journal of the National Cancer Institute. 1995;87(9):670-5.
13. Ramon YCT, Chirivella I, Miranda J, Teule A, Izquierdo A, Balmana J, et al. Mammographic density and breast cancer in women from high risk families. Breast cancer research : BCR. 2015;17:93.
14. Burt C. Factor Analysis and canonical correlations. Br J Math Stat Psychol. 1948;1(2):95-106.
15. Castello A, Buijsse B, Martin M, Ruiz A, Casas AM, Baena-Canada JM, et al. Evaluating the applicability of data-driven dietary patterns to independent samples with focus on measurement tools for pattern similarity. J Acad Nutr Diet 2016.
16. Garcia-Arenzana N, Navarrete-Munoz EM, Lope V, Moreo P, Vidal C, Laso-Pablos S, et al. Calorie intake, olive oil consumption and mammographic density among Spanish women. International journal of cancer Journal international du cancer. 2014;134(8):1916-25.
17. Castello A, Prieto L, Ederra M, Salas-Trejo D, Vidal C, Sanchez-Contador C, et al. Association between the Adherence to the International Guidelines for Cancer Prevention and Mammographic Density. PloS one. 2015;10(7):e0132684.
18. Nagata C, Matsubara T, Fujita H, Nagao Y, Shibuya C, Kashiki Y, et al. Associations of mammographic density with dietary factors in Japanese women. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2005;14(12):2877-80.
19. Qureshi SA, Couto E, Hilsen M, Hofvind S, Wu AH, Ursin G. Mammographic density and intake of selected nutrients and vitamins in Norwegian women. Nutrition and cancer. 2011;63(7):1011-20.

20. Sala E, Warren R, Duffy S, Welch A, Luben R, Day N. High risk mammographic parenchymal patterns and diet: a case-control study. British journal of cancer. 2000;83(1):121-6.
21. Castello A, Martin M, Ruiz A, Casas AM, Baena-Canada JM, Lope V, et al. Lower Breast Cancer Risk among Women following the World Cancer Research Fund and American Institute for Cancer Research Lifestyle Recommendations: EpiGEICAM Case-Control Study. PloS one. 2015;10(5):e0126096.
22. Nagel G, Mack U, von Fournier D, Linseisen J. Dietary phytoestrogen intake and mammographic density -- results of a pilot study. European journal of medical research. 2005;10(9):389-94.
23. Mishra GD, dos Santos Silva I, McNaughton SA, Stephen A, Kuh D. Energy intake and dietary patterns in childhood and throughout adulthood and mammographic density: results from a British prospective cohort. Cancer causes & control : CCC. 2011;22(2):227-35.
24. Thomson CA, Arendell LA, Bruhn RL, Maskarinec G, Lopez AM, Wright NC, et al. Pilot study of dietary influences on mammographic density in pre- and postmenopausal Hispanic and non-Hispanic white women. Menopause (New York, NY). 2007;14(2):243-50.
25. Renehan AG, Zwahlen M, Egger M. Adiposity and cancer risk: new mechanistic insights from epidemiology. Nature reviews Cancer. 2015;15(8):484-98.
26. Medina-Remon A, Casas R, Tressserra-Rimbau A, Ros E, Martinez-Gonzalez MA, Fito M, et al. Polyphenol intake from a Mediterranean diet decreases inflammatory biomarkers related to atherosclerosis: A sub-study of The PREDIMED trial. British journal of clinical pharmacology. 2016.
27. McCready J, Arendt LM, Rudnick JA, Kuperwasser C. The contribution of dynamic stromal remodeling during mammary development to breast carcinogenesis. Breast cancer research : BCR. 2010;12(3):205.
28. Castells X, Sala M, Ascunce N, Salas D, Zubizarreta R, Casamitjana M. Descripción del cribado del cáncer en España. Proyecto DESCRIC. Madrid: Plan de Calidad para el Sistema Nacional de Salud. Ministerio de Sanidad y Consumo. Agència d'Avaluació de Tecnologia i Recerca Mèdiques de Cataluña; 2007. Informes de Evaluación de Tecnologías Sanitarias, AATRM núm. 2006/01. 2007.
29. Garcia-Arenzana N, Navarrete-Munoz EM, Peris M, Salas D, Ascunce N, Gonzalez I, et al. Diet quality and related factors among Spanish female participants in breast cancer screening programs. Menopause (New York, NY). 2012;19(10):1121-9.
30. Garrido-Estepa M, Ruiz-Perales F, Miranda J, Ascunce N, Gonzalez-Roman I, Sanchez-Contador C, et al. Evaluation of mammographic density patterns: reproducibility and concordance among scales. BMC cancer. 2010;10:485.

