# RESIDENTIAL EXPOSURE TO TRAFFIC POLLUTION AND MAMMOGRAPHIC DENSITY IN PREMENOPAUSAL WOMEN

Jiménez T, Domínguez-Castillo A, Fernández de Larrea-Baz N, Lucas P, Sierra MÁ, Salas-Trejo D, Llobet R, Martínez I, Pino MN, Martínez-Cortés M, Pérez-Gómez B, Pollán M, Lope V, García-Pérez J. Residential exposure to traffic pollution and mammographic density in premenopausal women. Sci Total Environ. 2024 Jun 10;928:172463. doi: 10.1016/j.scitotenv.2024.172463. Epub 2024 Apr 12. PMID: 38615764.

# Residential exposure to traffic pollution and mammographic density in premenopausal women

**Authors:**

Tamara Jiménez[a,b], Alejandro Domínguez-Castillo[c], Nerea Fernández de Larrea-Baz[c,d], Pilar Lucas[c], María Ángeles Sierra[c,d], Dolores Salas-Trejo[d,e,f], Rafael Llobet[g], Inmaculada Martínez[e,f], Marina Nieves Pino[h], Mercedes Martínez-Cortés[h], Beatriz Pérez-Gómez[c,d], Marina Pollán[c,d], Virginia Lope[c,d,*,1], and Javier García-Pérez[c,d,1]

**Author´s afiliations:**

[a] Department of Preventive Medicine, Public Health and Microbiology, *Universidad Autónoma de Madrid (UAM)*, Madrid, Spain

[b] HM CINAC (*Centro Integral de Neurociencias AC*), *Hospital Universitario Puerta del Sur, Fundación HM Hospitales*, Móstoles, Spain

[c] Cancer and Environmental Epidemiology Unit, Department of Epidemiology of Chronic Diseases, National Center for Epidemiology, Carlos III Institute of Health (*Instituto de Salud Carlos III)*, Madrid, Spain

[d] Consortium for Biomedical Research in Epidemiology & Public Health (*CIBER en Epidemiología y Salud Pública – CIBERESP*), Spain

[e] Valencian Breast Cancer Screening Program, General Directorate of Public Health, Valencia, Spain

[f] Center for Public Health Research CSISP, FISABIO, Valencia, Spain

[g] Institute of Computer Technology, Universitat Politècnica de València, Valencia, Spain

[h] *Servicio de Prevención y Promoción de la Salud, Madrid Salud, Ayuntamiento de Madrid,* Madrid, Spain

***Corresponding author:**

Virginia Lope
Cancer and Environmental Epidemiology Unit
Department of Epidemiology of Chronic Diseases
National Center for Epidemiology
Carlos III Institute of Health
Avda. Monforte de Lemos, 5, 28029 Madrid, Spain
Tel.: +34-918222640
E-mail: **vicarvajal@isciii.es**

[1]**Joint senior authors**

**E-mail addresses:**

TJ: tamarajc91@gmail.com
AD-C: a.dominguez@isciii.es
NFL-B: nfernandez@isciii.es
PL: pmlucas@isciii.es
MAS: masierra@isciii.es
DS-T: salas_dol@gva.es
RL: rllobet@dsic.upv.es
IM: martinez_inm@gva.es
MNP: pinoemn@madrid.es
MM-C: martinezcme@madrid.es
BP-G: bperez@isciii.es
MP: mpollan@isciii.es
VL: vicarvajal@isciii.es
JG-P: jgarcia@isciii.es

## Abstract

***Background:*** Mammographic density (MD) is the most important breast cancer biomarker. Ambient pollution is a carcinogen, and its relationship with MD is unclear. This study aims to explore the association between exposure to traffic pollution and MD in premenopausal women.

***Methodology:*** This Spanish cross-sectional study involved 769 women attending gynecological examinations in Madrid. Annual Average Daily Traffic (AADT), extracted from 1944 measurement road points provided by the City Council of Madrid, was weighted by distances (d) between road points and women's addresses to develop a Weighted Traffic Exposure Index (WTEI). Three methods were employed: method-1 $((\frac{1}{d})AADT)$, method-2 $((\frac{1}{\sqrt{d}})AADT)$, and method-3 $((e^{(\frac{1}{\sqrt{d}})})AADT)$. Multiple linear regression models, considering both log-transformed percentage of MD and untransformed MD, were used to estimate MD differences by WTEI quartiles, through two strategies: "exposed (exposure buffers between 50 and 200 m) *vs*. not exposed (>200 m)"; and "degree of traffic exposure".

***Results:*** Results showed no association between MD and traffic pollution according to buffers of exposure to the WTEI (first strategy) for the three methods. The highest reductions in MD, although not statistically significant, were detected in the quartile with the highest traffic exposure. For instance, method-3 revealed a suggestive inverse trend ($e^{\beta}{}_{Q1}$=1.23, $e^{\beta}{}_{Q2}$=0.96, $e^{\beta}{}_{Q3}$=0.85, $e^{\beta}{}_{Q4}$=0.85, *p*-trend=0.099) in the case of 75 m buffer. Similar non-statistically significant trends were observed with Methods-1 and -2. When we examined the effect of traffic exposure considering the all the 1944 measurement road points in every participant (second strategy), results showed no association for any of the three methods. A slightly decreased MD, although not significant, was observed only in the quartile with the highest traffic exposure: $e^{\beta}{}_{Q4}$=0.98 (method-1), and $e^{\beta}{}_{Q4}$=0.95 (methods-2 and -3).

***Conclusions:*** Our results showed no association between exposure to traffic pollution and MD in premenopausal women. Further research is needed to validate these findings.

**Keywords:** traffic exposure, air pollution, breast density, premenopausal, breast cancer, DDM-Madrid

**Abbreviations:** WHO, World Health Organization; MD, Mammographic density; BMI, Body mass index; TRAP, Traffic-related air pollution; AADT, Annual Average Daily Traffic; WTEI, Weighted Traffic Exposure Index; IQRs, Interquartile ranges; 95%CIs, 95% confidence intervals; $NO_2$, nitrogen dioxide; $NO_x$, nitrogen oxides.

## 1. Introduction

Breast cancer is the first cause of cancer death and incidence in women worldwide (Bray et al., 2024). In Spain, a total of 35,001 women were diagnosed in 2023 (Sociedad Española de Oncología Médica, 2023), being the first cause of cancer among women. This highlights that it is a priority public health problem, even more when considering that the World Health Organization (WHO) estimates that both incidence and mortality will continue their upward trend in the coming decades, both nationally and globally (International Agency for Research on Cancer, 2024).

In terms of environmental exposures, in 2013 the International Agency on Research Cancer classified outdoor air pollution as a Group 1-carcinogen (carcinogenic to humans) (Loomis et al., 2013). This source of pollution has been identified as one of the leading causes of death worldwide (GBD 2017 Risk Factor Collaborators, 2018) and it is considered a real public health concern (Shmuel et al., 2017), with many urban areas exceeding the WHO air quality guidelines (Turner et al., 2020). Air pollution is defined as a complex mixture consisting of numerous suspected and known carcinogens and endocrine disrupting chemicals (Lisco et al., 2022; WHO/UNEP, 2013). Air pollution levels are higher in urban areas, where most people live (Turner et al., 2020). One of the biggest causes of air pollution is traffic and several studies suggest that increased traffic emissions, particularly in urban areas, are associated with increased risk of gynecological cancers (Liao et al., 2023) and higher rates of breast cancer (Andersen et al., 2017; Benedetti et al., 2017; Binachon et al., 2014; Mordukhovich et al., 2016). Particularly, exposure to traffic air pollution at specific times in the life course has been associated with a modest increase in breast cancer risk (Nie et al., 2007; Shmuel et al., 2017), although other studies have not found this association (Hart et al., 2016; Raaschou-Nielsen et al., 2011).

Mammographic density (MD) is the most important predictive biomarker for breast cancer (Boyd et al., 2011, 2007), and it is defined as the amount of fibroglandular tissue in the breast (seen as white color on a mammogram) relative to fatty tissue (seen as dark) (Yaffe, 2008). It has been described that the risk of breast cancer is 4 to 5 times higher in women with an MD>75% compared to women with a lower MD (Bond-Smith and Stone, 2019; Boyd et al., 2007; McCormack, 2006). MD has the potential to change over women’s lifetime (Lester et al., 2022);

indeed, MD progressively decreases with age, with the transition to menopause, with an increasing number of children or with a higher body mass index (BMI) (Assi et al., 2012; Huo et al., 2014). On the contrary, hormone replacement therapy seems to increase breast density (Assi et al., 2012; Huo et al., 2014), creating opportunities for primary prevention of breast cancer. However, these characteristics explain only 20-30% of the variation in MD (Boyd et al., 2005).

Higher MD has also been associated with air pollution (Eslami et al., 2022; Kotake et al., 2022; White et al., 2019; Yaghjyan et al., 2017), and some authors have suggested a possible etiological role of traffic-related air pollution (TRAP) on this association (Yaghjyan et al., 2017). Although the mechanism could be increased is still unknown (White et al., 2019), pathways related to xenoestrogens and carcinogens present in TRAP have been proposed (Hystad et al., 2015). However, the epidemiological evidence supporting the relationship between exposure to traffic pollution and MD is still scarce.

The aim of this study was to evaluate the association between residential exposure to traffic pollution and MD in premenopausal women in Spain.

## 2. Material and Methods

### 2.1. Study population

In 2013, the cross-sectional DDM-Madrid study recruited 1466 Spanish premenopausal women aged 39 to 50, who were invited to participate in the study when they attended to their gynecological check-ups at the *Madrid Salud* Medical Diagnostic Center between June 2013 and May 2015. These women lived in the province of Madrid and its surroundings. Further details regarding the study design have been previously published (Jiménez et al., 2023, 2021; Lope et al., 2020). Women answered a questionnaire on sociodemographic information, lifestyle habits, and personal and family medical history, administered face-to-face by trained interviewers. Participants also completed a 117-item food frequency questionnaire that included eating habits during the previous 12 months and that was validated in the Spanish population (Vioque et al., 2013). The women’s place of residence was collected and geocoded into ED50 / UTM zone 30 N coordinates. The participation rate was 88%. We excluded women with missing information on the address variable (n=24), and we restricted the analysis to the 896 participants living in the municipality of Madrid, since it is the only municipality in the province of Madrid with available traffic data. Therefore, this paper is a sub-study from the original DDM-Madrid study. Figure 1 represents a flow chart displaying the selection process of participants. After excluding women with analogical, instead of digital, images (n=18), women who did not have their MD measured (n=11), and those without information on at least one of the covariates (n=98), the final sample was based on 769 participants, whose geographic distribution is shown in Figure 2.

The DDM-Madrid study was approved by the Ethics and Animal Welfare Committee of the Carlos III Institute of Health and was carried out in accordance with the principles of the Declaration of Helsinki. All participants provided written informed consent prior to the inclusion in this study.

### 2.2. Traffic data

Traffic data for the period 2012-2013 have been obtained from the Madrid City Council open data portal (Ayuntamiento de Madrid, 2023). The register of this portal includes public information on the Annual Average Daily Traffic (AADT) measured at a total of 1944 road points, defined as the total number of vehicles passing through the different road points with vehicular traffic in one year divided by 365 days. These road points were geocoded into ED50 / UTM zone 30 N coordinates. Figure 2 shows the location of the 1944 AADT measurement road points.

