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Additional Information

Occupation, occupational exposures and mammographic density in Spanish women

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1 **ABSTRACT**

2 **Introduction:** Mammographic density (MD), the proportion of radiologically dense breast tissue, is a
3 strong risk factor for breast cancer. Our objective is to investigate the influence of occupations and
4 occupational exposure to physical, chemical, and microbiological agents on MD in Spanish
5 premenopausal women.
6

7 **Methods:** This is a cross-sectional study based on 1,362 premenopausal workers, aged 39-50, who
8 attended a gynecological screening in a breast radiodiagnosis unit of Madrid City Council. The work
9 history was compiled through a personal interview. Exposure to occupational agents was evaluated
10 using the Spanish job-exposure matrix MatEmESp. MD percentage was assessed using the validated
11 semi-automated computer tool DM-Scan. The association between occupation, occupational
12 exposures, and MD was quantified using multiple linear regression models, adjusted for age,
13 educational level, body mass index, parity, previous breast biopsies, family history of breast cancer,
14 energy intake, use of oral contraceptives, smoking, and alcohol consumption.
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16 **Results:** Although no occupation was statistically significantly associated with MD, a borderline
17 significant inverse association was mainly observed in orchard, greenhouse, nursery, and garden
18 workers ($\beta=-6.60$; 95% confidence interval (95%CI)=-14.27; 1.07) and information and communication
19 technology technicians ($\beta=-7.27$; 95%CI=-15.37; 0.84). On the contrary, a positive association was
20 found among technicians in art galleries, museums, and libraries ($\beta=8.47$; 95%CI=-0.65; 17.60). Women
21 occupationally exposed to fungicides, herbicides, and insecticides tended to have lower MD. The
22 percentage of density decreased by almost 2% for every 5 years spent in occupations exposed to the
23 mentioned agents.
24

25 **Conclusions:** Women involved in the agricultural sector and those exposed to pesticides in
26 occupational settings appear to have lower MD. Future studies are needed to confirm these results and
27 clarify possible biological mechanisms.
28

29 **Key words:** breast density; occupation; chemical agents; physical agents; job-exposure matrix, DDM-
30 Madrid
31

32 **Abbreviations**

33 MD: mammographic density

34 BMI: body mass index

35 IARC: International Agency for Research on Cancer

36 95%CI: 95% confidence interval

37 CNO: National Classification of Occupations

38 MatEmESp: Spanish job-exposure matrix
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40 **1. INTRODUCTION**

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1 Mammographic density (MD), defined as the percentage of radiologically dense fibrous and glandular
2 tissue seen on the mammographic image, represents an important breast cancer risk factor (Boyd et
3 al., 2007, 2005). A key feature of MD, compared to other established risk factors for breast cancer, is
4 its dynamic and modifiable nature. MD decreases progressively with age, transition to menopause,
5 number of children, and body mass index (BMI). On the contrary, the use of combined hormonal therapy
6 seems to increase this phenotype (Assi et al., 2012; Huo et al., 2014).
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10 Breast cancer is the most frequent tumor and the second cause of cancer death in Spanish women
11 (Ferlay et al., 2018) The origin of this tumor is multifactorial, and occupational factors have hardly been
12 considered in the risk assessment (Fenga, 2016). The number of recognized occupational carcinogens
13 has been increasing in recent decades. In 2017, 47 agents and 12 occupations or industries were
14 recognized by the International Agency for Research on Cancer (IARC) with sufficient evidence of
15 carcinogenicity in humans (Loomis et al., 2018). It has been estimated that around 5% of all cancers in
16 Spain can be directly attributed to exposures that are considered occupational (Kogevinas, 2012).
17 However, the true magnitude of the oncological workload could be greater, partly due to the new
18 substances that are continuously introduced into the work environment without having been previously
19 evaluated, and to the large number of possible carcinogens with still inconclusive evidence (IARC group
20 2B) (Kogevinas, 2012; Loomis et al., 2018). Some agents recognized by the IARC as carcinogens for
21 breast cancer have been detected in occupational settings, such as X-radiation, gamma radiation,
22 ethylene oxide, polychlorinated biphenyls, and night shift work involving circadian disruption (World
23 Health Organization, 2020).
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33 Previous studies detected an association between breast cancer risk and certain occupations, such as
34 teachers, nurses, social workers, cashiers, women who work in the cosmetic, chemical, and
35 pharmaceutical industry, hairdressers, and telephone operators (Goldberg and Labreche, 1996;
36 Kourmoussi and Alexopoulos, 2016; Lie et al., 2007; Pollán and Gustavsson, 1999). An association with
37 night shift work has also been found (Megdal et al., 2005). However, there is only two previous studies
38 that attempted to identify the occupations associated with higher MD, detecting higher risk among
39 teachers and nurses (García-Pérez et al., 2017), and lower risk among managers and administrators in
40 public sectors, agricultural workers and services and sales workers (Li et al., 2018). Regarding
41 occupational exposures, as far as we know, there are hardly any studies that have evaluated their
42 association with MD. While Lope et al. detected an increased MD among women occupationally
43 exposed to perchloroethylene, ionizing radiation, mold spores, and aliphatic/alicyclic hydrocarbon
44 solvents (Lope et al., 2018), other two studies associated this marker with self-reported history of night
45 shift work (Pedraza-Flechas et al., 2017; Peplonska et al., 2012).
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54 Given the limited information available, and the fact that published studies are based on predominantly
55 postmenopausal women, in whom the breast tissue involution and the fall in hormone levels could have
56 a significant influence, our objective is to identify the occupations associated with higher MD and to
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1 evaluate the influence of the occupational exposure to chemical, physical, and microbiological agents
2 on MD in Spanish premenopausal working women.
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4 **2. MATERIALS AND METHODS**

