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Lifelong exposure to residential greenspace and the premenstrual syndrome: A population-based study of Northern European women

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ABSTRACT

Background: The premenstrual syndrome (PMS) causes clinically relevant psychological and physical symptoms in up to 20% of women of reproductive age. To date, no studies have investigated the relationship between PMS and residential surrounding greenspace, although a green living environment has been reported to have beneficial associations with overall and reproductive health.
Objective: To investigate whether lifelong exposure to residential surrounding greenspace is associated with PMS and whether such an association is mediated by BMI, air pollution or physical activity.
Methods: This study used data collected in 2013–2015 from 1069 Scandinavian women aged 18–49 years, participating in RHINESSA, a European multi-centre and population-based cohort. Satellite-derived Normalised Difference Vegetation Index was used as a proxy of greenspace. Presence of eight common PMS symptoms and their sum (PMS symptom count) were used as outcomes. The associations were assessed by adjusted multilevel logistic and negative binomial regressions. Subsequently we carried out mediation analyses for physical activity, BMI and air pollution exposure.
Results: Higher exposure to residential surrounding greenspace was associated with "Anxiety or tension" (Odds Ratio 0.82, 95% Confidence Interval (CI): 0.70 – 0.95), "Depression or hopelessness" (0.84, 0.73 – 0.98), "Difficulty with sleeping" (0.82, 0.68 – 1.00) and "Breast tenderness and abdominal bloating" (0.84, 0.71 – 0.99) before or around the start of the menstrual period. There was also an association with a lower PMS symptom count (Risk Ratio: 0.94, 95% CI: 0.91 – 0.99). These associations were robust to sensitivity analyses and were not mediated by BMI, physical activity or air pollution.

Abbreviations: BMI, Body Mass Index; CI, Confidence Interval; IQR, Interquartile Range; NDVI, Normalised Difference Vegetation Index; NO_2, Nitrogen dioxide; OR, Odds Ratio; PCOS, Polycystic Ovary Syndrome; PMS, Premenstrual Syndrome; $PM_{2.5}$, Particulate matter with a diameter less than 2.5μm; PM_{10}, Particulate matter with a diameter between 2.5 and 10μm.

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Conclusions: Living in greener areas may be beneficial against PMS symptoms. Further studies are needed to confirm these novel findings and to explore the underlying biological mechanisms.

1. Introduction

During the preceding days of menstruation women often experience discomforting physical symptoms (e.g. pain, bloating, sleep problems) and psychological symptoms (e.g. anger, depression, anxiety), which together constitute the premenstrual syndrome (PMS). PMS can substantially affect quality of life and impair cognitive function, attention span, and self-esteem (Ghodrati et al. 2018; Slyepchenko et al. 2017). As such, it is of great public health interest at an individual and population levels because of its high prevalence in menstruating women. A comprehensive review reported a pooled PMS prevalence of 48% (A et al. 2014) and a study carried out in the United States reported that 20% of women have clinically relevant PMS and 5 – 8% of women experience severe PMS (Yonkers et al. 2008). The need for outpatient office visits and pain medication creates a direct economic consequence and decreased performance in the workplace due to lost productivity (presenteeism) (Posthuma et al. 1987; Shehadeh and Hamdan-Mansour 2018). Additionally, lost wages due to absenteeism lead to indirect economic consequences.

PMS occurs in women who have ovulatory cycles with a progesterone producing corpus luteum. Medical treatment is currently largely limited to contraceptives that suppress ovulation and the subsequent formation of the corpus luteum (Appleton 2018). Symptoms of PMS are commonly reduced with physical activity (Yesildere Saglam and Orsal 2020), but aggravated by obesity and smoking (Fernández et al. 2019; Masho et al. 2005). Recently, also air pollution has been suggested to the influence the risk of developing PMS symptoms (Lin et al. 2020). Exposure to greenspace on the other hand has been shown to improve physical health, mental health and general wellbeing (Gascon et al. 2015; Gidlow et al. 2016; Kondo et al. 2018; Lee et al. 2011; Roe et al. 2013; Twohig-Bennett and Jones 2018). More residential surrounding greenspace has been further associated with a delayed onset of menopause (Triebner et al. 2019) and higher levels of ovarian reserve hormones (Abareshi et al. 2020). The suggested health effects of greenspace have been suggested to be mediated through reduced stress (Twohig-Bennett and Jones 2018), improved mental health (Gascon et al., 2015), enhanced physical activity (Dadvand et al. 2012), improved social cohesion (Jennings and Bamkole 2019) and reduction of exposure to urban-related environmental hazards such as noise, heat, and air pollution (Bromberger et al. 1997; Dratva et al. 2009; Markevych et al. 2017). To date, there are no studies on the potential influence of residential surrounding greenspace on PMS, despite the above mentioned evidence suggesting an association between the exposure to greenspace and PMS, possibly through changes in sex hormone concentrations or more complex neurological pathways.