### 2.3. Mammographic density assessment

Mammograms were collected and anonymized. The craniocaudal projection of the left breast mammogram was used by a radiologist to calculate the percentage of MD using the DM-Scan software, a free semi-automated tool capable of identifying pixels corresponding to fatty tissue and pixels corresponding to dense tissue to measure MD percentage. This tool has shown high validity and reproducibility, proving to be more reliable and reproducible than visual inspection (Llobet et al., 2014; Pollán et al., 2013b).

### 2.4. Exposure assessment and statistical analyses (strategies)

Two strategies were implemented to assess the residential exposure to traffic pollution. For each of them, we developed a Weighted Traffic Exposure Index (WTEI), calculated as the sum of the AADT measurement road points around the participant's residence weighted by the Euclidean distance (d) between the residence and each AADT measurement road point (in meters), using three different weighting methods: a) Method 1: $\left(\frac{1}{d}\right) AADT$; b) Method 2: $\left(\frac{1}{\sqrt{d}}\right) AADT$; and c) Method 3: $\left(e^{\left(\frac{1}{\sqrt{d}}\right)}\right) AADT$.

1) First strategy ("exposed *vs.* not exposed"): assuming that there are participants exposed to traffic pollution and others not exposed, and in line with previous studies (DuPre et al., 2017; Puett et al., 2014), women with no measurement road points within a 200 m buffer around their residences were considered as "not exposed" to traffic pollution. For the remining women ("exposed"), we defined the WTEI for different buffers of proximity (exposure) to traffic pollution (50, 75, 100, 150, and 200 m) around their residences (according to the three above mentioned methods) as follows:

a) $WTEI_{Method1} = \sum_i (\frac{1}{d_i} AADT_i)$; b) $WTEI_{Method2} = \sum_i (\frac{1}{\sqrt{d_i}} AADT_i)$; and, c) $WTEI_{Method3} = \sum_i \left(e^{(\frac{1}{\sqrt{d_i}})} AADT_i\right)$, $i = 1, \ldots, no. of\ road\ points\ in\ each\ buffer$

Thus, 5 independent comparisons were made for each method: a) "≤50 m *vs*. >200 m"; b) "≤75 m *vs*. >200 m"; c) "≤100 m *vs*. >200 m"; d) "≤150 m *vs*. >200 m"; and e) "≤200 m *vs*. >200 m".

Figure 3 shows an example of the definition of the method 1 WTEI for a specific woman in different exposure buffers.

2) Second strategy ("degree of traffic exposure"): assuming that all the participants are exposed to some degree of traffic pollution, AADT from all the measurement road points were taken into account to calculate the WTEI for each participant, as follows:

a) $WTEI_{Method1} = \sum_i (\frac{1}{d_i} AADT_i)$; b) $WTEI_{Method2} = \sum_i (\frac{1}{\sqrt{d_i}} AADT_i)$; and, c) $WTEI_{Method3} = \sum_i \left(e^{(\frac{1}{\sqrt{d_i}})} AADT_i\right)$, $i = 1, \ldots, 1944\ road\ points$

Descriptive characteristics of women included in the study were analyzed and presented as absolute values and their corresponding percentages. The percentage of MD was calculated according to these characteristics, and we presented medians (and interquartile ranges (IQRs)) and means (and their corresponding 95% confidence intervals (95%CIs) and standard deviations).

The association between MD and exposure to traffic pollution (using the WTEI) was assessed using multiple linear regression models. For this purpose, we used two approaches considering:

a) Transformed MD measures: the response variable, the percentage of MD, was log-transformed to achieve the statistical assumptions for linear regression (Blair et al., 2022). Then, the estimated β coefficients and standard errors were exponentiated to calculate the ratio of geometric means, i.e., the relative change of the adjusted geometric mean of MD ($e^{\beta}$), comparing women among the different exposure categories (García-Pérez et al., 2017).
b) Untransformed MD measures: we used the untransformed percentage of MD as the response variable, estimating bootstrapped robust standard errors to calculate 95%CIs (DuPre et al., 2017; Gonçalves and White, 2005).

For all the models, the WTEI was created according to the aforementioned methods and strategies:

1) First strategy: women not exposed (living at >200 m from any road point) were considered as the reference group, and for each buffer of proximity, the WTEI was categorized into quartiles (one independent model for each buffer and method) based on its distribution in the exposed women within each buffer.

2) Second strategy: the WTEI was categorized into quartiles based on its distribution among all the participants (Q1 – low exposure, Q2 – medium exposure, Q3 – high exposure, and Q4 – very high exposure), and Q1 was considered as the reference group (one independent model for each method).

Regarding the choice of the method for weighting the AADT by the distance between the participants' homes and the AADT measurement points, ‘Method 1’ reflects the simplest form, that is, weighting by the inverse of the distance. However, with this method there is a large discrepancy in the values of the WTEI when applied to AADT measurement road points very close to the women's homes (principally, for distances <5 m). Figure 4A shows the shape of the $\left(\frac{1}{d}\right)AADT$ function, for the example of one road point with AADT=1. The value of the WTEI for a participant living at a distance of 1 m from this AADT measurement road point is 1, whereas the value for another participant living at a distance of 2 m from this AADT point is half this value, i.e., 0.5. This can be extrapolated to several AADT measurement road points at the same distances (1 and 2 m) and to any AADT values, i.e., the WTEI assigned to a woman with traffic points at 2 meters is 50% lower than the WTEI assigned to a woman with traffic points at 1 meter, and this is too large a reduction for such a small distance difference (between 1 and 2 meters). To solve this inconvenience, we proposed two additional methods, whose functions are shown in Figure 4B (‘Method 2’) and 4C (‘Method 3’). In ‘Method 2’, the shape of the function $\left(\frac{1}{\sqrt{d}}\right)AADT$ provides a difference (in %) between $WTEI_{(1\,m)}$ and $WTEI_{(2\,m)}$ of 29%, whereas in the ‘Method 3’, the shape of the function $e^{\left(\frac{1}{\sqrt{d}}\right)}AADT$ gives an even smaller reduction (25%).

All models were adjusted for potential and known confounders associated with MD (Huo et al., 2014): age (continuous); educational level (primary school or less, secondary school, university); BMI (continuous); parity (nulliparous, 1, 2, more than 2 children); previous breast biopsies (yes, no); family history of breast cancer (none, first degree, second degree); oral contraceptives consumption (never, past use, current use); tobacco consumption (never, former smoker, current smoker); alcohol consumption (never, <10 g/d, ≥10 g/d); energy intake (tertiles: <1657.6, 1657.6-2172.5, >2172.5 kcal/d); residing near industries pertaining to the industrial sectors associated with higher MD in a previous study by our group using the same population sample (Jiménez et al., 2022) (if the woman lived near industries belonging to “organic chemical industry” (at ≤1.5 km), “surface treatment of metals and plastic” (at ≤2.5 km), “pharmaceutical industry” (at ≤3 km), or “urban waste-water treatment plants” (at ≤3 km), she was classified as “yes”; otherwise, she was classified as “no”).

## 3. Results

### 3.1. Characteristics of the study population

The mean age of the participants was 44 ± 2.8 years. Descriptive characteristics of participating women are shown in Table 1. Most of them were younger than 45 years old (52.1%), had secondary or university education (96.6%), had a normal BMI (68.1%), had one or more children (70.7%), had no family history of breast cancer (76.6%) or previous biopsies (90.5%), had used or were using oral contraceptives (58.4%), were former or current smokers (61.4%), and with a moderate (<10 g/day) alcohol consumption (67.0%). The mean MD was higher in younger women (under 45 years old) (36.80%), with higher level of education (36.09%), in nulliparous (37.68%), in those with previous biopsies (40.41%), in women who had never used oral contraceptives (37.22%), and in those who had never consumed tobacco (37.22%).

### 3.2 Mammographic density and traffic pollution according to buffers of exposure ("exposed *vs.* not exposed" strategy)

In general, results showed no association between transformed MD measures and traffic pollution according to buffers of exposure to the WTEI for the three methods used (Table 2).

For all the methods, the highest decreases in MD, which were not statistically significant in the majority of the cases, were detected in the quartile with the highest exposure to traffic, with the exception of the 200 m buffer (method 3). For the first method, the 50 m buffer showed a non-statistically significant increased MD in women exposed to Q3 ($e^{\beta}{}_{Q3}$=1.24, 95%CI=(0.92-1.67)), whereas the remaining quartiles showed decreases in MD. In fact, the highest decrease in MD occurred in the highest quartile of WTEI ($e^{\beta}{}_{Q4}$=0.80, 95%CI=(0.60-1.08)). The following exposure buffers showed an increase in MD in the lower quartiles (Q1 for 75 and 100m; Q1 and Q2 for 150 m; and Q2 for 200 m) and a decrease in MD in the higher quartiles (Q2, Q3, and Q4 for 75 and 100 m; Q3 and Q4 for 150 and 200 m). For the second method, the 50 m buffer detected an increased MD in Q1 and Q3, and a decreased MD in Q2 and Q4. The remaining exposure buffers showed an increased MD in the lowest quartiles and a decreased MD in the highest quartiles, highlighting the statistically significant decreased MD in the 75 m buffer corresponding to Q4:

$e^{\beta}{}_{Q4}$=0.76; 95%CI=(0.61-0.96). For the third method, the results showed a suggestive inverse trend in the 75 m buffer ($e^{\beta}{}_{Q1}$=1.23, $e^{\beta}{}_{Q2}$=0.96, $e^{\beta}{}_{Q3}$=0.85, $e^{\beta}{}_{Q4}$=0.85, *p*-trend=0.099).

In relation to the association between untransformed MD measures and traffic pollution according to buffers of exposure to the WTEI for the three methods used (Table 3), results were similar to those of Table 2. It should be noted that the 75 m buffer showed the largest differences between the values of Q1 and Q4, where the values were decreasing from positive betas to negative betas, showing a non-statistically significant inverse trend for the three methods used: method 1 ($\beta_{Q1}$=5.39, $\beta_{Q2}$=-0.51, $\beta_{Q3}$=-2.50, $\beta_{Q4}$=-3.64, *p*-trend=0.223), method 2 ($\beta_{Q1}$=4.55, $\beta_{Q2}$=-0.03, $\beta_{Q3}$=-0.62, $\beta_{Q4}$=-5.19, *p*-trend=0.205), and method 3 ($\beta_{Q1}$=5.13, $\beta_{Q2}$=0.27, $\beta_{Q3}$=-2.74, $\beta_{Q4}$=-3.91, *p*-trend=0.201).

**3.3 Mammographic density and traffic pollution considering all the measurement road points ("degree of traffic exposure" strategy)**

When we examined the effect of traffic exposure considering the AADT for all the 1944 measurement road points in every participant, both in the transformed (Table 4) and untransformed (Table 5) MD measures, the results showed no association for any of the three methods used. A slightly decreased MD, although not statistically significant, was observed only in the quartile with the highest traffic exposure for the three methods: $e^{\beta}{}_{Q4}$=0.98 for the method 1, $e^{\beta}{}_{Q4}$=0.95 for the methods 2 and 3, in the case of transformed MD (Table 4); and $\beta_{Q4}$ (very high exposure)=-0.18 for the method 1, $\beta_{Q4}$ (very high exposure)=-0.80 for the methods 2 and 3, in the case of untransformed MD (Table 5).