5 **2.1 Study Population and data collection**

7 DDM-Madrid is a cross-sectional study conducted between June 2013 and May 2015 (Lope et al., 2019).
8 A sample of 1466 premenopausal workers, aged between 39 and 50, was recruited from the Madrid
9 City Medical Diagnostic Center (*Madrid Salud*), where the women went for their routine gynecological
10 examination. Women were invited to participate by phone prior to their screening visit. Those who
11 accepted signed an informed consent document and answered an epidemiological survey previously
12 used in the DDM-Spain study (DDM-Spain et al., 2012). This questionnaire was administered by three
13 interviewers on the same day as the one scheduled for their medical examination. The participants also
14 answered a 117-item food frequency questionnaire that included eating habits during the previous year,
15 and which has been previously validated in the Spanish population (INMA-Valencia Cohort Study et al.,
16 2013).
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24 The craniocaudal and mediolateral oblique views of the 2D mammograms of both breasts were
25 collected. The percentage of MD from the craniocaudal mammogram of the left breast was evaluated
26 by an experienced radiologist using the DM-Scan computer tool, a free semi-automated software that
27 quantifies MD in full-field digital images with high reproducibility and validity (Llobet et al., 2014; Pollán
28 et al., 2013). The internal consistency of the radiologist was evaluated by conducting a pilot study with
29 100 women whose mammograms were duplicated and read again. An intra-class correlation coefficient
30 of 0.87 was obtained between the first and second reading (95% confidence interval (95%CI)=0.82-
31 0.92). Women whose MD could not be measured were excluded, as well as those who had analogical
32 mammograms.
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39 The epidemiological questionnaire included a section on occupational history, with information on the
40 most recent occupation, the longest occupation, and time worked in each of them. Occupations were
41 coded according to the 2011 National Classification of Occupations (CNO-11) (Instituto Nacional de
42 Estadística (INE), 2020). The present study includes active women who had been working for at least
43 one year, or women who stopped working during the previous year but had worked for more than a year
44 in their last occupation.
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49 Occupational exposure to chemical, physical, and microbiological agents was assessed using the
50 Spanish job-exposure matrix (García et al., 2013; MatEmEsp.org, 2020). This matrix has been
51 developed specifically for Spanish workers, covering the period 1996-2005, and includes 52 chemical,
52 11 physical, and 2 microbiological agents, in alignment with those included in the Finnish job-exposure
53 matrix (Kauppinen et al., 2009). The estimates to develop the matrix were made by a panel of hygienists
54 and specialists with extensive experience in industrial hygiene in Spain. For each agent at each job title,
55 the prevalence of exposure (proportion of exposed workers) and the intensity of exposure (1-year
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1 average concentration levels) were quantitatively assessed. The matrix considers as “exposed
2 occupations” those in which at least 5% of the workers had a mean annual exposure level that exceeded
3 the reference exposure level, which was obtained from the 2012 Spanish occupational Threshold Limit
4 Values Document (Instituto Nacional de Seguridad e Higiene en el Trabajo (INSHT), 2012). In the case
5 of ionizing radiation, those that exceeded 0.2 mSv were considered as “exposed occupations”. Since
6 this matrix is based on the 1994 National Classification of Occupations (CNO-94), we had to recode the
7 occupations found in our study from the CNO-11 to the CNO-94. This task was carried out by the same
8 hygienists who developed the matrix.
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13 **2.2 Ethical approval**

