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ARTIGO ORIGINAL

Long-term Exposure to Ambient Air Pollution and its Association with Mental Well-Being, Depression and Anxiety: A Nationally Representative Study

Exposição de Longo-prazo a Poluição do Ar Ambiente e sua Associação com Bem-Estar Mental, Depressão e Ansiedade: Um Estudo Representativo a Nível Nacional

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ABSTRACT

Introduction: Exposure to ambient air pollution may play a role in the onset of common mental disorders like depressive and anxiety disorders. The association of long-term exposure to particles smaller than 10 µm (PM_{10}) with these diseases remains unclear. This study aimed to estimate the association of long-term exposure to PM_{10} with mental well-being and the frequency of probable diagnosis of common mental disorders.

Methods: A nationally representative cross-sectional study was done in mainland Portugal. Long-term exposure was estimated through one-year average concentrations of PM_{10}, calculated with data from the Portuguese Environment Agency, attributed individually considering individuals' postal codes of residence. The mental well-being and the probable diagnosis of common mental disorders were ascertained through the five-item Mental Health Inventory scale. Linear and Robust Poisson regression models were computed to estimate change percentages, prevalence ratios (PR), and their 95% confidence intervals (95% CI).

Results: The median (interquartile range) concentration of PM_{10} was 18.6 (15.3 - 19.3) µg/m³. The mental well-being score was 72 (56 - 84) points, on a scale from 0 to 100. A probable diagnosis of common mental disorders was found in 22.7% (95% CI: 20.0 to 25.6). Long-term exposure to PM_{10} was associated with a non-statistically significant decrease in the mental well-being score [for each 10 µg/m³ increment in one-year average PM_{10} concentrations, there was a 2% (95% CI: -8 to 4) decrease], and with a non-statistically significant increase in the common mental health frequency (PR = 1.012, 95% CI: 0.979 to 1.045).

Conclusion: We did not find statistically significant associations between long-term exposure to PM10 and mental well-being or the frequency of probable diagnosis of common mental disorders. These results may be explained by the reduced variability in the exposure values, given the geographical distribution and functioning of the network of air quality monitoring stations. This study contributes with evidence for low levels of air pollutants, being one of the first to adjust for individual and aggregate-level variables. Moreover, to the best of our knowledge, this was the first nationally representative, population-based study conducted on the Portuguese population using real-life data. Maintaining a robust and nationwide air quality monitoring network is essential for obtaining quality exposure data.
Keywords: Air Pollution/adverse effects; Anxiety Disorders; Depressive Disorders; Environmental Exposure; Mental Health; Particulate Matter/adverse effects; Stress, Psychological

RESUMO

Introdução: A exposição à poluição do ar ambiente poderá associar-se a doenças mentais comuns como as perturbações depressivas e ansiosas. A associação entre a exposição de longo prazo a partículas inferiores a 10 µm (PM_{10}) e estas doenças não está claramente estabelecida. Procurámos estimar a associação da exposição de longo prazo a PM_{10} com o bem-estar mental e a frequência de diagnóstico provável de doenças mentais comuns.

Métodos: Foi realizado um estudo transversal, representativo a nível nacional, em Portugal Continental. A exposição de longo prazo foi estimada através das concentrações médias de PM_{10} anuais, calculadas com dados da Agência Portuguesa do Ambiente e atribuídas individualmente considerando os códigos postais de residência de sete dígitos dos indivíduos. O bem-estar mental e o diagnóstico provável de doenças mentais comuns foram obtidos através da escala de cinco itens *Mental Health Inventory*. Aplicaram-se regressões lineares múltiplas e Poisson robustas para estimar percentuais de mudança, razões de prevalência (RP) e seus intervalos de confiança a 95% (IC 95%).

Resultados: A mediana (intervalo interquartil) da concentração de PM_{10} foi de 18,6 (15,3 - 19,3) µg/m³. A pontuação de bem-estar mental foi de 72 (56 - 84) pontos numa escala de 0 a 100. O diagnóstico provável de doenças mentais comuns foi observado em 22,7% (IC 95%: 20,0 a 25,6). A exposição de longo-prazo a PM^{10} associou-se à diminuição não estatisticamente significativa da pontuação de bem-estar mental [por cada aumento de 10 µg/m³ nas concentrações médias de PM_{10} anuais, ocorreu uma diminuição de 2% (IC 95%: -8 a 4)], e ao aumento não estatisticamente significativo da frequência de doenças mentais comuns (RP = 1,012, IC 95%: 0,979 a 1,045).

Conclusão: Não se verificaram associações estatisticamente significativas entre a exposição de longo prazo a PM_{10} e o bem-estar mental ou a frequência de diagnóstico provável de doenças mentais comuns. Os resultados podem ser explicados pela reduzida variabilidade observada nos valores de exposição, limitada pela disposição geográfica e funcionamento das estações de monitorização da qualidade do ar. Este estudo acrescenta evidência para níveis reduzidos de poluição atmosférica, sendo um dos primeiros a ajustar para variáveis individuais e populacionais. Foi também o primeiro estudo de base populacional, representativo a nível nacional, realizado na população portuguesa com dados de poluição efetivamente medidos.
Palavras-chave: Exposição Ambiental; Partículas em Suspensão/efeitos adversos; Perturbações de Ansiedade; Perturbações Depressivas; Poluição do Ar/efeitos adversos; Saúde Mental; Stress Psicológico