TABLES

Table 1: Composition of food groups based on the food frequency questionnaire of the "Determinants of Mammographic Density in Spain" study

FOOD GROUP	FOOD[a]
HIGH-FAT DAIRY	Whole-fat milk, w_1[b]·A+D enriched milk, w_1[b]·Folate enriched milk, double cream, condensed milk, whole-fat yogurt, semi-cured, cured or creamy cheese, custard, flan, pudding, ice-cream
LOW FAT DAIRY	Semi-skimmed and skimmed milk, Omega3 enriched milk[c], w_2[b]·A+D enriched milk, w_2[b]·Folate enriched milk, soy milk, soy yogurt, skimmed yogurt, cottage or fresh white cheese
EGGS	Eggs
WHITE MEAT	Chicken with skin, skinless chicken, game (turkey, rabbit, etc.)
RED MEAT	Pork, beef, lamb, liver (beef, pork or chicken), entrails, hamburger
PROCESSED MEAT	Serrano ham and other cold meat, sausages, bacon, pâte, foie-gras
WHITE FISH	1/3·all kind of fried fish, Fresh white fish (hake, sea bass, sea bream)
OILY FISH	1/3·all kind of fried fish, Fresh blue fish (Tuna, swordfish, sardines, anchovies, salmon), canned tuna, canned sardines or mackerel, salted and smoked fish
SEAFOOD/SHELLFISH	1/3·all kind of fried fish, Clams, mussels, oysters, squid, cuttlefish, octopus, prawn, crab, shrimp, lobster
LEAFY VEGETABLES	Spinach, chard, lettuce, endive, escarole
FRUITING VEGETABLES	Tomato, eggplant, zucchini, cucumber, pepper, artichoke
ROOT VEGETABLES	Carrot, pumpkin
OTHER VEGETABLES	Cooked cabbage, cauliflower or broccoli, onion, green beans, asparagus, mushrooms, corn, garlic, vegetable soup
LEGUMES	Legumes, soy sprouts
POTATOES	Roasted or boiled potatoes
FRUITS	Orange, mandarin, banana, apple, pear, peach, nectarine, apricot, watermelon, melon, grapes, plums or prunes (dried or fresh), strawberries, kiwi
NUTS	Almonds, peanuts, pine nuts, hazelnut
REFINED GRAINS	White-flour bread, rice, pasta
WHOLE GRAINS	Whole-grain bread and partial whole-grain bread, breakfast cereals, wheat germs
OLIVES AND VEGETABLE OIL	Olives, added olive oil to salads, bread and dishes, other vegetable oils (sunflower, corn, soybean)
OTHER EDIBLE FATS	Margarine, butter
SWEETS	Chocolate and other sweets, cocoa powder, plain cookies, chocolate cookies, pastries (croissant, donut, cake, pie or similar)
SUGARY	Jam, Honey, Sugar
JUICES	Tomato Juice, freshly squeezed orange juice, juice (other than freshly squeezed)
CALORIC DRINKS	Sugar-sweetened soft drinks
CONVENIENCE FOOD AND SAUCES	Fried potatoes, crisps, pizza, chicken and Serrano ham croquette, mayonnaise, tomato sauce, ketchup, fish sticks

[a]Log-transformed centered intake in grams.

[b]Weighted within the high and low fat dairy categories according to the consumption of whole, semi-skimmed and skimmed milk.

w_1 = whole /(whole + semi- skimmed + skimmed)

w_2 = (semi-skimmed + skimmed) /(whole + semi skimmed + skimmed)

w_1 and w_2 where 0.5 if consumption was 0 grams for whole, semi-skimmed and skimmed milk.