14 The DDM-Madrid study was conducted in accordance with the Declaration of Helsinki guidelines and
15 was approved by the Ethics and Animal Welfare Committee of the Carlos III Institute of Health.
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19 **2.3 Statistical analysis**

20 Characteristics of the participants were described with absolute values and percentages. Mean MD
21 values and their corresponding 95% CIs were also calculated according to the women characteristics
22 and compared using the Wald test.
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27 Multiple linear regression models were used to analyze the association of MD with occupations and with
28 the exposure to chemical, physical, and microbiological agents. An independent model for each
29 occupation and each agent was performed. The response variable was the percentage of MD. Models
30 were adjusted for age (continuous), educational level (primary school or less, secondary school,
31 university graduate), BMI (continuous), parity (nulliparous, 1, 2, >2 children), previous breast biopsies
32 (yes, no), family history of breast cancer (none, second degree only, first degree), daily caloric intake
33 (continuous), use of oral contraceptives (never, past use, current use), smoking status (never, ex-
34 smoker, current smoker), and alcohol consumption (never, <10 g/d, ≥10 g/d). We only considered those
35 occupations with at least 10 workers and those agents to which at least 10 women were exposed.
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42 Finally, the duration of exposure was also evaluated, both for each occupation and for each agent, using
43 the number of months exposed as an explanatory variable and analyzing the increase or decrease in
44 MD for every 5 years of exposure. All analyses were performed using STATA/MP 15.0 software.
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48 **3. RESULTS**

49 Results presented in this manuscript are based on 1362 women (93%). The general characteristics of
50 the study population, as well as the mean percentage of MD according to these characteristics, are
51 presented in Table 1. The mean percentage (\pm standard deviation) of MD in the study population was
52 34.3 ± 17.4 . The mean age was 44 years. More than half attended university (61%), had a normal BMI
53 (66%), had two or more children (53%), ever used oral contraceptives (59%), and consumed less than
54 10 g/day of alcohol (66%). Furthermore, 38% of women never smoked, and the mean calorie intake was
55 1978 ± 677 kcal/d. MD was significantly higher in women with lower BMI, in nulliparous women, in those
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1 who had never used oral contraceptives, in women with high caloric intake, and in workers who had
2 previous breast biopsies. The mean duration of the participants' last occupation was 16 years.
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4 Table 2 shows the association between MD and occupations with at least 10 workers. Although no
5 occupation was statistically significantly associated with MD, an inverse association was observed in
6 the information and communication technology sector ($\beta=-7.27$; 95%CI=-15.37; 0.84), and among
7 skilled workers in orchards, greenhouses, nurseries, and gardens ($\beta=-6.60$; 95%CI=-14.27; 1.07). In
8 contrast, technicians in art galleries, museums, and libraries ($\beta=8.47$; 95%CI=-0.65; 17.60) presented
9 higher MD. Regarding the analysis by duration of employment, we also did not observe an association.
10 It is only worth nothing that MD of women who worked in art galleries, museums, and libraries increased
11 by 3% for every 5 years worked in this occupation ($\beta=2.98$; 95%CI=-0.55; 6.51), while MD of information
12 and communication technology technicians decreased 2% ($\beta=-1.98$; 95%CI=-4.06; 0.11).
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19 With respect to the association between MD and occupational exposure to different chemical, physical,
20 and microbiological agents (Table 3), workers exposed to fungicides, herbicides, and insecticides of the
21 endosulfan type had lower MD ($\beta=-6.19$; 95%CI=-12.56; 0.19). The participants most exposed to these
22 agents were workers in orchards, greenhouses, nurseries, and gardens, as well as the agricultural,
23 forestry, and natural environment technicians (data not shown). In addition, exposure to other types of
24 insecticides (chlorpyrifos, methomyl and pyrethrin) also showed an inverse association with MD ($\beta=-$
25 5.73; 95%CI=-11.63; 0.17). Workers in the aforementioned sectors, as well as kitchen assistants and
26 cleaning staff in offices, hotels, and other similar establishments were exposed to these insecticides
27 (data not shown). Participants exposed to microbiological agents, specifically non-human bacteria and
28 mold spores, as well as workers exposed to gasoline, volatile sulfur compounds, and animal dust also
29 showed an inverse association with MD ($\beta=-6.60$; 95%CI=-14.27; 1.07). The workers in orchards,
30 greenhouses, nurseries, and gardens were the occupations exposed to the mentioned agents. Finally,
31 an inverse association was detected with exposure to wood dust ($\beta=-5.44$; 95%CI=-11.70; 0.82), an
32 agent to which a greater diversity of occupations were exposed.
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42 Regarding the exposure time (Table 3), we observed that MD decreased for every 5 years spent in
43 occupations exposed to herbicides, fungicides, insecticides of endosulfan type ($\beta=-1.53$; 95%CI=-3.32;
44 0.26), other types of insecticides ($\beta=-1.63$; 95%CI=-3.35; 0.08), and wood dust ($\beta=-1.61$; 95%CI=-3.43;
45 0.22).
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49 **4. DISCUSSION**