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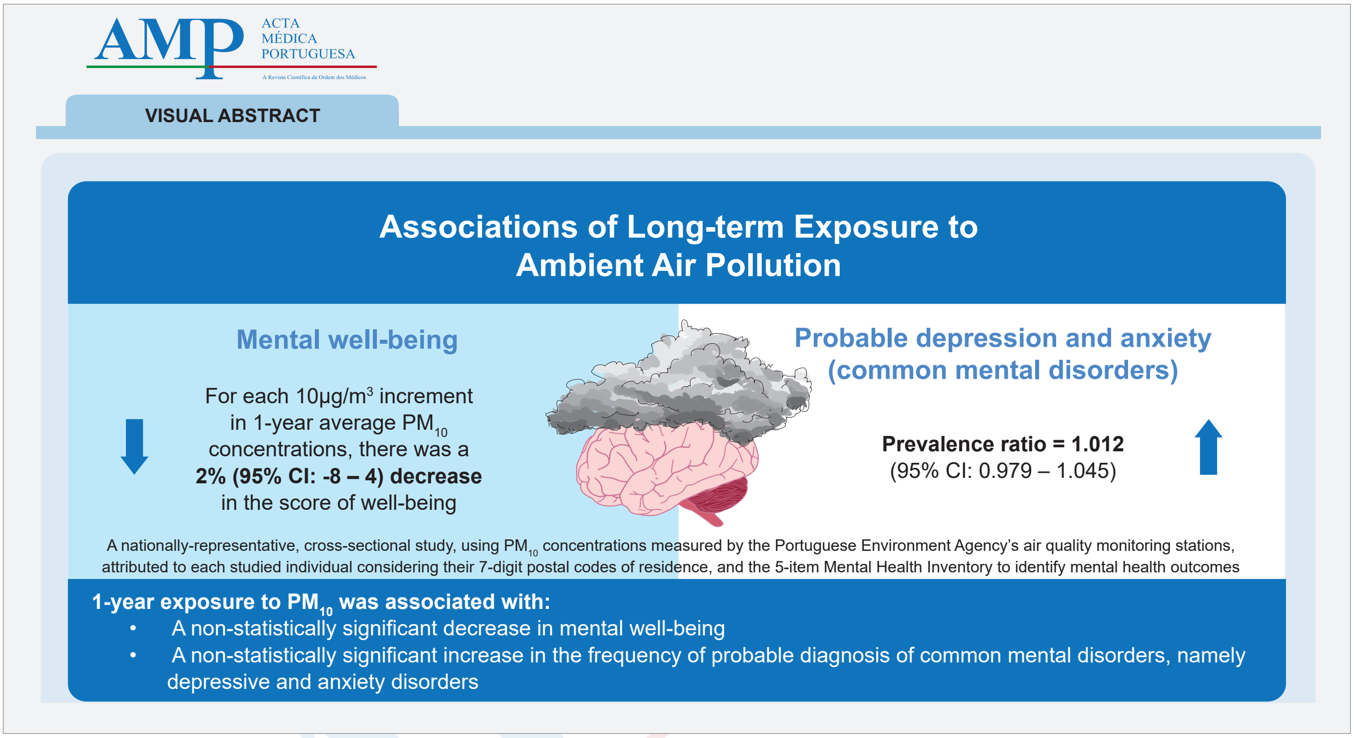

INTRODUCTION

Ambient air pollution is a global problem and a recognized risk factor for several diseases, including cancer, respiratory, and cardiovascular diseases.[1] Common mental disorders (CMD), namely depressive and anxiety disorders, are the main causes of disease burden worldwide.[3] Furthermore, with the COVID-19 pandemic, their prevalence rate was reported to increase by 28% and 26%, respectively.[3]

The causal path for depressive and anxiety disorders involves genetic, developmental, demographic, socioeconomic, and behavioral factors,[4] but knowledge about the interaction with environmental factors is still limited, especially in terms of exposure to ambient air pollution.[5] Particulate matter (PM) accounts for much of the impact of air pollution on health.[1,6] Some studies have already assessed the association between long-term exposure to particulate matter with a diameter lower than 10 micrometers (PM_{10}) and CMD.[7-12] However, evidence on this association remains inconsistent. In a recently published meta-analysis, for each 10 µg/m³ increment in PM_{10} atmospheric concentration, there was a 9.2% non-statistically significant increase in the incidence of depressive disorders [relative risk (RR) = 1.092, 95% confidence interval (95% CI): 0.988 - 1.206].[7]

Other meta-analyses reported a 8% non-statistically significant increase [odds ratio (OR) = 1.08, 95% CI: 0.98 - 1.19),[8] a 4% non-statistically significant increase (OR = 1.04, 95% CI: 0.85 - 1.26),[9] and even a 11% non-statistically significant decrease (OR = 0.89, 95% CI: 0.50 - 1.58)[10] in the prevalence of depressive disorders. Concerning anxiety disorders, for each 10 µg/m³ increment in PM_{10}, a recent meta-analysis reported a 12% statistically significant decrease in their prevalence (OR = 0.88, 95% CI: 0.78 - 0.98), and a 3% statistically significant increase in the prevalence of psychological stress (OR = 1.03, 95% CI: 1.00 - 1.05).[11] This last meta-analysis considered both short and long-term exposures, with considerable heterogeneity in the estimates [59% (p = 0.01) and 41% (p = 0.17), respectively], which was also noticed in other meta-analyses.[11]

Possible explanatory mechanisms for PM implication on CMD are neuroinflammatory and oxidative stress, dysregulation of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system, with the respective changes on neurotransmitters, neuromodulators, or their metabolites, and epigenetic alterations.[13,14] Some *in vivo* exposure studies in animal models demonstrated that PM may alter brain functions and gene expression in frontolimbic brain regions (associated with emotion processing),[15,16] as well as increase the expression of glucocorticoid-sensitive genes (and the levels of stress hormones).[17] Neuroimaging studies in humans demonstrated that exposure to air pollution was associated with an altered microstructure in the same brain regions.[18] The causal effect of PM_{10} on other chronic diseases may also explain part of the association due to the possible causal path between chronic multimorbidity and depression.[19]

Therefore, we hypothesized that, through neuroinflammatory mediation, changes in neurotransmitters and neuromodulators (or its metabolites), and through decreased neuroplasticity, ambient air pollution, more specifically long-term exposure to PM_{10}, might be associated with a decreased mental well-being and an increased frequency of CMD.