## 4. Discussion

In this cross-sectional study, we have evaluated the association between MD and residential exposure to traffic pollution, applying two strategies to develop an index that captures the exposure to daily traffic taking into account both the intensity of road traffic and the distance from the residence. In general, the results suggest no association between residential exposure to traffic pollution and MD in premenopausal women.

In the first strategy used in the analyses ("exposed *vs*. not exposed"), the results showed some discrepancies in certain exposure buffers, in the sense that the direction of the association changed between consecutive quartiles, lacking a dose-response trend, for the three weighting methods. In any case, the results in all the methods showed the highest decreases in MD, although not statistically significant in the majority of the cases, in the quartiles of higher traffic exposure for all the buffers, for both transformed and untransformed MD measures. In fact, a suggestive inverse trend for transformed MD measures was observed in the 75 m buffer for the third method. For the same exposure buffer, the estimates for untransformed percent MD, showed an increase in MD in the Q1, with a minimal change in Q2, and a decrease in MD in Q3 and Q4, compared to women living more than 200 m away from any AADT measurement road point. The choice of this reference category is consistent with that used by DuPree et al. (DuPre et al., 2017) in their study about distance to roadways and MD in women living in the US. However, the major difference between the two studies, in relation to the choice of the reference group, lies in the fact that DuPre et al. used as reference group women living ≥200 m from any type of road considered as A1-A2-A3 (A1: primary highways with limited access; A2: primary roads without limited access; A3: secondary and connecting roads), whereas we used women living >200 m from traffic points measured throughout roads with vehicular traffic similar to those of the study by DuPre et al. In that study, the authors used distances between 50 and 200 m as the exposure zone to traffic pollution, as we did in the present paper. The only difference is that DuPre et al. used distance to segments (roadways), whereas we used distance to road points measured throughout these segments (roadways). These distances have also been used by other authors in studies of proximity to traffic pollution and breast cancer incidence (Hart et al., 2016; Raaschou-Nielsen et al., 2011).

In the second strategy ("degree of traffic exposure"), the results showed a non-statistically significant inverse trend in the association between MD and traffic exposure, for all three methods, for both transformed and untransformed MD measures. It should be noted that the results shown in Table 4 for the methods 2 and 3 are identical: this is due to the fact that the participants corresponding to each WTEI exposure quartile are the same in both methods.

Regarding MD and traffic pollution, the first study addressing this issue was the Danish Diet, Cancer and Health cohort study (Huynh et al., 2015). This was a prospective cohort of women above age 50 (stratified by menopausal status), using a Danish AirGIS modeling system to assess TRAP by modeled levels of nitrogen dioxide ($NO_2$) and nitrogen oxides ($NO_x$). The authors found weak and inverse associations between MD and $NO_x$ exposure, whereas no association was found between MD and $NO_2$ exposure in premenopausal women. In our study, we have also found no association between MD in premenopausal women and traffic exposure modeled by the WTEI. Distance to roads was not associated with MD in premenopausal participants in the American Nurses' Health Studies cohort (DuPre et al., 2017). In this study, the authors used the residential proximity to three types of roadways, according to the traffic intensity, and two exposure buffers: <50 m, and 50-199 m. In addition, the exposure variable was included as a continuous variable in the multivariable linear regression models. In our study, we used five exposure buffers in the first strategy, ranging from 50 to 200 m, and these exposure variables were categorized into quartiles, with the aim of refining the exposure assessment.

TRAP is composed of several substances, including $NO_2$ and polycyclic aromatic hydrocarbons, which enter the body mainly by inhalation, and then pass into the bloodstream. Some of these substances are carcinogens, whereas others can promote oxidative stress, inflammation (Loomis et al., 2013) or act as endocrine disruptors (Sahay et al., 2019; Sapunar Zenteno et al., 2021; White et al., 2018; Wu et al., 2012), which can alter mammary gland development and increase MD (Gore et al., 2015; Gray et al., 2017; Hystad et al., 2015; Siddique et al., 2016; Sprague et al., 2013). Furthermore, it has been demonstrated that metallic air pollutants present in traffic-polluted environments can accumulate in breast tissue, some of which are known or suspected carcinogens (International Agency for Research on Cancer, 2012; Rodgers et al., 2018) and have xenoestrogenic properties that may modulate breast cancer (Choe et al., 2003; Kresovich et al., 2019). On the other hand, some exogenous substances can act as xenobiotic chemicals that have the property of interfering with adipose tissue and are capable of promoting lipid accumulation and adipogenesis (García-Mayor et al., 2012), altering endocrine functions. Thus, lipophilic compounds, due to their obesogenic property (Darbre, 2017), could contribute to modifying breast tissue composition, increasing adipose tissue and proportionally decreasing, consequently, the fibroglandular component. This hypothesis would be consistent with our findings of a decrease in MD, although not statistically significant among women more exposed to TRAP, and would suggest that the risk of breast cancer described by previous studies in association with traffic pollution (Praud et al., 2023) may not be mediated by increases in MD.

Regarding the limitations of our study, it should be noted that since this is a cross-sectional study, changes in MD over time could not be monitored. Moreover, all participants were recruited from a single center, limiting the generalizability of the findings, although their residences were distributed all over the city of Madrid, gathering variation in exposure levels. On the other hand, some covariates were self-reported and, therefore, subject to a possible recall bias. Another relevant aspect to mention is the small sample size in the smallest exposure buffers in the "exposed *vs*. not exposed strategy", which could limit the power to detect small effects. Regarding the exposure measure, we did not take into account the speed of the vehicles in each AADT measurement road point due to lack of data. This is a limitation since the amount of gaseous pollution emitted by the vehicles depends on whether vehicles are traveling at higher or lower speeds (Ren et al., 2023). Finally, although mammograms of both breasts and projections were available in the study, the craniocaudal image of the left breast was selected for the analyses. This fact should not imply a bias, since previous studies have shown a high correlation between MD measurements in both breasts (Balleyguier et al., 2019; Ciatto et al., 2005; Maskarinec et al., 2006), and in both projections (Pollán et al., 2013a).

Nevertheless, it should be highlighted that this is the first study analyzing the association between MD and TRAP in Spain. For this purpose, we have applied two methodological strategies to refine the exposure assessment to traffic pollution, developing a traffic exposure index using three different methods. On the other hand, mammograms were analyzed using a validated (Llobet et al., 2014) semi-automated tool that is widely used in the clinical practice, and were obtained as part of routine clinical practice, avoiding additional radiological tests. Data on traffic pollution (including a total of 1944 measurement point roads) were obtained from the official register of the City of Madrid, which is the entity responsible for air quality issues according to the Law 34/2007 on Air Quality and Atmospheric Protection in Spain (Ministerio de Medioambiente, 2007).

## 5. Conclusions

Although, in general, our findings do not support an association between exposure to traffic pollution and MD in premenopausal women, non-statistically significant decreases in MD were observed in zones with high traffic exposure, in line with the few previous studies on MD and traffic pollution existing in the literature. Further, future research is needed to confirm or refute these findings.

**Acknowledgments**

We would like to thank the participants in the DDM-Madrid study for their contribution to breast cancer research. This work was supported by the Carlos III Institute of Health (AESI PI15CIII/00029, AESI PI15CIII/00013, and EPY-505/19-PFIS). The article presents independent research. The views expressed are those of the authors and not necessarily those of the Carlos III Institute of Health.

## References

Andersen, Z.J., Stafoggia, M., Weinmayr, G., Pedersen, M., Galassi, C., Jørgensen, J.T., Oudin, A., Forsberg, B., Olsson, D., Oftedal, B., Marit Aasvang, G., Aamodt, G., Pyko, A., Pershagen, G., Korek, M., De Faire, U., Pedersen, N.L., Östenson, C.-G., Fratiglioni, L., Eriksen, K.T., Tjønneland, A., Peeters, P.H., Bueno-de-Mesquita, B., Plusquin, M., Key, T.J., Jaensch, A., Nagel, G., Lang, A., Wang, M., Tsai, M.-Y., Fournier, A., Boutron-Ruault, M.-C., Baglietto, L., Grioni, S., Marcon, A., Krogh, V., Ricceri, F., Sacerdote, C., Migliore, E., Tamayo-Uria, I., Amiano, P., Dorronsoro, M., Vermeulen, R., Sokhi, R., Keuken, M., de Hoogh, K., Beelen, R., Vineis, P., Cesaroni, G., Brunekreef, B., Hoek, G., Raaschou-Nielsen, O., 2017. Long-Term Exposure to Ambient Air Pollution and Incidence of Postmenopausal Breast Cancer in 15 European Cohorts within the ESCAPE Project. Environ. Health Perspect. 125, 107005. https://doi.org/10.1289/EHP1742

Assi, V., Warwick, J., Cuzick, J., Duffy, S.W., 2012. Clinical and epidemiological issues in mammographic density. Nat. Rev. Clin. Oncol. 9, 33–40. https://doi.org/10.1038/nrclinonc.2011.173

Ayuntamiento de Madrid, 2023. SICA. URL https://datos.madrid.es/portal/site/egob/menuitem.c05c1f754a33a9fbe4b2e4b284f1a5a0/?vgnextoid=4a2e4207bb864410VgnVCM1000000b205a0aRCRD&vgnextchannel=374512b9ace9f310VgnVCM100000171f5a0aRCRD (accessed 1.10.24).

Balleyguier, C., Arfi-Rouche, J., Boyer, B., Gauthier, E., Helin, V., Loshkajian, A., Ragusa, S., Delaloge, S., 2019. A new automated method to evaluate 2D mammographic breast density according to BI-RADS® Atlas Fifth Edition recommendations. Eur. Radiol. 29, 3830–3838. https://doi.org/10.1007/s00330-019-06016-y

Benedetti, M., Zona, A., Beccaloni, E., Carere, M., Comba, P., 2017. Incidence of Breast, Prostate, Testicular, and Thyroid Cancer in Italian Contaminated Sites with Presence of Substances with Endocrine Disrupting Properties. Int. J. Environ. Res. Public. Health 14, 355. https://doi.org/10.3390/ijerph14040355

Binachon, B., Dossus, L., Danjou, A.M.N., Clavel-Chapelon, F., Fervers, B., 2014. Life in urban areas and breast cancer risk in the French E3N cohort. Eur. J. Epidemiol. 29, 743–751. https://doi.org/10.1007/s10654-014-9942-z

Blair, L.K., Warner, E.T., James, P., Hart, J.E., VoPham, T., Barnard, M.E., Newton, J.D., Murthy, D.J., Laden, F., Tamimi, R.M., DuPre, N.C., 2022. Exposure to natural vegetation in relation to mammographic density in a Massachusetts-based clinical cohort. Environ. Epidemiol. Phila. Pa 6, e216. https://doi.org/10.1097/EE9.0000000000000216

Bond-Smith, D., Stone, J., 2019. Methodological Challenges and Updated Findings from a Meta-analysis of the Association between Mammographic Density and Breast Cancer. Cancer Epidemiol. Biomarkers Prev. 28, 22–31. https://doi.org/10.1158/1055-9965.EPI-17-1175

Boyd, N.F., Martin, L.J., Yaffe, M.J., Minkin, S., 2011. Mammographic density and breast cancer risk: current understanding and future prospects. Breast Cancer Res. 13, 223. https://doi.org/10.1186/bcr2942

Boyd, N.F., Rommens, J.M., Vogt, K., Lee, V., Hopper, J.L., Yaffe, M.J., Paterson, A.D., 2005. Mammographic breast density as an intermediate phenotype for breast cancer. Lancet Oncol. 6, 798–808. https://doi.org/10.1016/S1470-2045(05)70390-9

Boyd, N.F., Sun, L., Stone, J., Fishell, E., Jong, R.A., Chiarelli, A., 2007. Mammographic Density and the Risk and Detection of Breast Cancer. N Engl J Med 356227-236 10.