50 This study analyzes the association between occupation, occupational exposure to physical, chemical,
51 and microbiological agents and MD in a sample of more than 1300 workers in Madrid. Although, in
52 general, none of the occupations or occupational exposures studied were consistently associated with
53 MD, we found an inverse association among women employed in agricultural activities, and among
54 workers exposed to pesticides, gasoline, volatile sulfur compounds, animal and wood dust, and
55 microbiological agents.
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1 Women who worked in orchards, greenhouses, nurseries, and gardens had lower MD. Li et al, in a study
2 that included 4,867 Chinese women from the National Cancer Screening Program, also observed lower
3 MD among agricultural workers (Li et al., 2018). However, in another study that tried to identify
4 occupations associated with high MD, these professionals were not included (García-Pérez et al., 2017).
5 However, this finding is consistent with recent epidemiological studies that have shown lower breast
6 cancer risk in gardeners, farmers, carpenters or workers employed in the agricultural sector in general
7 (Kaneko et al., 2019; Katuwal et al., 2018). Workers employed in these activities are exposed to
8 pesticides and, to a lesser extent, to microbiological agents, gasoline (polycyclic aromatic
9 hydrocarbons), volatile sulfur compounds, and animal dust (MatEmEsp.org, 2020), compounds that
10 have been inversely associated with MD in our study. Lope et al (Lope et al., 2018) also found an inverse
11 relationship between MD and exposure to gasoline. However, they found no association with exposure
12 to pesticides, volatile sulfur compounds, and animal dust (Lope et al., 2018).
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21 The 13 study participants included in occupational category 3733 (Technicians in art galleries,
22 museums, and libraries) were all “library technicians” or “auxiliary library technicians”. The higher MD
23 detected in these workers is difficult to explain. Several previous studies have detected an excess risk
24 of breast cancer among these professionals (Pollán et al., 2001; Teitelbaum et al., 2003; Zheng et al.,
25 2002). One of them detected this association in young and parous women (Teitelbaum et al., 2003).
26 Pollán et al attributed the association observed among Swedish men to possible exposure to
27 electromagnetic fields of frequencies above the ELF-range from electronic security systems, or to the
28 sedentary behavior of these professionals (Pollán et al., 2001). The potential exposure to carcinogenic
29 chemicals has not been characterized in these professionals (Snedeker, 2006). This occupation
30 involves extensive handling of printed paper, yet little is known about transfer of dyes or inhalation of
31 paper treatments. The solvent formaldehyde is used in paper finishing and in manufacturing carbonless
32 paper (Snedeker, 2006) and, precisely, occupational exposure to this solvent was associated with higher
33 MD in Spanish women (Lope et al., 2018).
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42 Although some of the pesticides studied are probably or likely human carcinogens (captan, diuron),
43 mammary carcinogens (diuron), xenoestrogens (2-4D, diuron, endosulfan, and methomyl), and
44 cholinesterase inhibitors (chlorpyrifos), ecological studies have not found a general pattern of
45 association between exposure to these pesticides and breast cancer risk (Brody et al., 2004; Reynolds
46 et al., 2005). Regarding MD, while one study showed that women exposed to
47 dichlorodiphenyltrichloroethane (DDT) in utero had higher MD in their adult stage (Krigbaum et al.,
48 2020), two other studies showed lower breast density in women with high circulating levels of persistent
49 organic compounds (Diorio et al., 2013; Rusiecki et al., 2020). Given that these and other lipophilic
50 chemical compounds are mainly stored in adipose tissue, and that many of them induce an obesogenic
51 effect (La Merrill et al., 2013), we could hypothesize that these pesticides, stored in the fatty tissue of
52 the breast, could alter the structure of the breast tissue, increasing the fat (no dense) mass of the breast
53 and, thereby, decreasing the relative proportion of dense tissue.
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1 Regarding the limitations of the study, it should be noted that, due to the cross-sectional design,
2 interpretations of causality between MD and occupational factors cannot be made, and possible
3 variations in the MD of women over time cannot be taken into account. Second, it would have been very
4 interesting to evaluate the association of occupational exposures with the absolute area of dense and
5 non-dense breast tissue, to be able to confirm if the association detected with the agricultural sector is
6 due to an increase in the fatty tissue of the breast. However, we could not obtain this information
7 because the DICOM files did not contain the metadata that indicates the pixel size of the mammograms,
8 necessary to do the conversion from pixel to cm². Third, despite having adjusted the models for the main
9 established predictors, residual confounders, associated with specific occupations or with MD, may have
10 interfered with the detected associations. Fourth, since women were recruited in a single center in
11 Madrid, the external validity of the study is limited. Another limitation to consider is the problem of
12 multiple comparisons, the possibility of finding associations that are falsely positive or negative by
13 chance. However, due to the exploratory and hypothesis-generating nature of this study, we decided
14 not to adjust for multiple comparisons as proposed by Bender and Lange (Bender and Lange, 2001).
15 On the other hand, we have focused on the analysis of the last occupation and on expositions that took
16 place the previous year. We decided to do so because MD is a dynamic trait, and certain environmental
17 factors can modulate it (Nazari and Mukherjee, 2018). Thus, the influence of exogenous exposures on
18 density could cease when exposure is interrupted. Anyway, a sensitivity analysis was fitted including
19 women who reported being actively working in the same occupation during the last 5 years (93% of the
20 total sample), and the results were very similar to those observed in Table 2 and Table 3 (data not
21 shown). Another limitation is that the assessment of exposure using a job-exposure matrix implies a
22 classification bias, generally non-differential, caused by the variability of exposure within and between
23 occupational groups. This misclassification could imply an underestimation of the effects found.
24 However, the use of these matrices provides greater statistical power, by allowing the grouping of
25 workers from different occupations for which a similar range of exposure was estimated. Finally, we
26 must be cautious with associations based on a low number of exposed workers.