2. Methods

2.1. Study population

This study was based on data from the four Nordic centres of the RHINESSA ("Respiratory Health in Northern Europe, Spain and Australia") study, namely Bergen (Norway), Uppsala, Umea and Gothenburg (Sweden). Supplementary figure S1 shows the geographic locations of the study centres. The RHINESSA cohort constitutes a follow-up of the offspring of the population-based Respiratory Health in Northern Europe study and the European Community Respiratory Health Survey. Response rates were 40.2% for Bergen and 42.7% for the three Swedish centres. The recruitment was carried out between 2013 and 2015 and the simultaneous data collection consisted of a questionnaire on anthropometrics, lifestyle factors and reproductive health. Questionnaires were web-based in Norway, while in Sweden postal questionnaires were used. For the above-mentioned centres, registry data on residential address history was available. Further details about the cohort are presented elsewhere (www.rhinessa.net). All participants provided informed written consent and the study was approved by the respective regional ethics committees. Included in the analyses, were data from adult women at one time point, for whom we could estimate residential surrounding greenspace based on geocoded addresses. Excluded were women with a history of one or more of the following doctor-diagnosed gynaecological conditions that could affect menstruation: polycystic ovary syndrome (PCOS) (n = 86), endometriosis (n = 37), ovarian cysts (n = 242) and fibroids (n = 41). Excluded were also women using exogenous hormones for one or more of the following reasons: contraception (n = 642), hormone replacement therapy (n = 5), infertility (n = 23), gynaecological disorders (n = 9) and undisclosed reasons (n = 45). Since we carried out complete case analyses, we also excluded women with missing data on covariates (n = 94). As a result, the analytic sample comprised 1069 women (Fig. 1).

2.2. Outcome: PMS symptoms

Data on PMS symptoms were collected through a self-administered questionnaire. Eight binary outcome variables were based on affirmative answers to the following question, inquiring the presence/absence

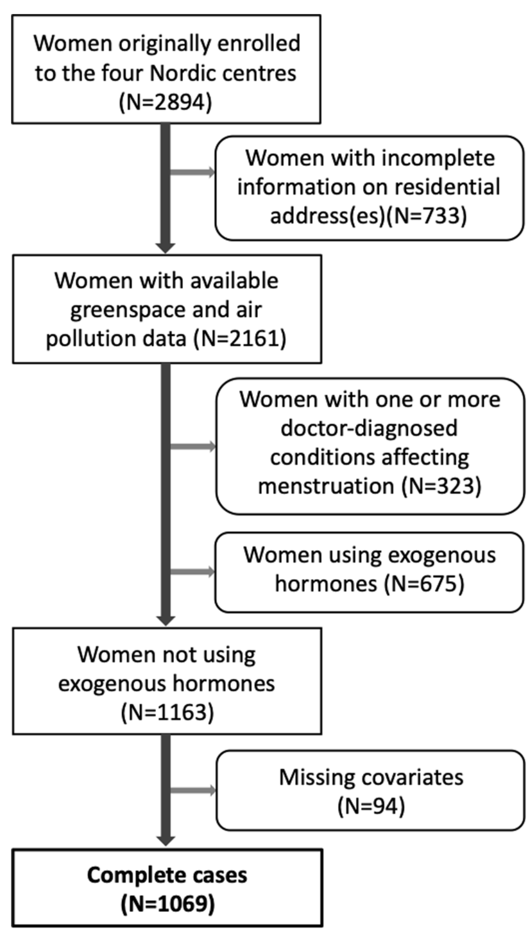

Fig. 1. Study population with inclusion criteria.