The present study aimed to estimate the association between long-term exposure to PM_{10} and the mental well-being score, and to estimate the association between long-term exposure to PM_{10} and the frequency of probable diagnosis of common mental disorders, in the population living in mainland Portugal.

METHODS

This study followed the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) reporting guidelines.

Study design and study population

We conducted a population-based, nationally-representative, cross-sectional study, in mainland Portugal. We used data from a restricted sample of the participants in the first Portuguese National Health Examination Survey (INSEF), implemented in Portugal between February 2nd and December 21st, 2015. The INSEF targeted 25- to 74-year-old non-institutionalized individuals, living in Portugal for at least 12 months, who were able to follow an interview in Portuguese. Self-reported data on demographic, socioeconomic, lifestyle and health variables was collected by INSEF. Data collection was performed through computer-assisted interviews made by healthcare professionals, trained according to the European Health Examination Survey guidelines. The design and implementation of this survey were detailed elsewhere.[20]

The study individuals were the INSEF participants from mainland Portugal who consented on data linkage, had their seven-digit postal codes of residence available in the database, and who were living within a 30-km radius from a background air quality monitoring station (with available data on PM_{10} atmospheric concentration), like previously detailed.[21-23] Additionally, we excluded individuals with missing data on any of the five items of the Mental Health Inventory (MHI-5) scale, the instrument used to operationalize the two outcomes in study.

Data availability statement

The datasets analyzed during the current study are not publicly available due to ethical restrictions. Data is available from the authors upon reasonable request.

Ethical considerations

In this study, no ethical or legal issues of confidentiality were raised, since all the data came from anonymized databases.

The INSEF had its scientific protocol approved by the Ethics Committee for Health of the National Health Institute Doutor Ricardo Jorge (INSA) (Internal Note No. 7/2011), by the National Data Protection Commission (Authorization No. 199/2001), and by the Ethics Commissions of the Northern Region Health Administration (Authorization No. 91/2014), the Regional Health Administration of Centro (Authorization No. 44/2014), the Regional Health Administration of Lisbon and Tagus Valley (Authorization No. 17/2014), the Algarve Regional Health Administration (Authorization No. 2742 of 04/03/2015), and the Health Service of the Autonomous Region of Madeira (Authorization No. 32/2014). All the participants were asked to sign a declaration of informed consent to participate in the INSEF, which consisted of accepting to respond to a general health interview, perform the physical examination, and donate a blood sample for clinical analysis.

The protocol of this study was also approved by the INSA Ethics Committee and by the Board of Review of the INSEF (INSA-IM60_05/February 2023).

Ambient air pollution assessment

Previous studies considered long-term exposure to PM_{10} as a period equal or higher than six months, with one year being the most common timeframe.[6-8,10,12] In this study, long-term exposure to PM_{10} was defined as the one-year average PM_{10} concentration (μg/m³), attributed to each individual according to their seven-digit postal code of residence, as the INSEF participants reported living in the same place for at least one year before their assessment day.

We computed individually allocated annual averages using the daily average PM_{10} concentrations available for the 365 days before each individual's assessment day. These daily averages were computed using the 24-hour PM_{10} concentrations available from each station. Hourly PM_{10} concentrations were obtained between February 2nd, 2014 (365 days before the first INSEF fieldwork day) and December 21st, 2015 (the last INSEF fieldwork day), through the air quality monitoring stations database (QualAR), available online at the Portuguese Environment Agency website (https://qualar.apambiente.pt/).

Only background stations located within 30 km from the individuals' residence, with daily and annually data collection efficiencies of at least 75%, were considered. For each individual, there was a unique allocated one-year average of exposure to PM_{10}. When two or more stations coexisted in the defined 30-km radius, we weighted annual average concentrations by the inverse of the squared distance between the individual's residence and each air quality monitoring station, as previously reported.[21-23]

Mental health outcomes definition and identification

We ascertained mental well-being and the frequency of probable diagnosis of CMD (proxy of prevalent CMD) through the scores obtained on MHI-5, in its numerical form (0 to 100 points) and categorical form (≤ 52 points or > 52 points), respectively. In its numerical form, a score of 0 represents the minimum on the continuum of mental well-being, while a score of 100 represents the maximum. In its categorical form, a score ≤ 52 represents a situation that requires proper clinical evaluation by a doctor (a 'Probable diagnosis of CMD'), while a score > 52 represents a situation that does not require proper clinical evaluation.

MHI-5 is a five-item self-reported questionnaire that measures negative and positive dimensions of mental health, in the four weeks prior to the day of assessment [Appendix 1 - Supplementary Fig. 1 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/21245/15477)].[24] It was nationally[25,26] and internationally[27,28] validated for the screening of major depressive disorder, affective disorders, (unipolar and bipolar depressive disorders) and anxiety disorders.

Covariates

Based on our literature review, we elaborated a directed acyclic graph, in DAGitty version 3.0 (https://dagitty.net/), to select the minimal sufficient set of variables needed to account for confounding during data analysis [Appendix 1 - Supplementary Fig. 2 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/21245/15477)].[19,23,29-31]

Age was categorized into four categories: 25 - 34 years, 35 - 49 years, 50 - 64 years, and 65 - 74 years, according to the cut-offs used in The World Mental Health Survey.[32] Sex and degree of urbanization were studied as available in the INSEF database: female/male and rural/urban, respectively.[20] Education level was categorized into three categories, considering the highest level of education completed and according to the 2011 International Standard Classification of Education (ISCED)[33]: low education (levels 0 - 2 of ISCED, 2011), medium education (levels 3 - 4 of ISCED, 2011), and high education (levels 5 - 8 of ISCED, 2011). Employment status was categorized into three categories, as in previous studies[34]: employed, unemployed, and other without a professional activity (student, retired, disabled, housewife, or other). Professional occupation was categorized into two categories, according to the International Standard Classification of Occupations (ISCO-08)[35]: white-collar (managers; professionals; technicians, and associate professionals; clerical support workers; and services, and sales workers) and blue-collar (skilled agricultural workers; craft, and related trades workers; plant, machine operators, and assemblers; and elementary occupations). Area-level socioeconomic deprivation is the Portuguese version of the European Deprivation Index, a variable available online for all the Portuguese boroughs, here used in terciles of increasing deprivation.[31,36] Individually allocated one-year average temperatures were obtained through a similar methodology to the one applied to estimate exposure to PM_{10}, making use of one-year average temperatures collected from the National Oceanic and Atmospheric Administration database.[21-23,37] Area-level walkability was obtained through the weighted sum of residential density, street connectivity, and a land use mix index, for all the boroughs of mainland Portugal, and is available upon reasonable request, in terciles of increasing walkability.