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42 One of the main strengths of the study is the high participation rate and its novelty. As far as we know,
43 there are only two previous articles that have studied the association of MD with occupations (García-
44 Pérez et al., 2017) or with occupational exposures other than night shift work (Lope et al., 2018), both
45 with a lower number of premenopausal women than those included in this analysis. Furthermore, all
46 mammograms were measured on a continuous scale using a validated computer-assisted method and
47 by a single reader that showed high internal consistency. Since the participants underwent their routine
48 gynecological examination at the Madrid medical diagnostic center, mammograms were obtained in the
49 context of routine clinical practice, without the need for additional mammograms, and using the same
50 equipment. Finally, we have used the first general population job-exposure matrix specifically designed
51 for the Spanish working population (García et al., 2013). MatEmESp has allowed us to relate exposure
52 to occupational agents to MD in an efficient and detailed way, without having to resort to matrices built
53 in other countries for other working populations.
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5. CONCLUSIONS

Although, in general, our findings point to an absence of association with the occupations and exposures studied, library technicians had a higher MD, while women involved in agricultural sector occupations had a lower MD. Occupational exposure to pesticides, gasoline, volatile sulfur compounds, animal dust, wood dust, and bacteria of non-human origin was also inversely associated with breast density. Further research is needed to confirm whether these results reflect real associations.