of common PMS symptoms: “Do you (or did you) usually experience the following symptoms the days before or around your menstrual periods?” (options: “Anger or irritability?”, “Anxiety or tension?”, “Tearfulness or increased sensitivity to rejection?”, “Feeling depressed or hopeless?”, “Difficulty with sleeping?”, “Abdominal pain (so that you need to take pain killers)?”, “Breast tenderness, abdominal bloating and/or swelling?”, and “Headaches?”). Missing observations were imputed as non-affirmative answers (n = 21). The Cronbach alpha coefficient for internal consistency was 0.73. We further built a PMS symptom count, ranging from zero to eight, by adding the affirmative answers pertaining to each of the above-mentioned PMS symptoms.

2.3. Exposure assessment

We applied the weighted average of the Normalised Difference Vegetation Index (NDVI) to characterise greenspace surrounding residential addresses of each participant since birth or since 1975 if born earlier, because address registries were not available for earlier time points (n = 103). NDVI is a satellite-derived index, calculated based on the knowledge that plants strongly absorb visible red light for use in photosynthesis while reflecting near-infrared light to prevent overheating. The equation for NDVI is based on spectral reflectance measurements acquired in corresponding light wavelengths and values are unitless ranging from −1 to +1, with higher numbers indicating more photosynthetically active land-cover (National Aeronautics and Space Administration 2018). Satellite images (30x30m) were retrieved every five years (1975 – 2015) during the most vegetation rich months. Residential surrounding greenspace was defined as the mean value of NDVI in a circular buffer of 100 m around each participant’s residential address(es). To calculate the weighted average of NDVI, which we used as final exposure variable, we averaged the available NDVI values, taking into account how long the respective participant had been living in each home. Negative NDVI pixels (water) were not excluded before calculating NDVI in line with Fuertes et al. (Fuertes et al. 2016). This NDVI variable did not only capture spatial contrasts, but also considered temporality (over several decades) even if the home address of a participant remained unchanged until the time of study participation. To confirm the robustness of this choice, we further abstracted residential surrounding greenspace across a 500 m buffer, and we additionally evaluated the current greenspace exposure at the time of the survey (100 m buffer).

2.4. Statistical analyses

Descriptive statistics for the study population were reported as mean and standard deviation for normally distributed continuous data and otherwise as median and interquartile range. Numbers and percentages were reported for categorical variables. We also present a comparison between the included study population and excluded observations (Supplementary Table S3).

2.4.1. Variables

2.4.1.1. Covariates. To make a selection of covariates we built a directed acyclic graph (www.dagitty.net) (Supplementary Figure S2). The minimal sufficient adjustment set for estimating the total effect of exposure to residential surrounding greenspace on PMS required adjustment for age (continuous) and socio-economic status. To adjust for the latter we utilised the highest parental education as a proxy (categorical; primary school, secondary school, university or college) as many young women had not completed their own education at the time of the survey.

2.4.1.2. Mediators. Nitrogen dioxide (NO_2) concentrations, particulate matter with a diameter less than 2.5 µm ($PM_{2.5}$) and between 2.5 and 10 µm (PM_{10}), as well as BMI and physical activity were deemed mediators. Physical activity was included as the self-reported frequency of exercise per week (options: never, less than once a week, once a week, 2–3 times a week, and almost every day). Air pollution was considered as the exposure to NO_2, $PM_{2.5}$ and PM_{10}. We used weighted averaged concentrations (µg/m^3) at the geocoded residential address(es) of each participant since her birth (or since 1975 if born earlier; n = 103), obtained by hybrid land use regression (LUR) models (de Hoogh et al. 2018; de Hoogh et al. 2016; Vienneau et al. 2013). Annual mean NO_2 and $PM_{2.5}$ were estimated from the grids created by applying hybrid LUR modelling frameworks with a resolution of 100 by 100 m (de Hoogh et al. 2018; de Hoogh et al. 2016). Annual mean PM_{10} exposures were extracted from surfaces based on another hybrid LUR model (Vienneau et al. 2013). We back- and forth-extrapolated the air pollution concentrations from the hybrid LUR models using the ratio method for each year from 1990 to 2015, following the procedure developed by the European Study of Cohorts for Air Pollution Effects (ESCAPE) project (2019). For years between 1975 and 1990, estimates from 1990 were used, in line with *Nordeide Kuiper et al.* as no air monitoring data were available for earlier time points (Kuiper et al. 2020; Nordeide Kuiper et al. 2021).