Four health status variables were used in the sensitivity analyses: two yes/no self-reported medical diagnoses of depression and chronic anxiety relative to the six months prior to the assessment time (or predicted to last for at least six months from that time), and two yes/no self-reported use of prescribed medication for these disorders (relative to the two weeks prior to the assessment time).[38]

Statistical analysis

Participants' characteristics were presented, for continuous variables, as mean ± standard deviation (SD) or as median [interquartile range (IQR)], according to the normality or not of their distributions, respectively, and, for categorical variables, as relative frequencies, specifically as percentages.

Pearson's chi-squared tests were used to assess the association between two categorical variables. Robust confidence intervals for generalized Hodges-Lehmann median differences were used to assess differences in numerical variables with non-normal distributions between two groups.[39]

The characteristics of the included and excluded individuals were compared, through descriptive and bivariate analysis, to assess selection bias.

We performed single-level multivariable analyses, even though we used individual and aggregated variables (at borough level) in our models, as the assumptions for carrying out a multilevel analysis were not met, namely because some boroughs had just one individual.

Regarding the numerical outcome, since no transformation was able to normalize the distribution of its residuals, we compared various generalized linear regression models (linear, gamma, Poisson, and negative binomial) using Akaike Information Criteria (AIC). We chose the model with the lowest AIC to ensure the best fit of the model. As the linear regression model was the best fit, but its assumptions were not met, we used the link function 'log' to help handle heteroscedasticity and transform the distribution of the response variable in a more symmetrical one. We estimated regression coefficients and calculated the percentage of change (% change) and its 95% CI, for each 10 µg/m³ increment in PM_{10}, through the formula 100 x (e^{β} – 1) x 10.[22]

Regarding the categorical outcome, since its frequency was higher than 10%,[40] we used the robust Poisson regression to estimate the prevalence ratio (PR) of probable diagnosis of CMD, and its 95% CI. The AIC confirmed the best fit of this model against log-binomial and negative binomial models.

As we confirmed that female individuals scored significantly higher in MHI-5 than males,[34] we performed stratified analyses by sex, for both outcomes.

Several sensitivity analyses were conducted to verify the robustness of the results and assess possible biases. First, to minimize the influence of reverse causality, we excluded individuals self-reported depression, chronic anxiety, or the use of prescribed medication for one or both. Second, we performed the analysis only in these individuals (those self-reporting at least one of the following: medical diagnosis of depression, medical diagnosis of anxiety, use of prescribed medication for depression, use of prescribed medication for anxiety). Third, to assess the validity of our analyses for the 30-km exposure radius, we fitted all the models considering only participants living within a 20-km radius of a background air quality monitoring station with sufficient PM_{10} data. No further radius reduction was tested, as it implied a near 50% sample reduction, which compromised the estimates' precision.

The statistical analysis was performed in Stata®, version 15. All estimates were weighted to account for different selection probabilities resulting from the complex sampling design, and to match the population distribution in terms of geographic region, age group and sex, unless specifically stated. The significance level was set at 5%.

RESULTS

A total of 2 398 individuals, distributed around 24 air quality monitoring stations, were included in the primary analysis [Appendix 1 - Supplementary Fig. 3 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/21245/15477)]. Included and excluded individuals were similar regarding most of the analyzed characteristics. Differences between the two groups were only found regarding the individual allocated one-year average temperature, and the area-level walkability terciles [Appendix 1 - Supplementary Table 1 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/21245/15477)].

The study population had higher percentages of female participants (52.6%, 95% IC: 50.2 - 55.1) and individuals belonging to the age groups 35 - 49 years (34.1%, 95% IC: 32.0 - 36.4) and 50 - 64 years (31.5%, 95% IC: 29.4 - 33.7) (Table 1). The median (IQR) individual allocated one-year average PM_{10} concentration was 18.6 (15.3 - 19.3) µg/m³ (Table 2, Fig. 1). The median (IQR) score of mental well-being was 72 (56 - 84) points, in a scale from 0 to 100. A probable diagnosis of CMD was found in 22.7% (95% CI: 20.0 - 25.6) (Table 1).

No statistically significant association was found between PM_{10} and mental well-being, after adjustment for all the defined potential confounders. Despite that, a nonsignificant decrease in the score of well-being was observed. For each 10 µg/m³ increment in PM_{10}, there was a 2% (95% CI: - 8,4) decrease in the score, or two points in 100. A subgroup analysis showed that the decrease tended to be higher in male (% change = -3; 95% CI: -13,7) than in female individuals (% change = -1; 95% CI: -9,6), but this association was not statistically significant (Table 3).

No statistically significant association was found between PM_{10} and the frequency of probable diagnosis of CMD, after adjustment. Nonetheless, a nonsignificant increase was observed (PR = 1.012, 95% CI: 0.979 - 1.045). Subgroup analyses showed that the association between PM_{10} and the prevalence of CMD tended to be higher in males (PR = 1.021, 95% CI:

0.945 - 1.102) than in females (PR = 1.011; 95% CI: 0.988 - 1.035), but this association was also not statistically significant (Table 4, Fig. 2).