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Table 1. Descriptive characteristics and mammographic density of the DDM-Madrid participants.

	n (%)	Mammographic density (%)			
		mean (95%CI)	<i>P</i> -value	<i>P</i> -value ^a	
Total	1362 (100)	34.3 (33.3; 35.2)			
Age, years			0.015	0.391	
<45	727 (53.4)	35.4 (34.1; 36.6)			
≥45	635 (46.6)	33.0 (31.7; 34.4)			
Education			0.001	0.344	
Primary school or less	60 (4.4)	31.0 (26.5; 35.4)			
Secondary school	475 (34.9)	32.6 (31.1; 34.1)			
University graduate	826 (60.7)	35.5 (34.3; 36.7)			
Age at menarche, years			0.007	0.512	
< 12	311 (23.0)	32.0 (30.1; 34.0)			
12-13	731 (54.1)	34.6 (33.4; 35.9)			
>13	309 (22.9)	35.8 (33.8; 37.8)			
Body mass index, kg/m ²			<0.001	<0.001	
<18.5	22 (1.6)	43.9 (35.8; 52.0)			
18.5-24.9	894(65.7)	38.9 (37.8; 40.0)			
25-29.9	309 (22.7)	26.9 (25.3; 28.6)			
≥30	136 (10.0)	19.0 (16.8; 21.3)			
Number of children			<0.001	0.001	
None	323 (23.7)	37.1 (35.1; 39.1)			
1	321 (23.6)	34.8 (32.8; 36.8)			
2	642 (47.1)	32.8 (31.6; 34.1)			
>2	76 (5.6)	32.1 (28.4; 35.7)			
Age at first child, years			0.140	0.119	
Nulliparous	323 (23.7)	37.1 (35.1; 39.1)			
<25	73 (5.4)	29.1 (25.2; 33.0)			
25-29	284 (20.9)	32.9 (31.1; 34.8)			
30-34	454(33.3)	33.3 (31.8; 34.9)			
>34	228 (16.7)	35.5 (33.1; 37.8)			
Breastfeeding, months			0.804	0.581	
< 3	354 (34.1)	33.1 (31.2; 35.0)			
4-6	386 (37.2)	33.7 (32.1; 35.3)			
> 6	298 (28.7)	33.4 (31.5; 35.3)			
Use of oral contraceptives			0.002	0.011	
Never	510 (37.7)	36.1 (34.5; 37.8)			
Past use	795 (58.8)	33.4 (32.2; 34.5)			
Current use	46 (3.4)	31.0 (26.5; 35.5)			
Energy intake, Kcal/day ^b			0.142	0.012	
<1672.1	403 (33.4)	33.4 (31.7; 35.1)			
1672.1-2151.1	403 (33.4)	35.8 (34.1; 37.5)			
>2151.1	403 (33.4)	35.2 (33.5; 36.9)			
Physical activity (MET-h/week)			0.002	0.911	
No	567(41.8)	32.9 (31.5; 34.3)			
≤12	340(25.1)	33.8 (31.9; 35.6)			
>12	449(33.1)	36.4 (34.7; 38.1)			
Tobacco consumption			0.037	0.151	
Never	518 (38.0)	35.5 (34.0; 37.0)			
Former smoker	480 (35.2)	33.9 (32.3; 35.4)			
Current smoker	364 (26.7)	33.1 (31.3; 34.9)			
Alcohol consumption, g/day			0.476	0.812	
Never	245 (20.3)	34.1 (31.8; 36.3)			
<10	793 (65.6)	35.0 (33.8; 36.2)			
≥10	170 (14.1)	35.2 (32.6; 37.8)			
Family history of breast cancer			0.877	0.858	
None	1058 (77.7)	34.2 (33.2; 35.2)			
Second degree only	211 (15.5)	34.8 (32.3; 37.3)			
First degree	93 (6.8)	34.0 (30.4; 37.5)			
Previous breast biopsy			<0.001	<0.001	

No	1222 (89.8)	33.5	(32.6; 34.5)		
Yes	139 (10.2)	41.0	(38.1; 43.9)		
Duration of employment, years				0.028	0.086
<12	489 (35.9)	35.3	(33.8; 36.9)		
12-20	465 (34.1)	34.5	(32.9; 36.1)		
>20	408 (30.0)	32.8	(31.1; 34.4)		

^a Adjusted for age and body mass index.