2.4.1.3. Effect modifiers. Urbanicity (continuous), current smoking (dichotomous; based on: “Are you a smoker?”; options: “No”, “Yes”), menstrual regularity (categorical; based on: “Do you have regular periods?’’ alternatives :‘‘yes’’; “no, they have never been regular’’; “no they have been irregular for a few months’’; and “no, my periods have stopped’’), parity (continuous) and cycle length (continuous) were treated as effect modifiers.

2.4.2. Main analyses

We cross-sectionally fitted two-level random intercept mixed effects logistic regression models, with eight individual symptoms of PMS as outcome (one at a time), as well as a negative binomial regression model with a PMS symptom count (sum of PMS symptoms) as outcome and in both cases NDVI was treated as the main exposure variable. All models apart from the ones stratified by study centre, included study centre (categorical) as random effects term. The main models were adjusted for age and socio-economic status. We reported all effect estimates for a one interquartile range (IQR) increment of NDVI.

2.4.3. Sensitivity analyses

We fitted a number of models with additional adjustment for urbanicity, current smoking, menstrual regularity, cycle length and number of pregnancies. We further limited our main analyses separately to only current non-smokers and only women reporting regular menstruations, as smoking could have anti-estrogenic effects, and irregular menstruations suggest an altered hormone balance and amenorrhea may indicate premature menopause or unknown underlying health conditions. We additionally stratified by study centre, age (tertiles) and parental education. Moreover, we repeated our main analyses, 1) using an alternative set of exposure that was abstracted based on a 500 m buffer, 2) using the current greenspace exposure (100 m) at the time of the survey and 3) excluding observations where the outcome was imputed.

2.4.4. Mediation analyses

For mediation analyses, we further assessed, BMI, physical activity and air pollution exposure. We fitted models using the R “lavaan” package to estimate average serial mediation effects (indirect effects) and direct effects. We used the default maximum likelihood estimator and non-parametric bootstrapping with 5000 simulation runs to abstract 95% confidence intervals (CI) for our estimates. We evaluated model fit with the Bayesian information criterion and further considered the comparative fit index. All analyses were performed using R (version

3.6.3).

3. Results

Descriptive statistics of the characteristics of participants altogether and by study centre, are presented in (Table 1).

An increase of one interquartile range in residential surrounding greenspace was associated with “Anxiety or tension” (Odds Ratio: 0.82, 95% Confidence Interval (CI): 0.70 – 0.95), “Depression or hopelessness” (0.84, 0.73 – 0.98), “Difficulty with sleeping” (0.82, 0.68 – 1.00) and “Breast tenderness and abdominal bloating” (0.84, 0.71 – 0.99) before or around the start of the menstrual period (Fig. 2) as well as the PMS symptom count (Risk Ratio: 0.94, 95% CI: 0.91 – 0.99), indicating a 6% decrease in the incidence rate ratio of the PMS symptom count for every IQR increase in NDVI. These findings were robust to additional adjustment (urbanicity, current smoking, menstrual regularity, cycle length and number of pregnancies) and across sensitivity analyses restricted to current non-smokers, observations where the outcome was not imputed as well as for women reporting regular menstruations and a greenspace buffer of 500 m (Supplementary figures S3-10, Supplementary Table S5). Models with current greenspace exposure as predictor did not reveal such associations (Supplementary figure S11). Associations were not mediated by BMI, physical activity or air pollutants.

The stratified analyses indicated that associations were similar across all four study centres, the strata by parental education and the strata across the three age tertiles, apart from “Difficulties with sleeping”, which seemed to be driven by the oldest women (33–49 years) (Supplementary figures S12-21).