[c]All the Omega3 enriched milk brands that have been examined are skimmed or semi-skimmed

Table 2: Description of anthropometric, sociodemographic and lifestyle characteristics for all women and by mammographic density classification (Boyd scale)(12).

		MAMMOGRAPHIC DENSITY				
CHARACTERISTICS	**ALL WOMEN** n=3548	**<10%** n=870	**10-25%** n=733	**25-50%** n=1136	**>50%** n=809	**p[a]**
Age (years) Mean±standard deviation	56.20±5.46	58.28±4.89	57.04±5.03	55.87±5.45	53.66±5.34	<0.001
BMI (Kg/m2) Mean±standard deviation	28.03±4.99	30.77±5.47	28.79±4.80	27.37±4.25	25.33±3.81	<0.001
Parity n(%)						<0.001
Nulliparous	318 (9%)[b]	48 (15%)[c]	47 (15%)[c]	110 (35%)[c]	113 (35%)[c]	
1	541 (15%)[b]	95 (18%)[c]	90 (17%)[c]	181 (33%)[c]	175 (32%)[c]	
2	1703 (48%)[b]	408 (24%)[c]	350 (21%)[c]	567 (33%)[c]	378 (22%)[c]	
≥3	986 (28%)[b]	319 (32%)[c]	246 (25%)[c]	278 (28%)[c]	143 (15%)[c]	
Menopausal Status n(%)						<0.001
Pre/Perimenopausal	816 (23%)[b]	107 (13%)[c]	108 (13%)[c]	268 (33%)[c]	333 (41%)[c]	
Postmenopausal	2732 (77%)[b]	763 (28%)[c]	625 (23%)[c]	868 (32%)[c]	476 (17%)[c]	
Smoking n(%)						<0.001
Never or former ≥6 months	2179 (61%)[b]	599 (28%)[c]	460 (21%)[c]	701 (32%)[c]	419 (19%)[c]	
Smoker or former <6 months	1369 (39%)[b]	271 (20%)[c]	273 (20%)[c]	435 (32%)[c]	390 (28%)[c]	
Family History of Breast Cancer n(%)						0.005
No	3289 (93%)[b]	815 (25%)[c]	696 (21%)[c]	1045 (32%)[c]	733 (22%)[c]	
Yes	259 (7%)[b]	55 (21%)[c]	37 (14%)[c]	91 (35%)[c]	76 (30%)[c]	
Use of Hormonal Replacement Therapy n(%)						0.117
No	3200 (90%)[b]	768 (24%)[c]	664 (21%)[c]	1026 (32%)[c]	742 (23%)[c]	
Yes	348 (10%)[b]	102 (29%)[c]	69 (20%)[c]	110 (32%)[c]	67 (19%)[c]	

Calorie Intake (kcal) Mean±standard deviation	2054±481	1989±471	2023±476	2076±472	2122±498	<0.001
Alcohol Intake (Ethanol in grs) Median(IQR)	0.85 (0.00-5.68)	0.04 (0.00-3.19)	0.89 (0.00-5.68)	0.85 (0.00-5.83)	1.20 (0.00-7.05)	<0.001
Quartiles(Q) of adherence to the Western dietary Pattern n(%)						<0.001
Q1	888(25%)[b]	285(32%)[c]	183(21%)[c]	251(28%)[c]	169(19%)[c]	
Q2	886(25%)[b]	218(25%)[c]	181(20%)[c]	302(34%)[c]	185(21%)[c]	
Q3	887(25%)[b]	205(23%)[c]	193(22%)[c]	276(31%)[c]	213(24%)[c]	
Q4	887(25%)[b]	162(18%)[c]	176(20%)[c]	307(35%)[c]	242(27%)[c]	
Quartiles(Q) of adherence to the Mediterranean dietary Pattern n(%)						0.725
Q1	887(25%)[b]	223(25%)[c]	200(23%)[c]	277(31%)[c]	187(21%)[c]	
Q2	887(25%)[b]	221(25%)[c]	180(20%)[c]	289(33%)[c]	197(22%)[c]	
Q3	886(25%)[b]	221(25%)[c]	173(20%)[c]	278(31%)[c]	214(24%)[c]	
Q4	888(25%)[b]	205(23%)[c]	180(20%)[c]	292(33%)[c]	211(24%)[c]	

[a] p-value for differences among mammographic density categories resulting from ANOVA test when comparing means, from Kruskal-Wallis test when comparing Medians and from Chi-Square tests when comparing percentages.
[b] Column percentages
[c] Row percentages

Table 3: Adjusted Logistic regression analyses of adherence to Western or Mediterranean dietary patterns on mammographic density--All women.