Bray, F., Laversanne, M., Sung, H., Ferlay, J., Siegel, R.L., Soerjomataram, I., Jemal, A., 2024. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA. Cancer J. Clin. https://doi.org/10.3322/caac.21834

Choe, S.-Y., Kim, S.-J., Kim, H.-G., Lee, J.H., Choi, Y., Lee, H., Kim, Y., 2003. Evaluation of estrogenicity of major heavy metals. Sci. Total Environ. 312, 15–21. https://doi.org/10.1016/S0048-9697(03)00190-6

Ciatto, S., Houssami, N., Apruzzese, A., Bassetti, E., Brancato, B., Carozzi, F., Catarzi, S., Lamberini, M.P., Marcelli, G., Pellizzoni, R., Pesce, B., Risso, G., Russo, F., Scorsolini, A., 2005. Categorizing breast mammographic density: intra- and interobserver reproducibility of BI-RADS density categories. The Breast 14, 269–275. https://doi.org/10.1016/j.breast.2004.12.004

Darbre, P.D., 2017. Endocrine Disruptors and Obesity. Curr. Obes. Rep. 6, 18–27. https://doi.org/10.1007/s13679-017-0240-4

DuPre, N.C., Hart, J.E., Bertrand, K.A., Kraft, P., Laden, F., Tamimi, R.M., 2017. Residential particulate matter and distance to roadways in relation to mammographic density: results from the Nurses' Health Studies. Breast Cancer Res. BCR 19, 124. https://doi.org/10.1186/s13058-017-0915-5

Eslami, B., Alipour, S., Omranipour, R., Naddafi, K., Naghizadeh, M.M., Shamsipour, M., Aryan, A., Abedi, M., Bayani, L., Hassanvand, M.S., 2022. Air pollution exposure and mammographic breast density in Tehran, Iran: a cross-sectional study. Environ. Health Prev. Med. 27, 28–28. https://doi.org/10.1265/ehpm.22-00027

García-Mayor, R.V., Larrañaga Vidal, A., Docet Caamaño, M.F., Lafuente Giménez, A., 2012. Disruptores endocrinos y obesidad: obesógenos. Endocrinol. Nutr. 59, 261–267. https://doi.org/10.1016/j.endonu.2011.11.008

García-Pérez, J., Pollán, M., Pérez-Gómez, B., González-Sánchez, M., Cortés Barragán, R.A., Maqueda Blasco, J., González-Galarzo, M.C., Alba, M.Á., Van Der Haar, R., Casas, S., Vicente, C., Medina, P., Ederra, M., Santamariña, C., Moreno, M.P., Casanova, F., Pedraz-Pingarrón, C., Moreo, P., Ascunce, N., García, M., Salas-Trejo, D., Sánchez-Contador, C., Llobet, R., Lope, V., 2017. Occupation and mammographic density: A population-based study (DDM-Occup). Environ. Res. 159, 355–361. https://doi.org/10.1016/j.envres.2017.08.028

GBD 2017 Risk Factor Collaborators, 2018. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet 392.

Gonçalves, S., White, H., 2005. Bootstrap Standard Error Estimates for Linear Regression. J. Am. Stat. Assoc. 100, 970–979. https://doi.org/10.1198/016214504000002087

Gore, A.C., Chappell, V.A., Fenton, S.E., Flaws, J.A., Nadal, A., Prins, G.S., Toppari, J., Zoeller, R.T., 2015. Executive Summary to EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. Endocr. Rev. 36, 593–602. https://doi.org/10.1210/er.2015-1093

Gray, J.M., Rasanayagam, S., Engel, C., Rizzo, J., 2017. State of the evidence 2017: an update on the connection between breast cancer and the environment. Environ. Health 16, 94. https://doi.org/10.1186/s12940-017-0287-4

Hart, J.E., Bertrand, K.A., DuPre, N., James, P., Vieira, V.M., Tamimi, R.M., Laden, F., 2016. Long-term Particulate Matter Exposures during Adulthood and Risk of Breast Cancer Incidence in the Nurses' Health Study II Prospective Cohort. Cancer Epidemiol. Biomarkers Prev. 25, 1274–1276. https://doi.org/10.1158/1055-9965.EPI-16-0246

Huo, C.W., Chew, G.L., Britt, K.L., Ingman, W.V., Henderson, M.A., Hopper, J.L., Thompson, E.W., 2014. Mammographic density—a review on the current understanding of its association with breast cancer. Breast Cancer Res. Treat. 144, 479–502. https://doi.org/10.1007/s10549-014-2901-2

Huynh, S., von Euler-Chelpin, M., Raaschou-Nielsen, O., Hertel, O., Tjønneland, A., Lynge, E., Vejborg, I., Andersen, Z.J., 2015. Long-term exposure to air pollution and

mammographic density in the Danish Diet, Cancer and Health cohort. Environ. Health 14, 31. https://doi.org/10.1186/s12940-015-0017-8
Hystad, P., Villeneuve, P.J., Goldberg, M.S., Crouse, D.L., Johnson, K., 2015. Exposure to traffic-related air pollution and the risk of developing breast cancer among women in eight Canadian provinces: A case–control study. Environ. Int. 74, 240–248. https://doi.org/10.1016/j.envint.2014.09.004
International Agency for Research on Cancer, 2024. Cancer Tomorrow. URL https://gco.iarc.fr/tomorrow/en (accessed 1.22.24).
International Agency for Research on Cancer, 2012. Arsenic, Metals, Fibres and Dusts, 100c ed.
Jiménez, T., García-Pérez, J., van der Haar, R., Alba, M.Á., Lucas, P., Sierra, M.Á., de Larrea-Baz, N.F., Salas-Trejo, D., Llobet, R., Martínez, I., Pino, M.N., Alguacil, J., González-Galarzo, M.C., Martínez-Cortés, M., Pérez-Gómez, B., Pollán, M., Lope, V., 2021. Occupation, occupational exposures and mammographic density in Spanish women. Environ. Res. 195, 110816. https://doi.org/10.1016/j.envres.2021.110816
Jiménez, T., Pollán, M., Domínguez-Castillo, A., Lucas, P., Sierra, M.Á., Castelló, A., Fernández de Larrea-Baz, N., Lora-Pablos, D., Salas-Trejo, D., Llobet, R., Martínez, I., Pino, M.N., Martínez-Cortés, M., Pérez-Gómez, B., Lope, V., García-Pérez, J., 2023. Mammographic density in the environs of multiple industrial sources. Sci. Total Environ. 876, 162768. https://doi.org/10.1016/j.scitotenv.2023.162768
Jiménez, T., Pollán, M., Domínguez-Castillo, A., Lucas, P., Sierra, M.Á., Fernández de Larrea-Baz, N., González-Sánchez, M., Salas-Trejo, D., Llobet, R., Martínez, I., Pino, M.N., Martínez-Cortés, M., Pérez-Gómez, B., Lope, V., García-Pérez, J., 2022. Residential proximity to industrial pollution and mammographic density. Sci. Total Environ. 829, 154578. https://doi.org/10.1016/j.scitotenv.2022.154578
Kotake, R., Yamauchi, H., Kimura, T., Tsunoda, H., Lee, M., 2022. An association between mammographic breast density and fine particulate matter among postmenopausal women. Environ. Sci. Pollut. Res. 30, 25953–25958. https://doi.org/10.1007/s11356-022-23529-0
Kresovich, J.K., Erdal, S., Chen, H.Y., Gann, P.H., Argos, M., Rauscher, G.H., 2019. Metallic air pollutants and breast cancer heterogeneity. Environ. Res. 177, 108639. https://doi.org/10.1016/j.envres.2019.108639
Lester, S.P., Kaur, A.S., Vegunta, S., 2022. Association Between Lifestyle Changes, Mammographic Breast Density, and Breast Cancer. The Oncologist 27, 548–554. https://doi.org/10.1093/oncolo/oyac084
Liao, H., Murithi, R.G., Lu, C., Yang, W., Liu, Z., Cao, L., 2023. Long-term exposure to traffic-related air pollution and temperature increases gynecological cancers. Build. Environ. 230, 109989. https://doi.org/10.1016/j.buildenv.2023.109989
Lisco, G., Giagulli, V.A., Iovino, M., Guastamacchia, E., Pergola, G.D., Triggiani, V., 2022. Endocrine-Disrupting Chemicals: Introduction to the Theme. Endocr. Metab. Immune Disord. - Drug Targets 22, 677–685. https://doi.org/10.2174/1871530321666210413124425
Llobet, R., Pollán, M., Antón, J., Miranda-García, J., Casals, M., Martínez, I., Ruiz-Perales, F., Pérez-Gómez, B., Salas-Trejo, D., Pérez-Cortés, J.-C., 2014. Semi-automated and fully automated mammographic density measurement and breast cancer risk prediction. Comput. Methods Programs Biomed. 116, 105–115. https://doi.org/10.1016/j.cmpb.2014.01.021
Loomis, D., Grosse, Y., Lauby-Secretan, B., Ghissassi, F.E., Bouvard, V., Benbrahim-Tallaa, L., Guha, N., Baan, R., Mattock, H., Straif, K., 2013. The carcinogenicity of outdoor air pollution. Lancet Oncol. 14, 1262–1263. https://doi.org/10.1016/S1470-2045(13)70487-X
Lope, V., del Pozo, M. del P., Criado-Navarro, I., Pérez-Gómez, B., Pastor-Barriuso, R., Ruiz, E., Castelló, A., Lucas, P., Sierra, Á., Salas-Trejo, D., Llobet, R., Martínez, I., Romieu, I.,