4. Discussion

This exploratory study integrated data of 1069 Northern European women from a well-established population-based cohort, with lifelong exposure of residential surrounding greenspace. To our knowledge, this is the first study investigating associations between exposure to greenspace and PMS. We observed that higher exposure to residential surrounding greenspace was associated with fewer PMS symptoms and with lower odds for four out of the eight investigated PMS symptoms. These findings were robust to a number of sensitivity analyses and not mediated by BMI, physical activity or air pollution. Our sensitivity analyses further indicate the importance of long-term exposure, as the models using current exposure at the time of the survey did not yield any significant results. Due to the lack of other studies, it was not possible to compare our findings with those of others. Yet, our observed associations are plausible considering a number of previous observations and might be attributed to emotional and physiological processes as theorised by Stress Reduction theory (Ulrich 1983) rather than to interrupting the overuse of directed attention according to the other of the two major theories, Attention Restoration theory (Kaplan 1995). Three out of the four observed associations were found for psychological symptoms, which aligns well with the ability of greenspace exposure to reduce stress and improve mental health (Beil and Hanes 2013; Ewert and Chang 2018; Tyrväinen et al. 2014; Van Den Berg and Custers 2011). Stress may worsen PMS symptoms and is reflected by a high level of cortisol, which, in turn, could be associated with an increased release of progesterone (Herrera et al. 2016; Kudielka and Kirschbaum 2005; Wirth et al. 2007). High levels of progesterone have been positively correlated with the occurrence of PMS symptoms (Redei and Freeman 1995). Also, progesterone itself may reduce the number of estrogen receptors, and may thus have anti-estrogenic effects in several tissues (Burns and Korach 2012). Higher cortisol, respectively stress levels are further associated with lower concentrations of 17β-estradiol (Roney and Simmons 2015), therefore it seems likely that this process is multi factorial, as 17β-estradiol and cortisol play crucial roles in many physiological processes, for instance the cortisol-mediated negative feedback on adrenocorticotropic hormone secretion (Sharma et al. 2014).

Table 1
Characteristics of the study population by study centre.