DIETARY PATTERNS	MODEL 1[a] OR (95%CI) [b]	MODEL 2[a] aOR (95%CI) [c]	MODEL 3[a] aOR (95%CI) [d]
WESTERN			
QUARTILES (Q)[e]			
Q1	1	1	1
Q2	1.11 (0.93-1.32)	1.09 (0.92-1.3)	1.06 (0.89-1.27)
Q3	1.13 (0.95-1.35)	1.11 (0.93-1.32)	1.05 (0.87-1.26)
Q4	1.34 (1.12-1.59)	1.35 (1.13-1.61)	1.25 (1.03-1.52)
p-trend[f]	0.002	0.001	0.039
Per 1-standard deviation increase[g]	1.11 (1.05-1.19)	1.12 (1.05-1.20)	1.09 (1.02-1.18)
MEDITERRANEAN			
QUARTILES (Q)[e]			
Q1	1	1	1
Q2	1.07 (0.90-1.27)	1.06 (0.89-1.26)	1.01 (0.85-1.20)
Q3	1.06 (0.89-1.27)	1.05 (0.88-1.25)	0.97 (0.80-1.16)
Q4	1.12 (0.94-1.34)	1.12 (0.94-1.34)	0.99 (0.81-1.21)
p-trend[f]	0.234	0.228	0.811
Per 1-standard deviation increase[g]	1.06 (0.99-1.13)	1.06 (1.00-1.13)	1.02 (0.95-1.09)

[a] All models included center as a random effect.
[b] Odds Ratio and 95% confidence interval adjusted by age and BMI.
[c] Odds Ratio and 95% confidence interval adjusted by age, BMI, parity, menopausal and smoking status, family history of BC and use of HRT.
[d] Odds Ratio and 95% confidence interval adjusted by age, BMI, parity, menopausal and smoking status, family history of BC, use of HRT, and calorie and alcohol intake.
[e] Odds Ratio and 95% confidence interval for quartiles of adherence.
[f] p value for trend resulting from the Wald test associated to the categorical variable include as continuous in the regression models.
[g] Odds Ratio and 95% confidence intervals per 1-standard deviation increase in the score of adherence to the specified dietary pattern.

Figure 1: Adjusted Odds Ratios (aOR) and 95% Confidence Intervals (95%CI) for the risk of high mammographic density in women in the fourth quartile of adherence to the Western dietary pattern according to women characteristics.

[a] All interaction models were adjusted by all the variables included in the figure and included center as a random effect.

Supplemental digital content I: Appendix 1: Researchers involved in the study "Determinants of Mammographic Density in Spain" (Determinantes de la Densidad Mamográfica en España).

Marina Pollán (IP), Adela Castelló, Nieves Ascunce, Dolores Salas-Trejo, Carmen Vidal, Carmen Sanchez-Contador, Carmen Santamariña, Carmen Pedraz-Pingarrón, Maria Pilar Moreno, Beatriz Pérez-Gómez, Virginia Lope, Nuria Aragonés, Jesús Vioque, Pilar Moreo, Mª Soledad Abad, Francisca Collado, Francisco Casanova, Jose Antonio Vázquez, Milagros García, Manuela Alcaraz, Mª Soledad Laso, Josefa Miranda, Francisco Ruiz Perales and Maria Ederra.

Supplemental digital content II: English translation of the food frequency questionnaire used to collect dietary information from the study "Determinants of Mammographic Density in Spain" (Determinantes de la Densidad Mamográfica en España).

FOOD FRECUENCY QUESTIONNAIRE OF DDM-SPAIN

Dear Madame, the aim of this part of the questionnaire is to assess your diet in the past year. Your answers will be very useful and that is why we demand you all your attention and collaboration. When a type of food does not match complete your consumption pattern you can try to answer approximately with the indicated quantities. We will help you with examples and instructions.