Chajès, V., Priego-Capote, F., Pollán, M., 2020. Serum Phospholipid Fatty Acids and Mammographic Density in Premenopausal Women. J. Nutr. 150, 2419–2428. https://doi.org/10.1093/jn/nxaa168
Maskarinec, G., Pagano, I., Lurie, G., Kolonel, L.N., 2006. A Longitudinal Investigation of Mammographic Density: The Multiethnic Cohort. Cancer Epidemiol. Biomarkers Prev. 15, 732–739. https://doi.org/10.1158/1055-9965.EPI-05-0798
McCormack, V.A., 2006. Breast Density and Parenchymal Patterns as Markers of Breast Cancer Risk: A Meta-analysis. Cancer Epidemiol. Biomarkers Prev. 15, 1159–1169. https://doi.org/10.1158/1055-9965.EPI-06-0034
Ministerio de Medioambiente, 2007. Ley 34/2007, de 15 de noviembre, de calidad del aire y protección de la atmósfera. URL https://www.boe.es/buscar/pdf/2007/BOE-A-2007-19744-consolidado.pdf (accessed 1.29.24).
Mordukhovich, I., Beyea, J., Herring, A.H., Hatch, M., Stellman, S.D., Teitelbaum, S.L., Richardson, D.B., Millikan, R.C., Engel, L.S., Shantakumar, S., Steck, S.E., Neugut, A.I., Rossner, P., Santella, R.M., Gammon, M.D., 2016. Vehicular Traffic–Related Polycyclic Aromatic Hydrocarbon Exposure and Breast Cancer Incidence: The Long Island Breast Cancer Study Project (LIBCSP). Environ. Health Perspect. 124, 30–38. https://doi.org/10.1289/ehp.1307736
Nie, J., Beyea, J., Bonner, M.R., Han, D., Vena, J.E., Rogerson, P., Vito, D., Muti, P., Trevisan, M., Edge, S.B., Freudenheim, J.L., 2007. Exposure to traffic emissions throughout life and risk of breast cancer: the Western New York Exposures and Breast Cancer (WEB) study. Cancer Causes Control 18, 947–955. https://doi.org/10.1007/s10552-007-9036-2
Pollán, M., Ascunce, N., Ederra, M., Murillo, A., Erdozáin, N., Alés-Martínez, J., Pastor-Barriuso, R., 2013a. Mammographic density and risk of breast cancer according to tumor characteristics and mode of detection: a Spanish population-based case-control study. Breast Cancer Res. BCR 15, R9. https://doi.org/10.1186/bcr3380
Pollán, M., Llobet, R., Miranda-García, J., Antón, J., Casals, M., Martínez, I., Palop, C., Ruiz-Perales, F., Sánchez-Contador, C., Vidal, C., Pérez-Gómez, B., Salas-Trejo, D., 2013b. Validation of DM-Scan, a computer-assisted tool to assess mammographic density in full-field digital mammograms. SpringerPlus 2, 242. https://doi.org/10.1186/2193-1801-2-242
Praud, D., Deygas, F., Amadou, A., Bouilly, M., Turati, F., Bravi, F., Xu, T., Grassot, L., Coudon, T., Fervers, B., 2023. Traffic-Related Air Pollution and Breast Cancer Risk: A Systematic Review and Meta-Analysis of Observational Studies. Cancers 15, 927. https://doi.org/10.3390/cancers15030927
Puett, R.C., Hart, J.E., Yanosky, J.D., Spiegelman, D., Wang, M., Fisher, J.A., Hong, B., Laden, F., 2014. Particulate matter air pollution exposure, distance to road, and incident lung cancer in the nurses’ health study cohort. Environ. Health Perspect. 122, 926–932. https://doi.org/10.1289/ehp.1307490
Raaschou-Nielsen, O., Andersen, Z.J., Hvidberg, M., Jensen, S.S., Ketzel, M., Sørensen, M., Hansen, J., Loft, S., Overvad, K., Tjønneland, A., 2011. Air pollution from traffic and cancer incidence: a Danish cohort study. Environ. Health 10, 67. https://doi.org/10.1186/1476-069X-10-67
Ren, L., Guo, X., Wu, J., Singh, A.K., 2023. Data mining and spatio-temporal characteristics of urban road traffic emissions: A case study in Shijiazhuang, China. PLOS ONE 18, e0295664. https://doi.org/10.1371/journal.pone.0295664
Rodgers, K.M., Udesky, J.O., Rudel, R.A., Brody, J.G., 2018. Environmental chemicals and breast cancer: An updated review of epidemiological literature informed by biological mechanisms. Environ. Res. 160, 152–182. https://doi.org/10.1016/j.envres.2017.08.045

Sahay, D., Terry, M.B., Miller, R., 2019. Is breast cancer a result of epigenetic responses to traffic-related air pollution? A review of the latest evidence. Epigenomics 11, 701–714. https://doi.org/10.2217/epi-2018-0158

Sapunar Zenteno, J., Ferrer Rosende, P., Chahuán Manzur, B., Vega, I.S., 2021. Breast cancer incidence and the air pollution level in the communes of Chile: an ecological study. ecancermedicalscience 15. https://doi.org/10.3332/ecancer.2021.1191

Shmuel, S., White, A.J., Sandler, D.P., 2017. Residential exposure to vehicular traffic-related air pollution during childhood and breast cancer risk. Environ. Res. 159, 257–263. https://doi.org/10.1016/j.envres.2017.08.015

Siddique, S., Kubwabo, C., Harris, S.A., 2016. A review of the role of emerging environmental contaminants in the development of breast cancer in women. Emerg. Contam. 2, 204–219. https://doi.org/10.1016/j.emcon.2016.12.003

Sociedad Española de Oncología Médica, 2023. Las cifras del cáncer en España, 2023. URL https://seom.org/images/Las_cifras_del_Cancer_en_Espana_2023.pdf (accessed 1.18.23).

Sprague, B.L., Trentham-Dietz, A., Hedman, C.J., Wang, J., Hemming, J.D., Hampton, J.M., Buist, D.S., Aiello Bowles, E.J., Sisney, G.S., Burnside, E.S., 2013. Circulating serum xenoestrogens and mammographic breast density. Breast Cancer Res. 15, R45. https://doi.org/10.1186/bcr3432

Turner, M.C., Andersen, Z.J., Baccarelli, A., Diver, W.R., Gapstur, S.M., Pope, C.A., Prada, D., Samet, J., Thurston, G., Cohen, A., 2020. Outdoor air pollution and cancer: An overview of the current evidence and public health recommendations. CA. Cancer J. Clin. 70, 460–479. https://doi.org/10.3322/caac.21632

Vioque, J., Navarrete-Muñoz, E.-M., Gimenez-Monzó, D., García-de-la-Hera, M., Granado, F., Young, I.S., Ramón, R., Ballester, F., Murcia, M., Rebagliato, M., Iñiguez, C., INMA-Valencia Cohort Study, 2013. Reproducibility and validity of a food frequency questionnaire among pregnant women in a Mediterranean area. Nutr. J. 12, 26. https://doi.org/10.1186/1475-2891-12-26

White, A.J., Bradshaw, P.T., Hamra, G.B., 2018. Air Pollution and Breast Cancer: a Review. Curr. Epidemiol. Rep. 5, 92–100. https://doi.org/10.1007/s40471-018-0143-2

White, A.J., Weinberg, C.R., O'Meara, E.S., Sandler, D.P., Sprague, B.L., 2019. Airborne metals and polycyclic aromatic hydrocarbons in relation to mammographic breast density. Breast Cancer Res. 21, 24. https://doi.org/10.1186/s13058-019-1110-7

WHO/UNEP, 2013. State of the science of endocrine disrupting chemicals - 2012. Edited by Åke Bergman, Jerrold J. Heindel, Susan Jobling, Karen A. Kidd and R. Thomas Zoeller. United National Environment Programme : World Health Organization, Geneva, Switzerland.

Wu, S., Deng, F., Wei, H., Huang, J., Wang, H., Shima, M., Wang, X., Qin, Y., Zheng, C., Hao, Y., Guo, X., 2012. Chemical constituents of ambient particulate air pollution and biomarkers of inflammation, coagulation and homocysteine in healthy adults: A prospective panel study. Part. Fibre Toxicol. 9, 49. https://doi.org/10.1186/1743-8977-9-49

Yaffe, M.J., 2008. Mammographic density. Measurement of mammographic density. Breast Cancer Res. 10, 209. https://doi.org/10.1186/bcr2102

Yaghjyan, L., Arao, R., Brokamp, C., O'Meara, E.S., Sprague, B.L., Ghita, G., Ryan, P., 2017. Association between air pollution and mammographic breast density in the Breast Cancer Surveilance Consortium. Breast Cancer Res. 19, 36. https://doi.org/10.1186/s13058-017-0828-3

**Figure 1**. Flow chart displaying the selection process of participants.

**Figure 2**. Geographic distribution of participants' homes and Annual Average Daily Traffic (AADT) measurement road points.

**Figure 3**. Example of definition of the Weighted Traffic Exposure Index (WTEI) for a specific participant in different exposure buffers.

**Figure 4**. Shape of the functions $\left(\frac{1}{d}\right)AADT$ (A), $\left(\frac{1}{\sqrt{d}}\right)AADT$ (B), and $e^{\left(\frac{1}{\sqrt{d}}\right)}AADT$ (C), for the example of 1 road point with AADT=1. d: distance; AADT: Annual Average Daily Traffic.

**Table 1.** Descriptive characteristics of the participants and mammographic density percentage according to women's characteristics.

| | | Mammographic density (%) | | |
|---|---|---|---|---|
| **Characteristic** | **n (%)** | **Median (IQR[a])** | **Mean (95%CI)** | **SD[b]** |
| **Total** | 769 (100.0) | 32.72 (25.02) | 35.00 (33.77; 36.23) | 17.41 |
| **Age (years)** | | | | |
| <45 | 401 (52.1) | 35.15 (26.06) | 36.80 (35.07;38.52) | 17.63 |
| ≥45 | 368 (47.9) | 30.88 (24.24) | 33.05 (31.31; 34.78) | 16.97 |
| **Education** | | | | |
| Primary school or less | 26 (3.4) | 30.59 (34.68) | 30.84 (23.65; 38.03) | 18.71 |
| Secondary school | 250 (32.5) | 31.80 (24.14) | 33.29 (31.28; 35.29) | 16.19 |
| University grade | 493 (64.1) | 33.53 (24.77) | 36.09 (34.52; 37.67) | 17.86 |
| **Body mass index (kg/m²)** | | | | |
| <18.5 | 15 (2.0) | 42.43 (17.53) | 38.43 (32.04; 44.81) | 12.62 |
| 18.5-24.9 | 524 (68.1) | 38.18 (24.30) | 39.33 (37.89; 40.76) | 16.77 |
| 25-29.9 | 161 (20.9) | 25.48 (18.82) | 27.03 (24.77; 29.30) | 14.67 |
| >30 | 69 (9.0) | 19.89 (18.56) | 20.03 (16.73; 23.34) | 14.01 |
| **Parity** | | | | |
| Nulliparous | 225 (29.3) | 35.79 (27.73) | 37.68 (35.27; 40.09) | 18.45 |
| 1 | 171 (22.2) | 30.43 (23.75) | 34.44 (31.75; 37.14) | 18.01 |
| 2 | 335 (43.6) | 32.45 (23.50) | 33.77 (32.01;35.53) | 16.41 |
| >2 | 38 (4.9) | 30.17 (17.42) | 32.57 (27.60; 37.55) | 15.64 |
| **Previous biopsies** | | | | |
| Yes | 73 (9.5) | 41.00 (22.98) | 40.41 (36.53; 44.29) | 16.92 |
| No | 696 (90.5) | 32.02 (24.59) | 34.44 (33.15; 35.73) | 17.37 |
| **Family history of breast cancer** | | | | |
| None | 589 (76.6) | 33.09 (25.75) | 35.21 (33.82; 36.61) | 17.27 |
| First degree | 52 (6.8) | 32.57 (17.05) | 33.42 (28.88; 37.97) | 16.71 |
| Second degree | 128 (16.6) | 32.20 (24.37) | 34.70 (31.51; 37.88) | 18.38 |
| **Oral contraceptives consumption** | | | | |
| Never | 320 (41.6) | 35.37 (26.78) | 37.22 (35.21; 39.23) | 18.37 |
| Past use | 423 (55.0) | 32.08 (24.04) | 33.49 (31.92; 35.06) | 16.46 |
| Current use | 26 (3.4) | 29.23 (17.29) | 32.34 (25.45; 39.22) | 17.91 |
| **Tobacco consumption** | | | | |
| Never | 297 (38.6) | 34.40 (26.20) | 37.22 (35.10; 39.34) | 18.62 |
| Former smoker | 262 (34.1) | 32.68 (23.25) | 33.36 (31.41; 35.31) | 16.09 |
| Current smoker | 210 (27.3) | 31.36 (25.49) | 33.92 (31.62; 36.21) | 16.97 |
| **Alcohol consumption (g/day)** | | | | |
| Never | 134 (17.4) | 32.08 (24.66) | 34.48 (31.54; 37.42) | 17.35 |
| <10 | 515 (67.0) | 32.56 (25.55) | 35.18 (33.66; 36.71) | 17.65 |
| ≥10 | 120 (15.6) | 33.43 (23.92) | 34.82 (31.86; 37.78) | 16.54 |
| **Energy intake consumption (kcal/day)** | | | | |
| < 1657.6 | 256 (33.3) | 31.16 (25.37) | 34.20 (32.04; 36.37) | 17.65 |
| 1657.6-2172.5 | 258 (33.6) | 34.55 (22.47) | 35.87 (33.85; 37.88) | 16.53 |
| >2172.5 | 255 (33.1) | 32.38 (27.54) | 34.93 (32.72; 37.15) | 18.05 |
| **To live near industries associated with higher MD** | | | | |
| Yes | 204 (26.5) | 33.65 (25.53) | 36.35 (34.02; 38.67) | 16.95 |
| No | 565 (73.5) | 32.56 (25.06) | 34.52 (33.07; 35.97) | 17.56 |