Results were robust in all the sensitivity analyses, with a slight change in the estimates of the analyses restricting for individuals without self-report of CMD, nor use of prescription medication, which showed a nonsignificant decrease in the probable diagnosis of CMD, after adjustment [Appendix 1 - Supplementary Tables 2 to 10 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/21245/15477)].

DISCUSSION

This study contributes to fill in the gap in evidence about the association between long-term air pollution and CMD. Our findings showed that individually allocated long-term exposure to PM_{10} was associated with a non-statistically significant decrease in mental well-being, and with a non-statistically significant increase in the frequency of probable diagnosis of common mental disorders. Our findings are consistent with recent meta-analyses estimates.[7-9]

A recent national cohort reported a statistically significant positive association of long-term exposure to PM_{10} and depressive disorders assessed by psychiatrists (gold-standard method).[41] However, another population-based cohort study found a non-statistically significant association with an increased risk of CMD.[42]

To our knowledge, this was one of the first studies to adjust not only for individual, but also for aggregate-level variables (namely area-level socioeconomic deprivation, degree of urbanization, and area-level walkability), which are being reported to account for bigger portions of the environmental effects on physical and mental health.[43-45] Moreover, this was the first nationally-representative, population-based study on these associations conducted in the Portuguese population

Furthermore, this study contributes to fill in the gap in evidence about the association between measured concentrations of air pollutants and CMD for low levels of air pollution. In fact, we assessed exposure to PM_{10} in Portugal, a country with a median of one-year average PM_{10} concentration (18.6 μg/m³) above the 15 μg/m³ recommended by the World Health Organization Global Air Quality Guidelines,[6] but well below the 40 μg/m³ annual value recommended by the European Union (EU Air Quality Directives 2008/50/EC and 2004/107/EC). In Asia, and even in several European countries (such as Belgium, Germany, the Netherlands, and Spain), higher median concentrations were observed, with equally larger variation intervals.[7,8] China, for instance, had medians of annual average PM_{10} concentrations ranging from 72.6 and 76.0 μg/m³, in the period from 2014 to 2015, to 155.6 μg/m³ between the maximum and minimum values observed, and India presented even more extreme levels.[46]

Although a minimum threshold for the effect of exposure to PM_{10} on mental health was not yet established,[7] the low variability of the observed exposure levels may explain the lack of statistical significance in our findings. It should be noted that the INSEF considered the distribution of the population in its sampling process, so its participants resided mostly in urban areas rather than rural areas, since the former had a higher number of individuals than the latter.[38] Moreover, in Portugal, most air quality monitoring stations are located on the coast, in urban areas, making it difficult to assess observed pollutant concentrations in rural areas.[23] Therefore, we recognize that exposure levels may have been somehow biased, which could also explain the lack of associations since it is expected that in INSEF there were higher median levels of PM_{10} concentrations than in Portugal generally, with a lower proportion of lower levels (typical of rural areas) for comparison, which limited not only the variability of our exposure values but also the power of this study.[47]

It is important to acknowledge that our findings reflect the influence of a single air pollutant, and not a joint exposure to multiple air pollutants, as in real-life. It is also important to note that studies reporting statistically significant results are more likely to be published, preventing authors from establishing methodological comparisons that allow the leveraging of new and more robust studies.[48] Recent meta-analyses that studied the association between air pollution and CMD reported publication bias on this topic.[11,48]

Considering the estimates of our subgroup analyses, sex might play a modulating role between exposure to PM_{10} and mental well-being, or CMD. Recent findings from a longitudinal, joint exposure study support this hypothesis.[42] Nonetheless, as our findings were not statistically significant, this interpretation must be done with caution, and more studies are needed to understand the role of this variable in the studied associations.

Strengths and limitations

Our study has several strengths. First, it contributes to a better understanding of the associations between long-term exposure to air pollution and mental health outcomes at low concentration levels. Second, we assessed individually allocated long-term exposures, obtained from ground air quality monitoring stations measurements (real data and not modeled data), following a robust and previously reviewed methodology.[21-23] Third, we used an analytical methodology to confirm the absence of selection bias and the national representativeness of this study. Fourth, all the estimates were weighted to account for different selection probabilities and to match the population distribution in terms of geographic region, age group and sex, allowing us to infer the results for the Portuguese population aged 25 to 75 years old. Fifth, the INSEF database, the main source of the data for this study, has been developed following standard quality procedures, providing reliable information about the covariates in study, which contributed to minimize confounding and classification bias.[38] Sixth, we controlled for confounding for a minimally defined set based on the best available evidence, including individual and aggregate-level variables. Finally, we compared different statistical models for our estimates, choosing the best fitting ones according to standard statistical procedures, which increased not only their validity, but also contributed to overcome the unreliable estimation provided by odds ratios, in the case of cross-sectional studies addressing outcomes which are not rare.[40]

Some limitations of our study should also be noted. First, we focused on PM_{10} as sufficient data from other air pollutants (for instance, $PM_{2.5}$, nitrogen dioxide, or ozone) was not available in the air quality monitoring stations database of the Portuguese Environment Agency. We could have chosen to assess exposure through modeled values, but we chose to stick to objectively measured values to increase exposure validity. Second, this study was a cross-sectional study, and thus reverse causality and survival biases might exist, even if it is not likely due to the nature of the exposure. A recent meta-analysis reported the existence of a statistically significant and positive association between exposure to PM_{10} and suicide, which increases the possibility of survival bias in this study.[49] Another recent meta-analysis found that, despite the association between long-term exposure to PM_{10} and depression was not statistically significant when the subgroup of cross-sectional studies was considered, it was statistically significant when only cohort studies were considered.[8] To lessen the impact of a possible reverse causality bias, as well as to reduce the misclassification bias of the outcomes, we sought to ensure that the exposure occurred before the beginning of the outcomes, using the annual average computed for the 365 days prior to the day of the assessment of each of the INSEF participants. The observed results were robust in the sensitivity analyses, indicating these biases are unlikely. Third, we assessed exposure to air pollution from a static point of view, considering the seven-digit postal code of residence of each of the studied individuals as the fixed reference (and not their everyday movements), which might not reflect the real exposure levels of a dynamic life. To minimize exposure misclassification bias, we performed inverse distance weighting to attribute individual exposures in individuals with more than two stations nearby, not only for a 30-km radius but also for a 20-km radius, in our sensitivity analyses, with robust results. No further reduction of the exposure radius was possible due to the loss of a considerable part of our sample and power. Fourth, CMD not only have long latency periods, but they are also frequently underdiagnosed, with their caseness being complex to establish and the validity of self-reported diagnoses being questionable.[50,51] Moreover, the latency of the exposure effects, which is also unknown,[52] must be long. To minimize outcome misclassification, we used the MHI-5 scale to operationalize our outcomes, and not data on self-reported diagnoses. Furthermore, as mentioned, our sensitivity analyses results were robust. Lastly, some residual confounding is inevitable, even if a comprehensive set of covariates was used for adjustment.