For each type of food, please average your use of these foods in the past year. You must take into account when food is to consume alone or when it is to add to other foods. For example, if you prepare eggs consider when you eat them alone (E.g. fried or boiled) and when you add them to another food. If you have eaten a 2-eggs omelet every two days you will answer "1 daily". Do not take into account the eggs used to prepare baked goods or sweets.

Do not forget to fill up every line

I. DAIRY PRODUCTS		Never ó <1 month	1-3 per mo	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6+ per day
Milk (One glass, 200 cc)	Whole	1	2	3	4	5	6	7	8	9
	Semi-skimmed	1	2	3	4	5	6	7	8	9
	Skimmed or low fat	1	2	3	4	5	6	7	8	9
	Other milk: with Soy	1	2	3	4	5	6	7	8	9
	with Omega-3	1	2	3	4	5	6	7	8	9
	with Calcium and vitamins A+D	1	2	3	4	5	6	7	8	9
	with Folate	1	2	3	4	5	6	7	8	9
Condensed milk (1 table spoon)		1	2	3	4	5	6	7	8	9
Full cream, e.g. added coffee, whipped (1 table spoon)		1	2	3	4	5	6	7	8	9
Full fat or Greek yogurt (125 g carton)		1	2	3	4	5	6	7	8	9
Low fat yogurt (125 g carton)		1	2	3	4	5	6	7	8	9
Soy yogurt (125 g carton)		1	2	3	4	5	6	7	8	9
Cottage cheese, low fat soft cheese (medium serving, 100 g)		1	2	3	4	5	6	7	8	9
Cheese e.g. Cheddar, Brie, Edam (medium serving, 50 g)		1	2	3	4	5	6	7	8	9
Custard, cream caramel, pudding (one)		1	2	3	4	5	6	7	8	9
Ice cream (1 cup or cornet)		1	2	3	4	5	6	7	8	9
II. EGGS, MEAT, FISH		Never ó <1 month	1-3 per mo	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6+ per day
Poultry eggs (one)		1	2	3	4	5	6	7	8	9
Chicken WITH skin (one medium size serving, 90 g)		1	2	3	4	5	6	7	8	9
Chicken WITHOUT skin (one medium size serving, 90 g)		1	2	3	4	5	6	7	8	9
Meat as main dish: roast, steak, mince, stew or casserole (one medium size serving, 125g)	Beef	1	2	3	4	5	6	7	8	9
	Pork	1	2	3	4	5	6	7	8	9
	Lamb	1	2	3	4	5	6	7	8	9
Game: rabbit, quail, duck (one medium size serving, 100g)		1	2	3	4	5	6	7	8	9
Hamburger (one medium, 100 g)		1	2	3	4	5	6	7	8	9
Liver beef, pork, chicken (one medium serving, 100g)		1	2	3	4	5	6	7	8	9