[a] Interquartile range.
[b] Standard deviation.
[c] Variable in tertiles.
[d] Mammographic density.

**Table 2.** Association between transformed mammographic density measures and traffic pollution according to buffers of exposure to the Weighted Traffic Exposure Index (WTEI) and methods used ("exposed *vs*. not exposed" strategy).

| | | METHOD 1: (1/d)AADT[a] | | | METHOD 2: (1/√d)AADT[a] | | | METHOD 3: ($e^{(1/\sqrt{d})}$)AADT[a] | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Buffer** | **Exposure category (WTEI quartile)** | **n** | **$e^{\beta}$ (95%CI)[b]** | ***p*-trend** | **n** | **$e^{\beta}$ (95%CI)[b]** | ***p*-trend** | **n** | **$e^{\beta}$ (95%CI)[b]** | ***p*-trend** |
| | Reference (not exposed: >200 m)[c] | 307 | 0 | - | 307 | 0 | - | 307 | 0 | - |
| 50 m | Q1 | 18 | 0.96 (0.73-1.27) | | 18 | 1.03 (0.77-1.36) | | 20 | 0.99 (0.75-1.29) | |
| | Q2 | 19 | 0.99 (0.76-1.30) | | 19 | 0.97 (0.74-1.28) | | 16 | 1.03 (0.77-1.39) | |
| | Q3 | 16 | 1.24 (0.92-1.67) | | 16 | 1.13 (0.84-1.53) | | 17 | 1.02 (0.76-1.37) | |
| | Q4 | 16 | 0.80 (0.60-1.08) | 0.698 | 16 | 0.83 (0.62-1.12) | 0.613 | 16 | 0.91 (0.67-1.22) | 0.723 |
| 75 m | Q1 | 33 | 1.17 (0.93-1.46) | | 33 | 1.15 (0.92-1.43) | | 32 | 1.23 (0.99-1.55) | |
| | Q2 | 30 | 0.93 (0.74-1.17) | | 33 | 0.96 (0.77-1.19) | | 33 | 0.96 (0.77-1.19) | |
| | Q3 | 30 | 0.94 (0.75-1.18) | | 27 | 1.02 (0.80-1.29) | | 27 | 0.85 (0.66-1.08) | |
| | Q4 | 29 | 0.84 (0.66-1.06) | 0.158 | 29 | 0.76 (0.61-0.96) | 0.112 | 30 | 0.85 (0.68-1.07) | 0.099 |
| 100 m | Q1 | 47 | 1.04 (0.86-1.25) | | 47 | 1.07 (0.89-1.29) | | 46 | 1.16 (0.96-1.39) | |
| | Q2 | 54 | 0.99 (0.83-1.18) | | 53 | 1.01 (0.85-1.20) | | 53 | 0.90 (0.75-1.07) | |
| | Q3 | 46 | 0.94 (0.78-1.14) | | 44 | 0.88 (0.72-1.06) | | 46 | 0.99 (0.82-1.20) | |
| | Q4 | 46 | 0.89 (0.74-1.07) | 0.231 | 49 | 0.91 (0.76-1.09) | 0.174 | 48 | 0.85 (0.71-1.02) | 0.120 |
| 150 m | Q1 | 82 | 1.04 (0.90-1.20) | | 81 | 1.02 (0.89-1.18) | | 83 | 1.09 (0.95-1.26) | |
| | Q2 | 88 | 1.07 (0.93-1.23) | | 88 | 1.04 (0.91-1.20) | | 82 | 0.95 (0.82-1.10) | |
| | Q3 | 82 | 0.99 (0.85-1.14) | | 80 | 1.05 (0.90-1.21) | | 84 | 1.09 (0.95-1.26) | |
| | Q4 | 81 | 0.90 (0.78-1.05) | 0.358 | 84 | 0.89 (0.77-1.03) | 0.430 | 84 | 0.87 (0.76-1.01) | 0.320 |
| 200 m | Q1 | 110 | 1.00 (0.88-1.13) | | 109 | 1.06 (0.93-1.20) | | 109 | 1.04 (0.91-1.18) | |
| | Q2 | 123 | 1.09 (0.96-1.23) | | 123 | 1.00 (0.89-1.14) | | 121 | 0.97 (0.86-1.10) | |
| | Q3 | 118 | 0.97 (0.86-1.10) | | 116 | 0.99 (0.87-1.12) | | 117 | 0.99 (0.87-1.12) | |
| | Q4 | 111 | 0.95 (0.84-1.08) | 0.603 | 114 | 0.97 (0.86-1.11) | 0.594 | 115 | 1.02 (0.90-1.16) | 0.981 |

[a] d: distance; AADT: Annual Average Daily Traffic.
[b] $e^{\beta}$ were estimated using multiple linear regression models (an independent model for each buffer and method), adjusted for age, education, body mass index, parity, previous breast biopsies, family history of breast cancer, oral contraceptives use, tobacco consumption, alcohol consumption, energy intake, and residing near industries associated with higher mammographic density.
[c] The reference group (women not exposed (>200 m) to AADT measurement road points) is the same for all the buffers.

**Table 3.** Association between untransformed mammographic density measures and traffic pollution according to buffers of exposure to the Weighted Traffic Exposure Index (WTEI) and methods used ("exposed *vs*. not exposed" strategy).

| | | METHOD 1: (1/d)AADT[a] | | | | METHOD 2: (1/√d)AADT[a] | | | | METHOD 3: ($e^{(1/\sqrt{d})}$)AADT[a] | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Buffer** | **Exposure category (WTEI quartile)** | **n** | **β[b]** | **95%CI[c]** | ***p*-trend** | **n** | **β[b]** | **95%CI[c]** | ***p*-trend** | **n** | **β[b]** | **95%CI[c]** | ***p*-trend** |
| | Reference (not exposed: >200 m)[d] | 307 | 0 | - | | 307 | 0 | - | | 307 | 0 | - | |
| 50 m | Q1 | 18 | -1.17 | (-8.70; 6.36) | | 18 | 1.10 | (-6.11; 8.32) | | 20 | -0.36 | (-6.84; 6.12) | |
| | Q2 | 19 | -1.02 | (-8.29; 6.25) | | 19 | -2.03 | (-9.51; 5.45) | | 16 | -0.29 | (-8.19; 7.61) | |
| | Q3 | 16 | 6.61 | (-2.62; 15.84) | | 16 | 3.23 | (-5.88; 12.34) | | 17 | 2.11 | (-5.98; 10.20) | |
| | Q4 | 16 | -4.54 | (-11.96; 2.88) | 0.908 | 16 | -2.59 | (-10.54; 5.36) | 0.834 | 16 | -1.99 | (-9.72; 5.73) | 0.913 |
| 75 m | Q1 | 33 | 5.39 | (-0.28; 11.07) | | 33 | 4.55 | (-1.00; 10.09) | | 32 | 5.13 | (-0.26; 10.52) | |
| | Q2 | 30 | -0.51 | (-6.04; 5.02) | | 33 | -0.03 | (-5.96; 5.90) | | 33 | 0.27 | (-6.40; 6.94) | |
| | Q3 | 30 | -2.50 | (-7.97; 2.98) | | 27 | -0.62 | (-7.01; 5.78) | | 27 | -2.74 | (-8.65; 3.18) | |
| | Q4 | 29 | -3.64 | (-8.83; 1.54) | 0.223 | 29 | -5.19 | (-9.73; -0.65) | 0.205 | 30 | -3.91 | (-8.69; 0.87) | 0.201 |
| 100 m | Q1 | 47 | 0.62 | (-4.42; 5.66) | | 47 | 0.92 | (-3.82; 5.66) | | 46 | 3.03 | (-1.47; 7.52) | |
| | Q2 | 54 | 0.83 | (-4.14; 5.81) | | 53 | 1.98 | (-3.01; 6.98) | | 53 | -1.30 | (-6.67; 4.07) | |
| | Q3 | 46 | -1.16 | (-6.18; 3.85) | | 44 | -3.91 | (-8.74; 0.92) | | 46 | -0.29 | (-5.51; 4.93) | |
| | Q4 | 46 | -2.51 | (-6.81; 1.78) | 0.394 | 49 | -1.54 | (-5.86; 2.79) | 0.332 | 48 | -3.25 | (-7.52; 1.02) | 0.219 |
| 150 m | Q1 | 82 | 0.24 | (-3.52; 4.00) | | 81 | 0.14 | (-3.60; 3.89) | | 83 | 1.94 | (-1.68; 5.55) | |
| | Q2 | 88 | 2.78 | (-1.31; 6.86) | | 88 | 2.24 | (-1.40; 5.88) | | 82 | -0.43 | (-4.16; 3.31) | |
| | Q3 | 82 | -0.37 | (-4.07; 3.34) | | 80 | 0.83 | (-2.81; 4.47) | | 84 | 2.07 | (-1.99; 6.13) | |
| | Q4 | 81 | -2.82 | (-6.92; 1.29) | 0.365 | 84 | -3.20 | (-6.62; 0.22) | 0.376 | 84 | -3.54 | (-6.80; -0.27) | 0.285 |
| 200 m | Q1 | 110 | -1.05 | (-4.56; 2.46) | | 109 | 0.91 | (-2.22; 4.05) | | 109 | 0.52 | (-3.00; 4.05) | |
| | Q2 | 123 | 3.22 | (-0.19; 6.63) | | 123 | 0.79 | (-2.61; 4.18) | | 121 | -0.34 | (-3.62; 2.94) | |
| | Q3 | 118 | -1.16 | (-4.28; 1.96) | | 116 | -0.48 | (-4.10; 3.15) | | 117 | 0.33 | (-3.00; 3.66) | |
| | Q4 | 111 | -1.51 | (-4.82; 1.80) | 0.564 | 114 | -1.42 | (-4.71; 1.87) | 0.411 | 115 | -0.63 | (-3.75; 2.50) | 0.775 |

[a] d: distance; AADT: Annual Average Daily Traffic.
[b] β coefficients estimated using multiple linear regression models (an independent model for each buffer and method), adjusted for age, education, body mass index, parity, previous breast biopsies, family history of breast cancer, oral contraceptives use, tobacco consumption, alcohol consumption, energy intake, and residing near industries associated with higher mammographic density.
[c] 95% confidence intervals were calculated using bootstrapped robust standard errors.
[d] The reference group (women not exposed (>200 m) to AADT measurement road points) is the same for all the buffers.