	All	Bergen	Gothenburg	Umea	Uppsala
N	1069	464	140	227	238
Anthropometrics, mean (SD)					
Age [y]	29.80 (7.22)	28.54 (6.94)	30.88 (7.15)	31.59 (6.88)	29.91 (7.68)
BMI [kg/m^2]	23.52 (4.27)	23.68 (4.36)	23.90 (4.52)	23.28 (4.02)	23.19 (4.17)
Current smoker, N (%)	105 (9.8)	49 (10.5)	20 (14.3)	17 (7.5)	19 (8.0)
Parental education, N (%)					
Primary school	94 (8.8)	28 (6.0)	22 (15.7)	20 (8.8)	24 (10.1)
Secondary school	285 (26.6)	125 (26.9)	56 (40.0)	61 (26.9)	43 (18.1)
University or College	691 (64.6)	312 (67.1)	62 (44.3)	146 (64.3)	171 (71.8)
Physical activity, N (%)					
Never	32 (3.0)	10 (2.2)	6 (4.3)	10 (4.4)	6 (2.5)
Less than once a week	141 (13.2)	48 (10.4)	24 (17.1)	32 (14.1)	37 (15.6)
Once a week	205 (19.2)	92 (19.9)	31 (22.1)	42 (18.5)	40 (16.9)
2–3 times a week	461 (43.2)	221 (47.7)	49 (35.0)	91 (40.1)	100 (42.2)
Almost every day	228 (21.4)	92 (19.9)	30 (21.4)	52 (22.9)	54 (22.8)
Mean exposure (lifelong), median (IQR)					
NDVI 100 m buffer	0.54 [0.48, 0.60]	0.53 [0.48, 0.59]	0.55 [0.50, 0.62]	0.53 [0.46, 0.58]	0.56 [0.49, 0.62]
NDVI 300 m buffer	0.55 [0.49, 0.60]	0.55 [0.49, 0.60]	0.56 [0.50, 0.61]	0.53 [0.47, 0.59]	0.56 [0.50, 0.62]
NDVI 500 m buffer	0.55 [0.49, 0.60]	0.55 [0.50, 0.59]	0.57 [0.50, 0.62]	0.53 [0.47, 0.59]	0.56 [0.50, 0.63]
Nitrogen dioxide [μg/m^3]	17.80 [13.39, 20.96]	19.36 [16.71, 21.14]	23.51 [20.09, 27.16]	11.99 [9.28, 14.65]	16.00 [12.60, 19.08]
Particulate matter <2.5μm [μg/m^3]	8.82 [7.91, 9.91]	8.67 [8.05, 9.04]	12.07 [11.33, 12.73]	7.48 [6.22, 8.09]	9.83 [8.87, 10.38]
Particulate matter <10μm [μg/m^3]	13.98 [12.75, 15.04]	14.03 [13.39, 14.75]	16.76 [15.99, 17.58]	11.56 [10.76, 12.25]	14.17 [13.33, 15.02]
Symptoms of PMS[1], N(%)					
Anger or irritability	705 (65.9)	329 (70.8)	83 (59.3)	141 (62.1)	152 (63.9)
Anxiety or tension	353 (33.0)	176 (37.8)	41 (29.3)	63 (27.8)	73 (30.7)
Tearfulness or sensitivity to rejection	625 (58.4)	268 (57.6)	84 (60.0)	127 (55.9)	146 (61.3)
Depressed or hopeless	486 (45.4)	181 (38.9)	69 (49.3)	119 (52.4)	117 (49.2)
Difficulty with sleeping	162 (15.1)	79 (17.0)	22 (15.7)	25 (11.0)	36 (15.1)
Abdominal pain	596 (55.7)	265 (57.0)	73 (52.1)	127 (55.9)	131 (55.0)
Breast tenderness, abdominal bloating	777 (72.6)	355 (76.3)	99 (70.7)	155 (68.3)	168 (70.6)
Headaches	309 (28.9)	151 (32.5)	46 (32.9)	50 (22.0)	62 (26.1)
			3.69 (2.29)		

(continued on next page)

Table 1 (*continued*)

	All	Bergen	Gothenburg	Umea	Uppsala
N	1069	464	140	227	238
PMS[1] symptom count, mean (SD)	3.75 (2.18)	3.88 (2.11)		3.56 (2.12)	3.72 (2.28)

[1]Premenstrual syndrome

Additionally, exposure to greenspace is known to be associated with reduced risk of mood disorders such as anxiety and depression (Gascon et al. 2015), which could increase the risk of developing PMS symptoms (Forrester-Knauss et al. 2011). Greenspace has also been suggested, though not consistently, to increase physical activity (Markevych et al. 2017), which, in turn, has been associated with lower risk of PMS symptoms (Yesildere Saglam and Orsal 2020). Our mediation analysis, however, did not support such a mediatory role for physical activity. Moreover, greenspace could reduce perceived loneliness and enhance social cohesion, which could as well be associated with lower risk of PMS symptoms (Maddineshat et al. 2016). Another potential mechanism underlying our observed associations could be the ability of greenspace in reducing exposure to air pollution (Dadvand et al. 2012; Eisenman et al. 2019) which, in turn has been associated with higher risk of PMS (Lin et al. 2020). We observed however no suggestions for such a mediatory role of air pollution.

Despite our questionnaire specifically referring to the days around the menstrual period, it cannot be excluded that the self-reported psychological symptoms overlap with mental health in general, thus depending on personal psychological traits and background stress levels. Our observed associations might be amplified in women with fragile mental health and therefore also reflect the general health benefits of greenspace. Concerning the associations with physical PMS symptoms, it is known that social interaction and physical activity both could reduce pain and further emerging evidence suggests that greenspace exposure may reduce pain via phytoncides, negative air ions, sunlight exposure as well as environmental microbiota (Stanhope et al. 2020). Although we observed a clear association between residential surrounding greenspace and PMS, we can only speculate about potential mechanisms.