CONCLUSION

This nationally-representative, population-based cross-sectional study found that long-term exposure to PM_{10}, at the observed levels, was associated with a non-statistically significant decreased score in mental well-being, and with a non-statistically significant increased frequency of probable diagnosis of common mental disorders. These results may be explained by the reduced variability in the exposure values, limited also by the geographical distribution and data availability of the network of air quality monitoring stations.

Considering that the European Union air quality standards are more permissive than the World Health Organization Global guidelines, that no threshold is known for the dose-response curve of air pollution and its health effects, and that virtually everyone is exposed to air pollutants at different levels, more studies on this topic are needed. These studies could confirm the reported findings and provide, along with this study, solid evidence that can serve as the basis for the formulation of more restrictive air quality control policies in the European Union, and for the design of public health interventions tailored to the most vulnerable populations. Maintaining a robust and nationwide air quality monitoring network is essential for obtaining accurate exposure data, which plays a pivotal role in supporting research endeavors.

Future studies should assess joint exposures to multiple pollutants, evaluated dynamically through a longitudinal study design with a follow-up period of several years, providing estimates of its association with incident mental health disorders.

LEARNING POINTS

- This study underscored the potential link between long-term exposure to ambient air pollution, specifically PM10, and mental health outcomes. Despite finding non-statistically significant associations, the observed trends suggest that even low levels of air pollution might adversely affect mental well-being. These findings highlight the need for continued research in this area, particularly studies that can confirm these trends and provide more robust evidence. Future studies should explore joint exposures to multiple pollutants and employ longitudinal designs to assess the long-term effects of air pollution on mental health.
- The study emphasized the importance of maintaining a robust and nationwide air quality monitoring network. Accurate and comprehensive exposure data is essential for conducting high-quality research and supporting evidence-based policy decisions.

PREVIOUS AWARDS AND PRESENTATIONS

A poster of this work was presented in *the IV Congresso Nacional dos Médicos de Saúde Pública*.

AUTHOR CONTRIBUTIONS

LPG: Conceptualization, methodology, formal analysis and investigation, writing - original draft preparation.
MSU: Software, validation, formal analysis, investigation, writing - review & editing.
RG: Investigation, writing - review & editing, supervision.
CM: Investigation, writing - review & editing.
CMD: Resources, investigation, writing - review & editing, supervision.
VC: Investigation, writing - review & editing.
CGQ, DSR: Software, data curation, Investigation, Writing - review & editing.
VG: Software, investigation, writing - review & editing, project administration.
All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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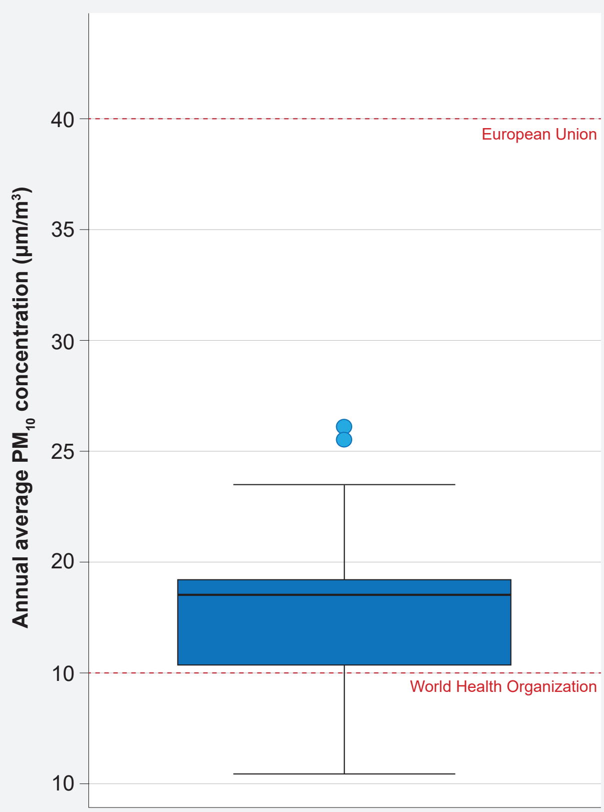

Figure 1 – Boxplot of the individually allocated one-year average PM_{10} concentrations, as measured in the mainland Portugal, compared to the recommended values of the World Health Organization Global Air Quality Guidelines and of the European Union Air Quality Directives

PM_{10}: particulate matter with an aerodynamic diameter less than or equal to 10 micrometers.