Trips, brains, sweetbreads (one serving, 100 g)	1	2	3	4	5	6	7	8	9
Serrano or cocked ham (one serving, 50 g)	1	2	3	4	5	6	7	8	9
Other Cold meat: salami type sausage, salami, bologna (one serving, 50 g)	1	2	3	4	5	6	7	8	9
Sausages and similar (one, 50 g)	1	2	3	4	5	6	7	8	9
Pâté, liver pâté (medium serving, 50 g)	1	2	3	4	5	6	7	8	9
Pork fat (lard), bacon (2 slides, 50 g)	1	2	3	4	5	6	7	8	9
Fish fried and mixed (1 medium serving, 100 g)	1	2	3	4	5	6	7	8	9
White fish fried or grilled fish: haddock, sole, gilthead (1 serving, 100 g)	1	2	3	4	5	6	7	8	9
Blue fish boiled or grilled: tuna fish, swordfish, bonito (1 serving, 100 g)	1	2	3	4	5	6	7	8	9
Other dark meat fish: mackerel, sardines, anchovy, salmon (1 serving, 100 g)	1	2	3	4	5	6	7	8	9
Canned tuna fish in oil (small can)	1	2	3	4	5	6	7	8	9
Canned sardines or mackerel in oil (small can)	1	2	3	4	5	6	7	8	9
Salted fish and/or smoked fish: anchovy, cod, salmon (small serving, 50g)	1	2	3	4	5	6	7	8	9
Clams, mussels, oysters (one serving, 100 g)	1	2	3	4	5	6	7	8	9
Squid, sepia, octopus (one serving, 100 g)	1	2	3	4	5	6	7	8	9
Shellfish: prawns, crabs, lobster (one serving 100 g)	1	2	3	4	5	6	7	8	9
III. VEGETABLES AND LEGUMES	Never ó <1 month	1-3 per mo	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6+ per day
Spinach or beet, cooked (1 medium serving, 100 g)	1	2	3	4	5	6	7	8	9
Cabbage, cauliflower, broccoli, cooked (1 medium serving, 100 g)	1	2	3	4	5	6	7	8	9
Lettuce, green salad (1 medium serving, 60 g)	1	2	3	4	5	6	7	8	9
Onions (1 medium size, 50 g)	1	2	3	4	5	6	7	8	9
Tomatoes (1 medium size, 100 g)	1	2	3	4	5	6	7	8	9
Tomato juice (one glass, 200cc)	1	2	3	4	5	6	7	8	9
Tomato sauce (half a cup, 100 cc)	1	2	3	4	5	6	7	8	9
Carrot, pumpkin (1 or small dish, 50 g)	1	2	3	4	5	6	7	8	9
French been, cooked (1 serving, 100 g)	1	2	3	4	5	6	7	8	9
Aubergine, marrow, cucumber (one, 100 g)	1	2	3	4	5	6	7	8	9
Peppers (one, 75 g)	1	2	3	4	5	6	7	8	9
Artichokes (1 serving, 100 g)	1	2	3	4	5	6	7	8	9
Asparagus (1 serving, 75 g)	1	2	3	4	5	6	7	8	9
Mushrooms (1 serving, 100 g)	1	2	3	4	5	6	7	8	9
Sweet corn (1 serving or small can, 82 g)	1	2	3	4	5	6	7	8	9
Soya sprouts (a handful, 30g)	1	2	3	4	5	6	7	8	9
Wheat germ (a handful, 10g)	1	2	3	4	5	6	7	8	9
Legumes: lentils, chickpeas, dark or white beans (1 medium dish, 140 g)	1	2	3	4	5	6	7	8	9
IV. FRUITS	Never ó <1 month	1-3 per mo	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6+ per day
Oranges, mandarins (one)	1	2	3	4	5	6	7	8	9
Orange juice, fresh fruit (small glass, 125 cc)	1	2	3	4	5	6	7	8	9
Bananas (one)	1	2	3	4	5	6	7	8	9
Apple, pears (one medium size)	1	2	3	4	5	6	7	8	9
Peaches, apricots (one medium size)	1	2	3	4	5	6	7	8	9
Watermelon, melon (1 slice medium)	1	2	3	4	5	6	7	8	9
Grapes (medium bunch of grapes or dessert dish)	1	2	3	4	5	6	7	8	9
Prunes, plum, dried or fresh (one)	1	2	3	4	5	6	7	8	9
Strawberries (7-8 units)	1	2	3	4	5	6	7	8	9