^b Variable in tertiles

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Table 2. Association between mammographic density, occupation, and duration of employment.

Code ^a	Occupation ^b	n	Exposed vs non-exposed			Time of exposure			
			β^c	(95%CI)	P-value	Mean ^d	β^e	(95%CI)	P-value
1	Directors and managers	11	-1.89	(-11.50; 7.73)	0.701	137	-1.35	(-5.02; 2.32)	0.471
2	Technicians and intellectual and scientific professionals	271	-0.64	(-2.95; 1.68)	0.590	181	-0.28	(-0.97; 0.40)	0.417
21	Healthcare professionals	19	1.75	(-5.65; 9.16)	0.643	204	0.33	(-1.73; 2.39)	0.756
2121	Non specialized nurses	11	5.85	(-3.79; 15.48)	0.234	216	1.46	(-1.16; 4.08)	0.275
232	Other teachers and teaching professionals	11	-4.18	(-13.79; 5.42)	0.393	201	-1.81	(-4.39; 0.77)	0.169
2329	Teachers and teaching professionals not classified under other headings	10	-2.68	(-12.79; 7.44)	0.604	197	-1.47	(-4.22; 1.28)	0.294
24	Professionals in the physical, chemical, mathematical, and engineering sciences	20	-1.47	(-8.86; 5.93)	0.697	205	-0.26	(-2.27; 1.75)	0.801
246	Technicians engineers (except agricultural, forestry, electrical electronic, and ICT)	10	-7.64	(-19.09; 3.81)	0.191	174	-2.26	(-5.89; 1.37)	0.222
26	Specialists in organization of public administration and companies, and in marketing	105	-2.15	(-5.45; 1.14)	0.201	161	-0.80	(-1.90; 0.30)	0.155
262	Specialists in organization and administration	102	-2.18	(-5.53; 1.17)	0.202	159	-0.88	(-2.02; 0.25)	0.126
2623	Specialists in public administration	97	-2.42	(-5.85; 1.00)	0.165	159	-0.96	(-2.13; 0.20)	0.103
282	Sociologists, historians, psychologists, and other professionals in social science	80	2.42	(-1.38; 6.23)	0.212	186	0.17	(-0.95; 1.29)	0.766
2824	Labor and social education professionals	70	2.92	(-1.11; 6.94)	0.156	182	0.30	(-0.89; 1.48)	0.626
29	Culture and entertainment professionals	20	-3.75	(-10.96; 3.46)	0.307	167	0.03	(-2.27; 2.33)	0.978
291	Archivists, librarians, conservators, and related	19	-5.40	(-12.81; 2.01)	0.153	159	-0.85	(-3.37; 1.67)	0.509
2912	Librarians, documentalists, and related	18	-5.66	(-13.28; 1.96)	0.145	158	-0.88	(-3.48; 1.71)	0.503
3	Technicians, support professionals	181	-0.30	(-2.90; 2.29)	0.818	183	0.04	(-0.71; 0.79)	0.922
31	Science and engineering technicians	16	3.00	(-5.76; 11.81)	0.500	186	2.17	(-1.02; 5.35)	0.182
33	Health technicians and professionals in alternative therapies	16	3.20	(-5.26; 11.65)	0.458	175	1.29	(-1.59; 4.16)	0.379
331	Laboratory health, diagnostic tests, and prosthetics technicians	10	0.56	(-10.18; 11.29)	0.919	182	0.71	(-2.59; 4.01)	0.673
36	Support professionals for administration management; forces and security forces technicians	65	-1.39	(-5.45; 2.66)	0.501	151	-0.01	(-1.37; 1.35)	0.985
361	Administrative and specialized assistants	20	-4.32	(-11.30; 2.67)	0.226	186	-1.01	(-3.00; 0.99)	0.323
3613	Management and administrative assistants	17	-4.19	(-11.79; 3.41)	0.280	198	-0.87	(-2.94; 1.21)	0.415
362	Customs, tax, and related agents that work in tasks of the public administration	45	0.09	(-4.81; 4.99)	0.972	135	0.81	(-1.01; 2.63)	0.380
3622	Support professionals of the public administration of social services	24	-1.40	(-8.14; 5.33)	0.683	128	1.04	(-1.58; 3.67)	0.435
3629	Other support professionals of the public administration for inspection and control tasks and similar tasks	13	6.44	(-2.70; 15.58)	0.167	154	2.31	(-0.84; 5.45)	0.150
37	Professionals supporting legal, social, cultural, sports, and related services	68	0.75	(-3.25; 4.75)	0.713	208	0.13	(-0.90; 1.16)	0.805
372	Sports women, trainers, sports activity instructors; recreational activity monitors	47	-0.52	(-5.27; 4.24)	0.832	236	-0.12	(-1.24; 1.01)	0.840
3723	Sports activities instructors	46	-0.49	(-5.30; 4.32)	0.842	239	-0.11	(-1.24; 1.02)	0.844
3733	Technicians in art galleries, museums, and libraries	13	8.47	(-0.65; 17.60)	0.069	130	2.98	(-0.55; 6.51)	0.098
38	Information and communication technology technicians	15	-7.27	(-15.37; 0.84)	0.079	216	-1.98	(-4.06; 0.11)	0.064
4	Accounting, administrative, and other office employees	646	1.25	(-0.53; 3.04)	0.169	209	0.12	(-0.34; 0.57)	0.618
430	Other administrative employees without public service tasks	628	1.34	(-0.45; 3.12)	0.142	210	0.15	(-0.30; 0.61)	0.505
4309	Administrative employees without public service tasks not classified under other headings	624	1.33	(-0.45; 3.11)	0.144	210	0.16	(-0.30; 0.61)	0.500
5	Catering, personal protection, and sales service workers	76	0.92	(-3.04; 4.88)	0.649	159	0.53	(-0.78; 1.84)	0.430
56	Health care workers in health services	10	0.99	(-8.64; 10.62)	0.840	163	0.67	(-2.40; 3.75)	0.668
583	Building maintenance and cleaning supervisors, supers, and housekeepers	31	-1.82	(-8.09; 4.44)	0.568	128	-0.81	(-3.49; 1.88)	0.555