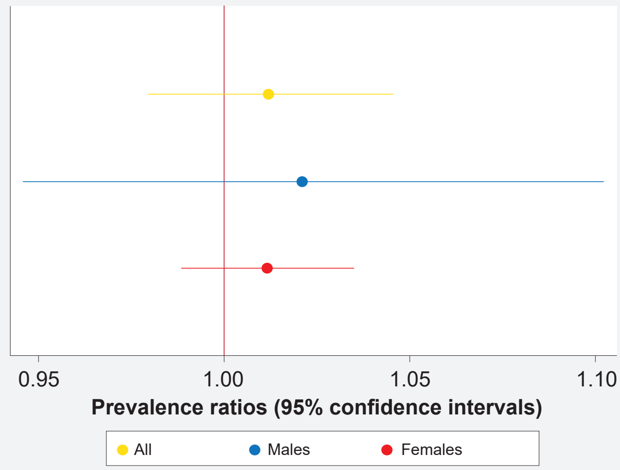

Figure 2 – Prevalence ratios plot for the association between individually allocated one-year average PM_{10} concentrations and the probable diagnosis of common mental disorders

PM_{10}: particulate matter with an aerodynamic diameter less than or equal to 10 micrometers.

The dots are estimates of the prevalence ratios, the lines intersecting the dots are the intervals of confidence for these estimates.

Table 1 – Estimates for the characteristics in study of the included individuals

	n	Sample estimates (%/median)[$]	Weighted estimates (95% CI) (%/median)[$]	
Exposure				
Individual allocated 1-year average PM_{10} (µg/m³)	2398	19.0	18.6	(18.4, 18.7)
Covariates				
Sex				
Female	1294	54.0	52.6	(50.2, 55.1)
Male	1104	46.0	47.4	(44.9, 49.9)
Age group				
25 - 34 years	353	14.7	18.9	(17.2, 20.7)
35 - 49 years	826	34.4	34.1	(32.0, 36.4)
50 - 64 years	827	34.5	31.5	(29.4, 33.7)
65 - 74 years	392	16.4	15.5	(13.9, 17.2)
Education level*				
Low[a]	679	28.3	26.5	(24.4, 28.7)
Medium[b]	1279	53.4	53.5	(50.2, 56.8)
High[c]	439	18.3	20.0	(16.7, 23.7)
Employment status*				
Employed	1448	60.4	62.3	(59.4, 65.0)
Unemployed	272	11.4	11.4	(9.7, 13.4)
Other[d]	677	28.2	26.3	(24.1, 28.7)
Professional occupation*				
White-collar[e]	1376	62.3	62.9	(58.5, 67.1)
Blue-collar[f]	834	37.7	37.1	(32.9, 41.5)
Area-level socioeconomic deprivation terciles				
Low deprivation (T1)	475	19.8	16.0	(10.5, 24.5)
Moderate deprivation (T2)	609	25.4	31.6	(19.3, 47.2)
High deprivation (T3)	1314	54.8	52.4	(37.8, 66.6)
Individual allocated 1-year average temperature (ºC)	2398	15.2	15.0	(14.8, 15.3)
Area-level walkability terciles				
Low walkability (T1)	84	3.5	1.3	(0.6, 2.9)
Moderate walkability (T2)	574	23.9	18.4	(13.5, 24.6)
High walkability (T3)	1740	72.6	80.3	(73.2, 85.9)
Degree of urbanization				
Rural	702	29.3	28.2	(22.7, 34.5)
Urban	1696	70.7	71.8	(65.5, 77.3)
Outcomes				
Mental well-being[§]	2398	72.0	72.0	(70.7, 73.3)
Probable diagnosis of common mental health disorders				
Yes	555	23.1	22.7	(20.0, 25.6)
No	1843	76.9	77.3	(74.4, 80.0)

95% CI: 95% confidence intervals; PM10: particulate matter with an aerodynamic diameter less than or equal to 10 µm T1: first tercile; T2: second tercile; T3: third tercile.
*: 1 missing in education level, 1 missing in employment status, 188 missing in professional occupation.
$: percentages or medians were presented according to the type of variable being described (categorical or continuous, respectively).
§: Assessed through the score on 5-item Mental Health Inventory, being 0 the absence of mental well-being and 100 the complete mental well-being.
a: Low education: levels 0 - 2 of ISCED, 2011 (no education, primary education).
b: Medium education: levels 3 - 4 of ISCED, 2011 (basic, secondary, post-secondary education).
c: High education: levels 5 - 8 of ISCED, 2011 (higher education).
d: Other without professional activity: students, retired people, housewives, other.
e: White-collar: managers, professionals, technicians and associate professional, clerical support workers, and services and sales workers.
f: Blue-collar: skilled agricultural workers, craft and related trades workers, plant and machine operators, and elementary occupations.

Table 2 – Characteristics of the included individuals (n = 2398) and comparison between groups of probable diagnosis of common mental health disorders

	Total (n = 2398)		Probable diagnosis of CMD (n = 555)		Without probable diagnosis of CMD (n = 1843)		*p*-value/95% CI[$]
Individual allocated 1-year average PM_{10} (µg/m³) – median (IQR)	18.6	(15.3, 19.3)	18.3	(15.2,19.2)	18.6	(15.3,19.3)	(0.012, 0.423)
Sex - %							< 0.001
Female	52.6		70.4		47.4		
Male	47.4		29.6		52.6		
Age group - %							0.072
25 - 34 years	18.9		14.3		20.2		
35 - 49 years	34.1		31.1		35.0		
50 - 64 years	31.5		37.3		29.9		
65 - 74 years	15.5		17.3		14.9		
Education level* - %							< 0.001
Low[a]	26.5		33.2		24.5		
Medium[b]	53.5		53.2		53.6		
High[c]	20.0		13.6		21.9		
Employment status* - %							< 0.001
Employed	62.3		51.5		65.4		
Unemployed	11.4		14.3		10.6		
Other[d]	26.3		34.2		24.0		
Professional occupation* - %							0.071
White-collar[e]	62.9		58.1		64.2		
Blue-collar[f]	37.1		41.9		35.8		
Area-level socioeconomic deprivation terciles - %							0.087
Low deprivation (T1)	16.0		16.4		15.9		
Moderate deprivation (T2)	31.6		36.0		30.3		
High deprivation (T3)	52.4		47.6		53.8		
Individual allocated 1-year average temperature (ºC) – median (IQR)	15.0	(14.8, 16.7)	14.9	(14.6, 16.7)	15.2	(14.8, 16.7)	(0.015, 0.141)
Area-level walkability terciles - %							0.489
Low walkability (T1)	1.3		1.5		1.3		
Moderate walkability (T2)	18.4		20.6		17.7		
High walkability (T3)	80.3		77.9		81.0		
Degree of urbanization - %							0.051
Rural	28.2		33.0		26.9		
Urban	71.8		67.0		73.1		