**Table 4.** Association between transformed mammographic density measures and traffic pollution exposure considering all the measurement road points to calculate the Weighted Traffic Exposure Index (WTEI), according to the methods used ("degree of traffic exposure" strategy).

| | METHOD 1: (1/d)AADT[a] | | | METHOD 2: (1/√d)AADT[a] | | | METHOD 3: ($e^{(1/\sqrt{d})}$)AADT[a] | | |
|---|---|---|---|---|---|---|---|---|---|
| **Exposure category (WTEI quartile)** | **n** | **$e^{\beta}$ (95%CI)[b]** | ***p*-trend** | **n** | **$e^{\beta}$ (95%CI)[b]** | ***p*-trend** | **n** | **$e^{\beta}$ (95%CI)[b]** | ***p*-trend** |
| Reference: Q1 (low exposure) | 195 | 0 | | 195 | 0 | | 195 | 0 | |
| Q2 (medium exposure) | 197 | 1.07 (0.95-1.21) | | 197 | 1.00 (0.89-1.13) | | 197 | 1.00 (0.89-1.13) | |
| Q3 (high exposure) | 186 | 1.00 (0.89-1.13) | | 186 | 1.03 (0.91-1.16) | | 186 | 1.03 (0.91-1.16) | |
| Q4 (very high exposure) | 191 | 0.98 (0.87-1.10) | 0.524 | 191 | 0.95 (0.84-1.07) | 0.461 | 191 | 0.95 (0.84-1.07) | 0.461 |

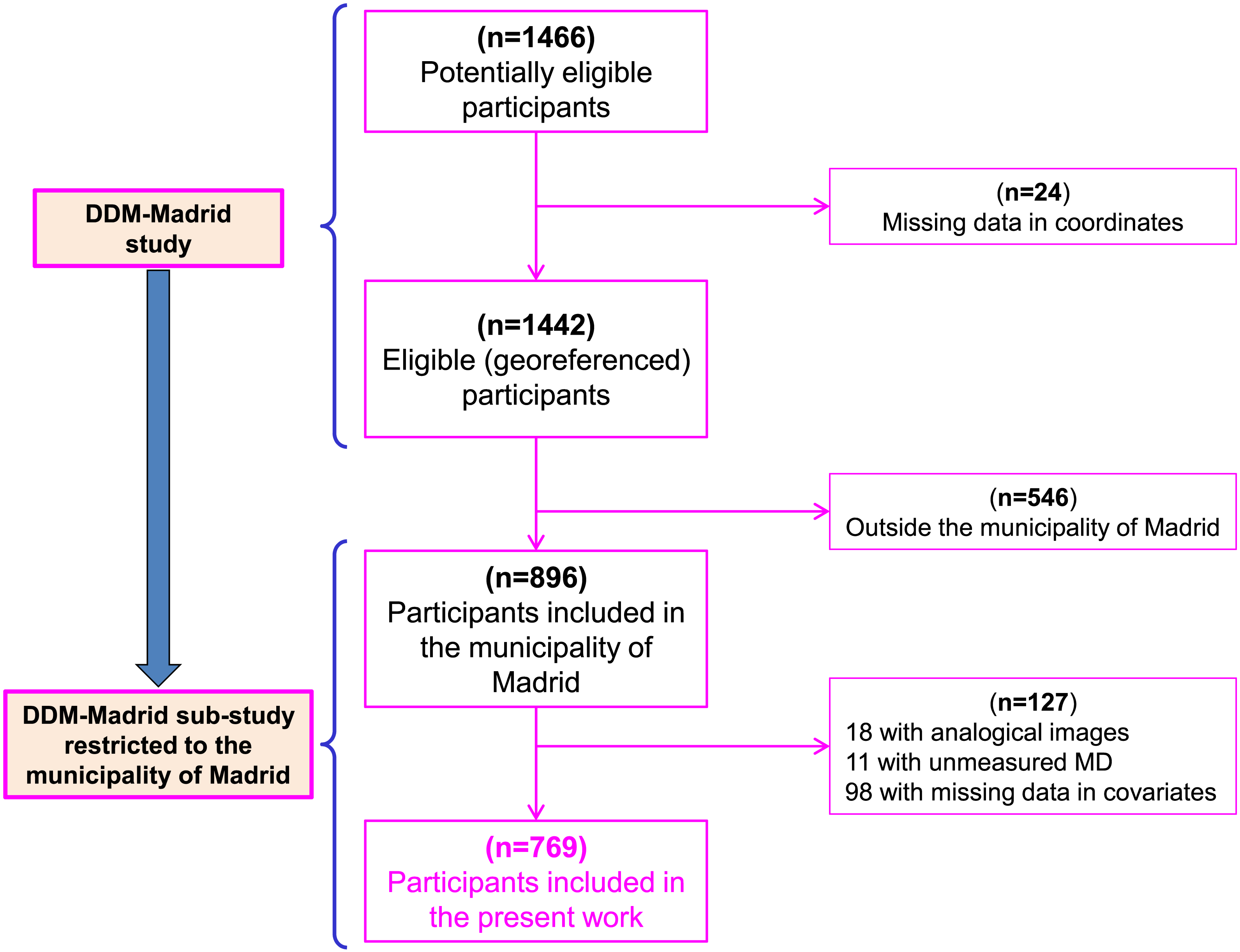
[a] d: distance; AADT: Annual Average Daily Traffic.

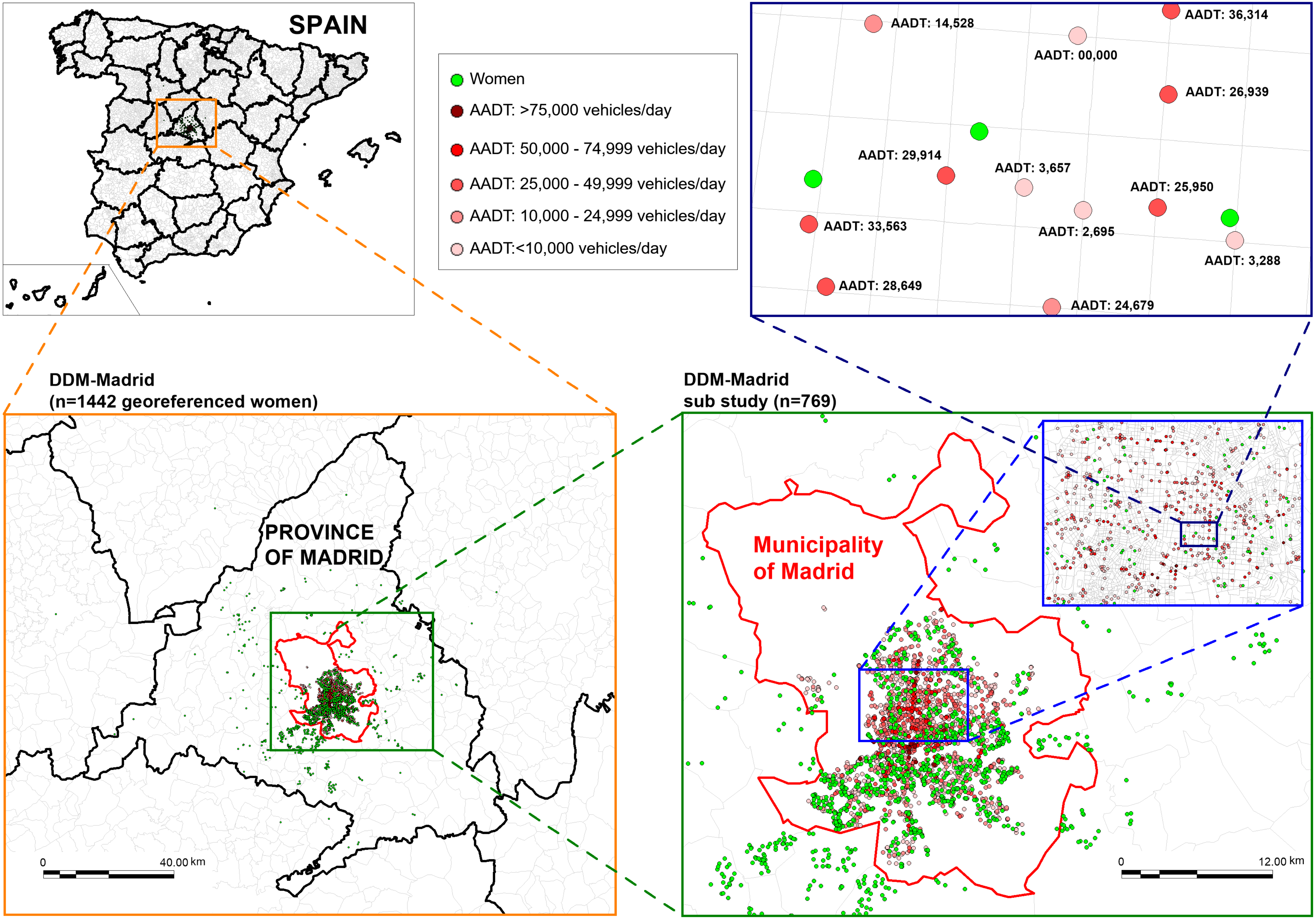
[b] $e^{\beta}$ were estimated using multiple linear regression models (an independent model for each method), adjusted for age, education, body mass index, parity, previous breast biopsies, family history of breast cancer, oral contraceptives use, tobacco consumption, alcohol consumption, energy intake, and residing near industries associated with higher mammographic density.

