

**Title:** Impact of moderate wine consumption in breast cancer risk.

**Authors' full names and surnames:** Francesc Casanovas-Garriga<sup>1</sup>, Simona Costanzo<sup>2,3</sup>, Augusto Di Castelnuovo<sup>2</sup>, Roger Borràs<sup>4,5</sup>, Ana María Ruiz-León<sup>1,6,7,8,9</sup>, Rosa Casas<sup>1,6,7,9\*</sup>, Ramon Estruch<sup>1,6,7,9\*</sup>

**Affiliation (institutions and country):** <sup>1</sup>Department of Internal Medicine, Hospital Clinic, Institut d'Investigació Biomèdica August Pi I Sunyer (IDIBAPS), Barcelona, Spain; <sup>2</sup>Research Unit of Epidemiology and Prevention, IRCCS NEUROMED, Pozzilli (IS), Italy; <sup>3</sup>Research Center in Epidemiology and Preventive Medicine (EPIMED), Department of Medicine and Surgery, University of Insubria, Varese, Italy; <sup>4</sup>Cardiovascular Institute, Hospital Clínic, IDIBAPS, Universitat Autònoma de Barcelona, Barcelona, Spain.; <sup>5</sup>Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Instituto de Salud Carlos III, Madrid, Spain.; <sup>6</sup>CIBER OBN (Fisiopatología de la Obesidad y la Nutrición), Instituto de Salud Carlos III, Madrid, Spain; <sup>7</sup>Institut de Recerca en Nutrició i Seguretat Alimentària (INSA-UB), University of Barcelona, Barcelona, Spain; <sup>8</sup>Fundación Dieta Mediterránea, Barcelona, Spain; <sup>9</sup>Faculty of Medicine and Life Sciences, University of Barcelona, Barcelona, Spain

\*Equal contribution

**Background:** Breast Cancer (BC) was, in 2022, the most frequently diagnosed cancer and the most prevalent cause of cancer mortality in women globally. A key feature of the Mediterranean diet (MedDiet) is the moderate consumption of wine with meals. The MedDiet offers a variety of health benefits and has been linked to a lower risk of BC and improved survival rates thanks to anti-inflammatory and antioxidant properties, and interactions with hormone receptors. Wine contains various (poly)phenolic substances that have demonstrated anti-oncogenic effects at molecular level in BC. However, epidemiological studies have produced controversial results regarding the relationship between moderate wine consumption and BC risk.

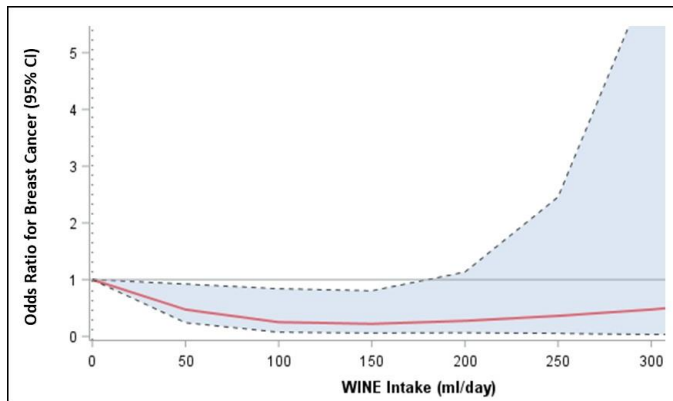
**Objectives:** To evaluate the potential protective effect of moderate wine consumption on BC risk.

**Methods:** This analysis employed a case-control design, drawing from a cohort of 188 women from the PREDIMED study. The population included 47 cases of breast cancer, diagnosed during follow-up and confirmed through clinical records, and 141 controls who remained cancer-free, matched to cases by age, sex, and BMI. The exposure variables were the levels and average wine consumption, as assessed through FFQs administered at multiple time points during follow-up. Conditional logistic regression models were used in SAS to examine the association between exposures and breast cancer. Dose-response analyses were conducted using natural cubic splines with three knots.

**Results:** The average wine consumption during follow-up, analyzed as a continuous exposure per 1 drink (100 mL), was associated with a non-significant 55% reduction in breast cancer risk (Table; P=0.059). All categories of wine consumption, including former drinkers, were associated with a reduced risk of breast cancer compared to abstainers.

	<b>N°Case/N°Control</b>	<b>Odds ratio (95 % CI)</b>
<b>Average wine consumption</b>	47/141	0.45 (0.19- 1.03)
<b>Categories of wine consumption</b>		
<i>Abstainers</i>	29/46	-1-
<i>Former</i>	3/24	0.14 (0.03-0.57)
<i>1-50 mL/day</i>	11/36	0.30 (0.10-0.86)
<i>50-100 mL/day</i>	2/19	0.08 (0.01-0.47)
<i>≥ 100 mL/day</i>	2/16	0.12 (0.02-0.68)

As illustrated in the dose-response curve, an increased risk of breast cancer was observed only for wine intake exceeding 150 mL per day (1.5 glasses).



**Discussion and Conclusion:** These results contrast with current general guidelines and scientific evidence, which link even low-to-moderate wine consumption to a greater risk of breast cancer, suggesting no such risk at these levels. The observed outcomes can be partially attributed to the reduced population size that was studied. Therefore, it is essential that these analyses are replicated in larger cohorts to ensure the validity of the results.

**Keywords:** Mediterranean Diet, Breast Cancer, Wine in Moderation, Polyphenols, Lifestyle

**Summarized CV of the first author:** Francesc Casanovas Garriga is a PhD Student in the Cardiovascular Risk, Nutrition and Aging group, in IDIBAPS, Faculty of Medicine and Health Science, University of Barcelona, Spain. He obtained a BSc in Genetics for Universitat Autònoma de Barcelona (UAB) and a MSc in Translational Medicine at Universitat de Barcelona. Since joining the Cardiovascular Risk, Nutrition and Aging group, led by Dr. Ramon Estruch, in 2021, he has been involved in several research projects, such as PREDIMED-PLUS. His PhD Thesis Project focuses in Protective mechanisms associated to moderate wine consumption on cardiovascular disease and cancer.