CMD: common mental health disorders; 95% CI: 95% confidence intervals; PM_{10}: particulate matter with an aerodynamic diameter less than or equal to 10 µm T1: first tercile; T2: second tercile; T3: third tercile.
*: 1 missing in education level, 1 missing in employment status, 188 missing in professional occupation.
$: percentages or medians were presented according to the type of variable being described (categorical or continuous, respectively).
§: Assessed through the score on 5-item Mental Health Inventory, being 0 the absence of mental well-being and 100 the complete mental well-being.
a: Low education: levels 0 - 2 of ISCED, 2011 (no education, primary education).
b: Medium education: levels 3 - 4 of ISCED, 2011 (basic, secondary, post-secondary education).
c: High education: levels 5 - 8 of ISCED, 2011 (higher education).
d: Other without professional activity: students, retired people, housewives, other.
e: White-collar: managers, professionals, technicians and associate professional, clerical support workers, and services and sales workers.
f: Blue-collar: skilled agricultural workers, craft and related trades workers, plant and machine operators, and elementary occupations.
All the estimates were weighted to account for different selection probabilities and population distribution.

Table 3 – Percent change in mental well-being, measured in a scale from 0 to 100, for each 10 µg/m^3 increment in annual average PM_{10} concentrations, among all individuals, and by sex

	n	% change* (95% CI)	
All included individuals			
Crude model	2 398	5	(- 4, 14)
Adjusted model 1[a]	2 398	5	(- 4, 14)
Adjusted model 2[b]	2 210	4	(- 5, 12)
Adjusted model 3[c]	2 210	3	(- 6, 11)
Adjusted model 4[d]	2 210	-2	(- 8, 4)
Male individuals			
Crude model	1 104	4	(- 7, 15)
Adjusted model 1[a]	1 104	3	(- 8, 15)
Adjusted model 2[b]	1 061	3	(- 9, 15)
Adjusted model 3[c]	1 061	2	(- 10, 14)
Adjusted model 4[d]	1 061	-3	(- 13, 7)
Female individuals			
Crude model	1 294	7	(-1, 15)
Adjusted model 1[a]	1 294	7	(-1, 15)
Adjusted model 2[b]	1 149	4	(-4, 12)
Adjusted model 3[c]	1 149	3	(-5, 11)
Adjusted model 4[d]	1 149	-1	(-9, 6)

PM_{10}: particulate matter with an aerodynamic diameter less than or equal to 10 µm 95% CI: 95% confidence interval.
*: Percent change was computed through the formula 100×(exp(regression coefficient)−1)×10, per 10 µg/m^3 increment in annual average PM_{10} concentrations, having the coefficients been computed through linear regression models with the link function 'log'.
a: Adjusted for sex (only when all individuals included), and age group.
b: Adjusted for sex (only when all individuals included), age group, education level, employment status, and professional occupation.
c: Adjusted for sex (only when all individuals included), age group, education level, employment status, and professional occupation, and area-level socioeconomic deprivation terciles.
d: Adjusted for sex (only when all individuals included), age group, education level, employment status, professional occupation, area-level socioeconomic deprivation terciles, individual allocated 1-year average temperature, area-level walkability terciles, degree of urbanization.
All the estimates were weighted to account for different selection probabilities and population distribution.

Table 4 – Prevalence ratios computed through modified Poisson regression models for the association between individually allocated long-term PM_{10} concentrations and the probable diagnosis of common mental disorders, among all individuals, and by sex

	n	PR (95%CI)	
All included individuals			
Crude model	2 398	0.972	(0.927, 1.018)
Adjusted model 1[a]	2 210	0.973	(0.931, 1.016)
Adjusted model 2[b]	2 210	0.982	(0.939, 1.028)
Adjusted model 3[c]	2 210	0.990	(0.951, 1.031)
Adjusted model 4[d]	2 210	1.012	(0.979, 1.045)
Male individuals			
Crude model	1 104	0.976	(0.886, 1.076)
Adjusted model 1[a]	1 104	0.978	(0.888, 1.077)
Adjusted model 2[b]	1 061	0.979	(0.881, 1.088)
Adjusted model 3[c]	1 061	0.987	(0.911, 1.069)
Adjusted model 4[d]	1 061	1.021	(0.945, 1.102)
Female individuals			
Crude model	1 294	0.970	(0.937, 1.003)
Adjusted model 1[a]	1 294	0.970	(0.939, 1.002)
Adjusted model 2[b]	1 149	0.983	(0.951, 1.015)
Adjusted model 3[c]	1 149	0.989	(0.958, 1.022)
Adjusted model 4[d]	1 149	1.011	(0.988, 1.035)

PM_{10}: particulate matter with an aerodynamic diameter less than or equal to 10 µm; 95% CI: 95% confidence interval.
*: Percent change was computed through the formula 100×(exp(regression coefficient)−1)×10, per 10 µg/m^3 increment in annual average PM_{10} concentrations, having the coefficients been computed through linear regression models with the link function 'log'.
a: Adjusted for sex (only when all individuals included), and age group.
b: Adjusted for sex (only when all individuals included), age group, education level, employment status, and professional occupation.
c: Adjusted for sex (only when all individuals included), age group, education level, employment status, and professional occupation, and area-level socioeconomic deprivation terciles.
d: Adjusted for sex (only when all individuals included), age group, education level, employment status, professional occupation, area-level socioeconomic deprivation terciles, individual allocated 1-year average temperature, area-level walkability terciles, degree of urbanization.
All the estimates were weighted to account for different selection probabilities and population distribution.