Kiwi (one)	1	2	3	4	5	6	7	8	9
Olives (15 small olives)	1	2	3	4	5	6	7	8	9
Dried fruit: almonds, peanuts, pinions, hazelnut (1 small dish or small packet, 30g)	1	2	3	4	5	6	7	8	9
V. BREAD, CEREALS AND SIMILAR	Never ó <1 month	1-3 per mo	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6+ per day
White bread (small piece or 3 slides, 60 g)	1	2	3	4	5	6	7	8	9
Brown or whole bread (small piece or 3 slides, 60 g)	1	2	3	4	5	6	7	8	9
Breakfast cereals (30 g dried, 1 cup)	1	2	3	4	5	6	7	8	9
Chips (fried potatoes in oil) (1 serving, 100 g)	1	2	3	4	5	6	7	8	9
Potatoes: boiled, grilled (1 medium)	1	2	3	4	5	6	7	8	9
Chips (1 small bag, 25-30 g)	1	2	3	4	5	6	7	8	9
Rice cooked (1 medium dish)	1	2	3	4	5	6	7	8	9
Pasta: spaghetti, noodles, macaroni and similar (1 dish)	1	2	3	4	5	6	7	8	9
Pizza (1 portion, 200 g)	1	2	3	4	5	6	7	8	9
VI. OILS, FAT AND SWEETS	Never ó <1 month	1-3 per mo	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6+ per day
Olive oil added to salads, bread or food (1 table spoon)	1	2	3	4	5	6	7	8	9
Other vegetables oils (idem): girasol, corn, soy (1 1 table spoon)	1	2	3	4	5	6	7	8	9
Margarine added to bread or food (1 1 table spoon or spread on bread)	1	2	3	4	5	6	7	8	9
Butter added to bread or meals (spread butter on bread)	1	2	3	4	5	6	7	8	9
Biscuits (one)	1	2	3	4	5	6	7	8	9
Chocolate cookies (1 double cookie)	1	2	3	4	5	6	7	8	9
Baked goods: croissant, donut, small sponge cake, brownies, cake or similar (one)	1	2	3	4	5	6	7	8	9
Chocolate and similar (1 piece or candy bar or 2 chocolates)	1	2	3	4	5	6	7	8	9
Drinking chocolate, cocoa and similar (1 tbs of powder)	1	2	3	4	5	6	7	8	9
VII. DRINKS AND OTHERS	Never ó <1 month	1-3 per mo	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6+ per day
Red wine (1 glass, 125 cc)	1	2	3	4	5	6	7	8	9
White, rose or sparkling wine and champagne (1 glass, 125 cc)	1	2	3	4	5	6	7	8	9
Sherry, dry wine, vermouth (small glass, 50 cc)	1	2	3	4	5	6	7	8	9
Cider (1 glass, 125 cc)	1	2	3	4	5	6	7	8	9
Beer (1 glass or small bottle, 200 cc)	1	2	3	4	5	6	7	8	9
No-alcohol beer (1 glass or small bottle, 200 cc)	1	2	3	4	5	6	7	8	9
Fruit and cream spirits (20-25º) (small glass, 50 cc)	1	2	3	4	5	6	7	8	9
Brandy, gin, rum, whiskey, vodka 40º (small glass, 50 cc)	1	2	3	4	5	6	7	8	9
Sugar-sweetened soft drinks (one, 250 cc)	1	2	3	4	5	6	7	8	9
Diet soft drinks (one, 250 cc)	1	2	3	4	5	6	7	8	9
Tap water (one glass, 250cc)	1	2	3	4	5	6	7	8	9
Still bottled water (one glass, 250cc)	1	2	3	4	5	6	7	8	9
Sparkly bottled water (one glass, 250cc)	1	2	3	4	5	6	7	8	9
Bottled fruit juice (one glass, 200cc)	1	2	3	4	5	6	7	8	9
Coffee (1 cup)	1	2	3	4	5	6	7	8	9
Decaffeinated coffee (1 cup)	1	2	3	4	5	6	7	8	9
Red, green, blank of green tea (1 cup)	1	2	3	4	5	6	7	8	9
Other teas like chamomile or mint (1 cup)	1	2	3	4	5	6	7	8	9
Vegetable soup and puree (1 serving, 250 g)	1	2	3	4	5	6	7	8	9
Serrano ham or chicken croquettes (one)	1	2	3	4	5	6	7	8	9

Fish fingers (one)	1	2	3	4	5	6	7	8	9
Mayonnaise (1 1 table spoon)	1	2	3	4	5	6	7	8	9
Ketchup (1 1 table spoon)	1	2	3	4	5	6	7	8	9
Added salt (1 pinch)	1	2	3	4	5	6	7	8	9
Garlic (1 clove)	1	2	3	4	5	6	7	8	9
Jam, honey (1 1 table spoon)	1	2	3	4	5	6	7	8	9
Added sugar (1 tea spoon)	1	2	3	4	5	6	7	8	9
Added spices (1 tea spoon)	1	2	3	4	5	6	7	8	9