The major strength of our study was the availability of data on lifelong exposure to residential surrounding greenspace and air pollution, based on the detailed address history for each participant. Our study also faced some limitations. The largely Caucasian study population may not be representative for other ethnicities and excluding those using exogenous hormones might mean that we could have effectively excluded some of those participants with more severe symptoms, as these drugs are used to treat PMS. However, including those participants might have biased our analyses as including women on drugs that are likely to suppress PMS symptoms, would increase information bias. Our current analysis may therefore be more relevant to women with mild to moderate PMS. The above assumption probably explains the higher prevalence of some PMS symptoms as well as the higher symptom count among those participants who were excluded (Table S3). Also the evaluation of PMS symptoms by self reported questionnaire is crude and may add to the limitations of this study. It is further possible that the main analyses included, apart from women with irregular menstruations, also women with premature menopause. Our results indicate however that this is of little concern, as differences between the main analysis and the analysis among women with regular menstruations are likely explained by loss of statistical power. Furthermore, we cannot exclude residual confounding, since we used NDVI as compared to other non-static indexes, and did not have information on the intensity of symptoms, time spent in the neighbourhood, the types of vegetation or quality aspects of greenspace, greenspace exposure at work or while commuting and information on the general mental health status, which may have somewhat altered our results. Also, potential confounding through socio-economic status cannot be completely ruled out as we adjusted the analyses only for a proxy (parental education level). However, study populations from Scandinavia generally show little variability in socio-economic status and cities are comparatively small and characterised by having few industrial areas. Compared to the general population in the same age range, the RHINESSA population did not differ substantially when looking at demographic distributions (e.g. in terms of current smoking or educational level) (Johannessen et al. 2014). The results of the mediation analysis may further have been altered somewhat by a potential temporal misalignment between the reporting of physical activity and the specific greenspace exposure.

5. Conclusions

Our findings suggest that women residing in more vegetated residences across their lifespan are less likely to experience PMS symptoms. Our findings, if confirmed by future studies, could provide an evidence base for implementing policies aiming at reducing the personal, familial, and societal burden of this prevalent condition in our rapidly urbanising world.

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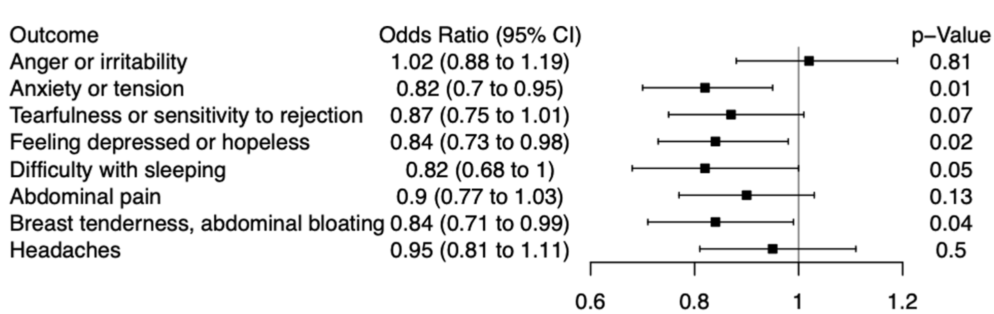

Fig. 2. Results of the main model, adjusted for age, parental education and study centre; The x-axis represents the Odds Ratio per one interquartile range increase (observed in the study sample) of **residential surrounding greenspace** (100 m buffer).

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CRediT authorship contribution statement

Kai Triebner: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Iana Markevych:** Conceptualization, Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Randi J Bertelsen:** Funding acquisition, Writing – review & editing. **Bente Sved Skottvoll:** Data curation, Writing – review & editing. **Steinar Hustad:** Writing – review & editing. **Bertil Forsberg:** Funding acquisition, Writing – review & editing. **Karl A Franklin:** Funding acquisition, Writing – review & editing. **Mathias Holm:** Funding acquisition, Writing – review & editing. **Eva Lindberg:** Funding acquisition, Writing – review & editing. **Joachim Heinrich:** Funding acquisition, Writing – review & editing. **Francisco Gómez Real:** Conceptualization, Funding acquisition, Investigation, Methodology, Writing – review & editing. **Payam Dadvand:** Conceptualization, Funding acquisition, Investigation, Methodology, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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