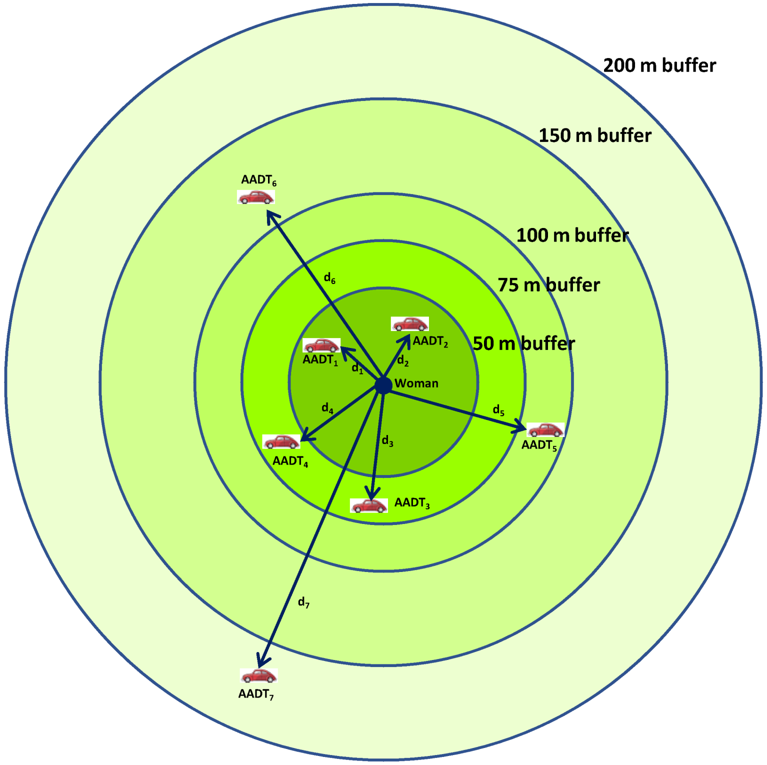
**Table 5.** Association between untransformed mammographic density measures and traffic pollution exposure considering all the measurement road points to calculate the Weighted Traffic Exposure Index (WTEI), according to the methods used ("degree of traffic exposure" strategy).

| | METHOD 1: (1/d)AADT[a] | | | | METHOD 2: (1/√d)AADT[a] | | | | METHOD 3: $(e^{(1/\sqrt{d})})$AADT[a] | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Exposure category (WTEI quartile)** | **n** | **β[b]** | **95%CI[c]** | ***p*-trend** | **n** | **β[b]** | **95%CI[c]** | ***p*-trend** | **n** | **β[b]** | **95%CI[c]** | ***p*-trend** |
| Reference: Q1 (low exposure) | 195 | 0 | - | | 195 | 0 | - | | 195 | 0 | - | |
| Q2 (medium exposure) | 197 | 3.25 | (0.07; 6.42) | | 197 | 1.83 | (-1.41; 5.07) | | 197 | 1.83 | (-1.28; 4.94) | |
| Q3 (high exposure) | 186 | 0.80 | (-2.11; 3.70) | | 186 | 0.94 | (-2.15; 4.03) | | 186 | 0.94 | (-2.38; 4.26) | |
| Q4 (very high exposure) | 191 | -0.18 | (-2.98; 2.63) | 0.582 | 191 | -0.80 | (-4.16; 2.56) | 0.560 | 191 | -0.80 | (-4.00; 2.39) | 0.524 |

[a] d: distance; AADT: Annual Average Daily Traffic.
[b] β coefficients estimated using multiple linear regression models (an independent model for each method), adjusted for age, education, body mass index, parity, previous breast biopsies, family history of breast cancer, oral contraceptives use, tobacco consumption, alcohol consumption, energy intake, and residing near industries associated with higher mammographic density.
[c] 95% confidence intervals were calculated using bootstrapped robust standard errors.


DDM-Madrid study
DDM-Madrid sub-study restricted to the municipality of Madrid
(n=1466) Potentially eligible participants
(n=24) Missing data in coordinates
(n=1442) Eligible (georeferenced) participants
(n=546) Outside the municipality of Madrid
(n=896) Participants included in the municipality of Madrid
(n=127)
18 with analogical images
11 with unmeasured MD
98 with missing data in covariates
(n=769) Participants included in the present work

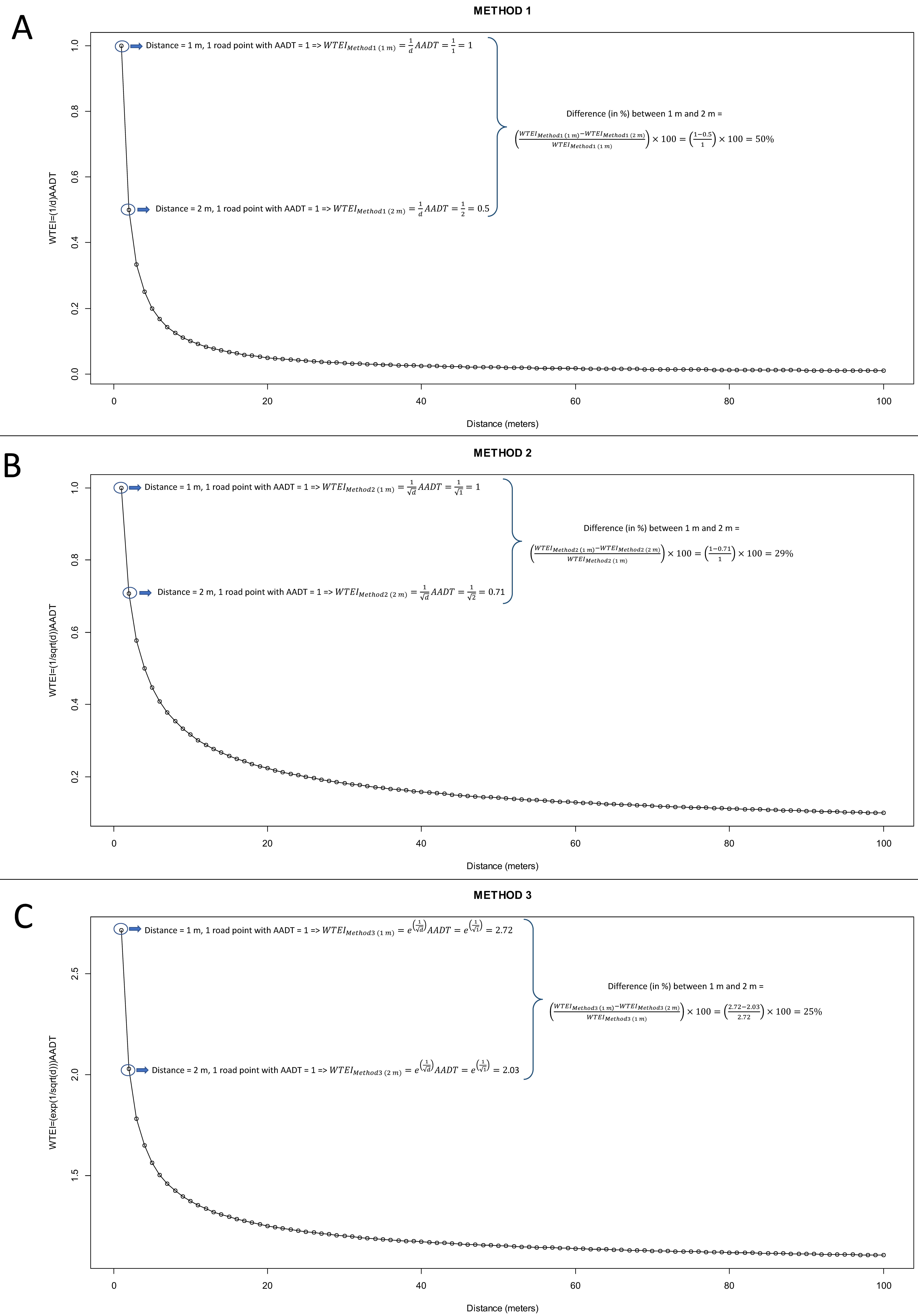

SPAIN
Women
AADT: >75,000 vehicles/day
AADT: 50,000 - 74,999 vehicles/day
AADT: 25,000 - 49,999 vehicles/day
AADT: 10,000 - 24,999 vehicles/day
AADT:<10,000 vehicles/day
AADT: 14,528
AADT: 36,314
AADT: 00,000
AADT: 26,939
AADT: 29,914
AADT: 3,657
AADT: 25,950
AADT: 33,563
AADT: 2,695
AADT: 3,288
AADT: 28,649
AADT: 24,679
DDM-Madrid
(n=1442 georeferenced women)
PROVINCE
OF MADRID
0
40.00 km
DDM-Madrid
sub study (n=769)
Municipality
of Madrid
0
12.00 km




$$WTEI_{Method1} = \sum_i \left(\frac{1}{d_i} AADT_i\right) = \frac{1}{d_1} AADT_1 + \frac{1}{d_2} AADT_2 \text{ (for a 50 m buffer)}$$

$$WTEI_{Method1} = \sum_i \left(\frac{1}{d_i} AADT_i\right) = \frac{1}{d_1} AADT_1 + \frac{1}{d_2} AADT_2 + \frac{1}{d_3} AADT_3 + \frac{1}{d_4} AADT_4 + \frac{1}{d_5} AADT_5$$
(for a 100 m buffer)

$$WTEI_{Method1} = \sum_i \left(\frac{1}{d_i} AADT_i\right) = \frac{1}{d_1} AADT_1 + \frac{1}{d_2} AADT_2 + \frac{1}{d_3} AADT_3 + \frac{1}{d_4} AADT_4 + \frac{1}{d_5} AADT_5 + \frac{1}{d_6} AADT_6 + \frac{1}{d_7} AADT_7 \text{ (for a 200 m buffer)}$$


A
METHOD 1
Distance = 1 m, 1 road point with AADT = 1 => $WTEI_{Method1\ (1\ m)} = \frac{1}{d}AADT = \frac{1}{1} = 1$
Distance = 2 m, 1 road point with AADT = 1 => $WTEI_{Method1\ (2\ m)} = \frac{1}{d}AADT = \frac{1}{2} = 0.5$
Difference (in %) between 1 m and 2 m =
$\left(\frac{WTEI_{Method1\ (1\ m)} - WTEI_{Method1\ (2\ m)}}{WTEI_{Method1\ (1\ m)}}\right) \times 100 = \left(\frac{1-0.5}{1}\right) \times 100 = 50\%$
WTEI=(1/d)AADT
Distance (meters)
B
METHOD 2
Distance = 1 m, 1 road point with AADT = 1 => $WTEI_{Method2\ (1\ m)} = \frac{1}{\sqrt{d}}AADT = \frac{1}{\sqrt{1}} = 1$
Distance = 2 m, 1 road point with AADT = 1 => $WTEI_{Method2\ (2\ m)} = \frac{1}{\sqrt{d}}AADT = \frac{1}{\sqrt{2}} = 0.71$
Difference (in %) between 1 m and 2 m =
$\left(\frac{WTEI_{Method2\ (1\ m)} - WTEI_{Method2\ (2\ m)}}{WTEI_{Method2\ (1\ m)}}\right) \times 100 = \left(\frac{1-0.71}{1}\right) \times 100 = 29\%$
WTEI=(1/sqrt(d))AADT
Distance (meters)
C
METHOD 3
Distance = 1 m, 1 road point with AADT = 1 => $WTEI_{Method3\ (1\ m)} = e^{\left(\frac{1}{\sqrt{d}}\right)}AADT = e^{\left(\frac{1}{\sqrt{1}}\right)} = 2.72$
Distance = 2 m, 1 road point with AADT = 1 => $WTEI_{Method3\ (2\ m)} = e^{\left(\frac{1}{\sqrt{d}}\right)}AADT = e^{\left(\frac{1}{\sqrt{1}}\right)} = 2.03$
Difference (in %) between 1 m and 2 m =
$\left(\frac{WTEI_{Method3\ (1\ m)} - WTEI_{Method3\ (2\ m)}}{WTEI_{Method3\ (1\ m)}}\right) \times 100 = \left(\frac{2.72-2.03}{2.72}\right) \times 100 = 25\%$
WTEI=(exp(1/sqrt(d)))AADT
Distance (meters)