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5831	Maintenance and cleaning supervisors in offices, hotels, and other establishments	12	2.20	(-7.98; 12.38)	0.672	164	0.12	(-3.36; 3.60)	0.945
5833	Building superintendents	19	-4.22	(-12.11; 3.67)	0.294	106	-2.14	(-6.32; 2.04)	0.316
59	Protection and security services workers	27	2.60	(-3.79; 8.99)	0.426	189	0.68	(-1.18; 2.54)	0.476
5923	Local police women	21	3.42	(-3.77; 10.61)	0.352	201	0.82	(-1.22; 2.86)	0.430
6120	Skilled workers in orchards, greenhouses, nurseries, and gardens	20	-6.60	(-14.27; 1.07)	0.092	225	-1.46	(-3.42; 0.51)	0.147
7	Craftswomen and skilled workers in manufacturing and construction industries (except facility and machinery operators)	70	-0.15	(-4.39; 4.08)	0.944	157	0.06	(-1.41; 1.52)	0.941
7899	Officers, operators, and craftswomen of other trades not classified under other headings	69	-0.76	(-5.03; 3.51)	0.728	154	-0.31	(-1.82; 1.19)	0.681
9	Elementary occupations	83	-2.26	(-5.88; 1.35)	0.220	132	-0.85	(-2.36; 0.65)	0.267
9431	Ordinances	76	-2.10	(-5.88; 1.68)	0.277	135	-0.66	(-2.22; 0.89)	0.404

^a Coded according to the 2011 National Classification of Occupations.

^b Occupations with at least 10 exposed workers.

^c Adjusted for age, education, body mass index, parity, oral contraceptives use, previous breast biopsies, family history of breast cancer, smoking, energy intake, and alcohol consumption.

^d Mean of months spent in the corresponding occupation.

^e Increase or decrease in the percentage of mammographic density for every 5 years spent in the corresponding occupation. Adjusted for age, education, body mass index, parity, oral contraceptives use, previous breast biopsies, family history of breast cancer, smoking, energy intake, and alcohol consumption.