Supplementary materials

Outdoor artificial light at night and reproductive endocrine and glucose homeostasis and polycystic ovary syndrome in women of reproductive age

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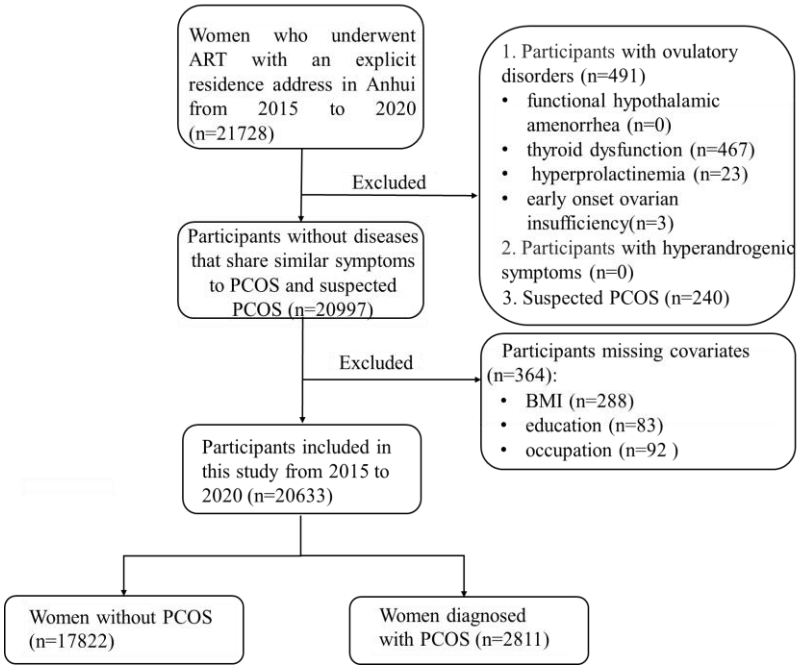

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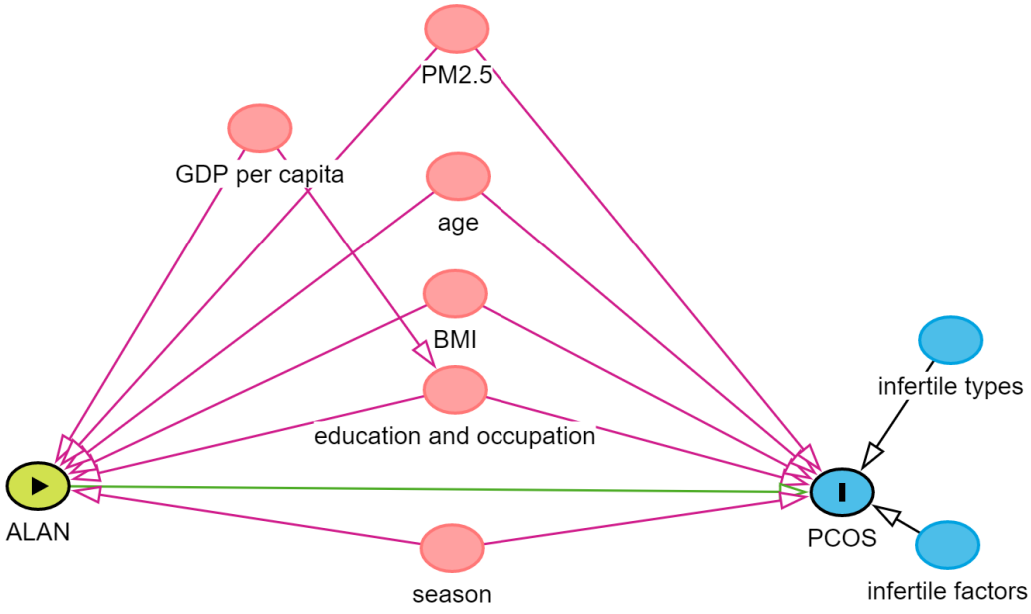

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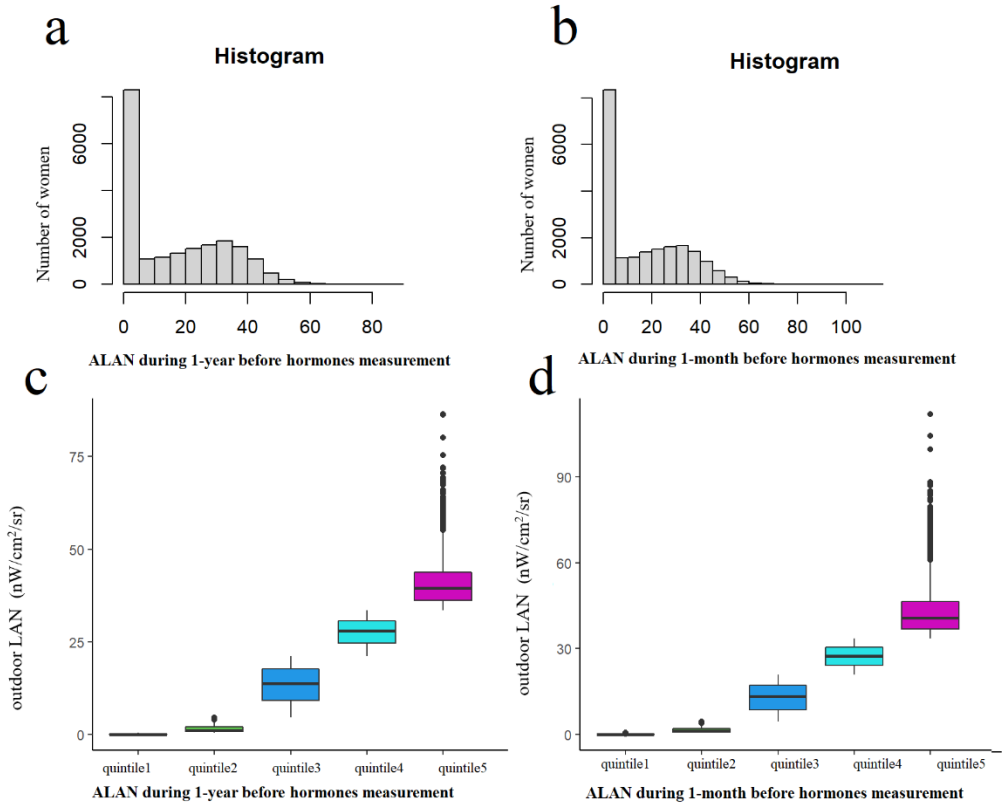

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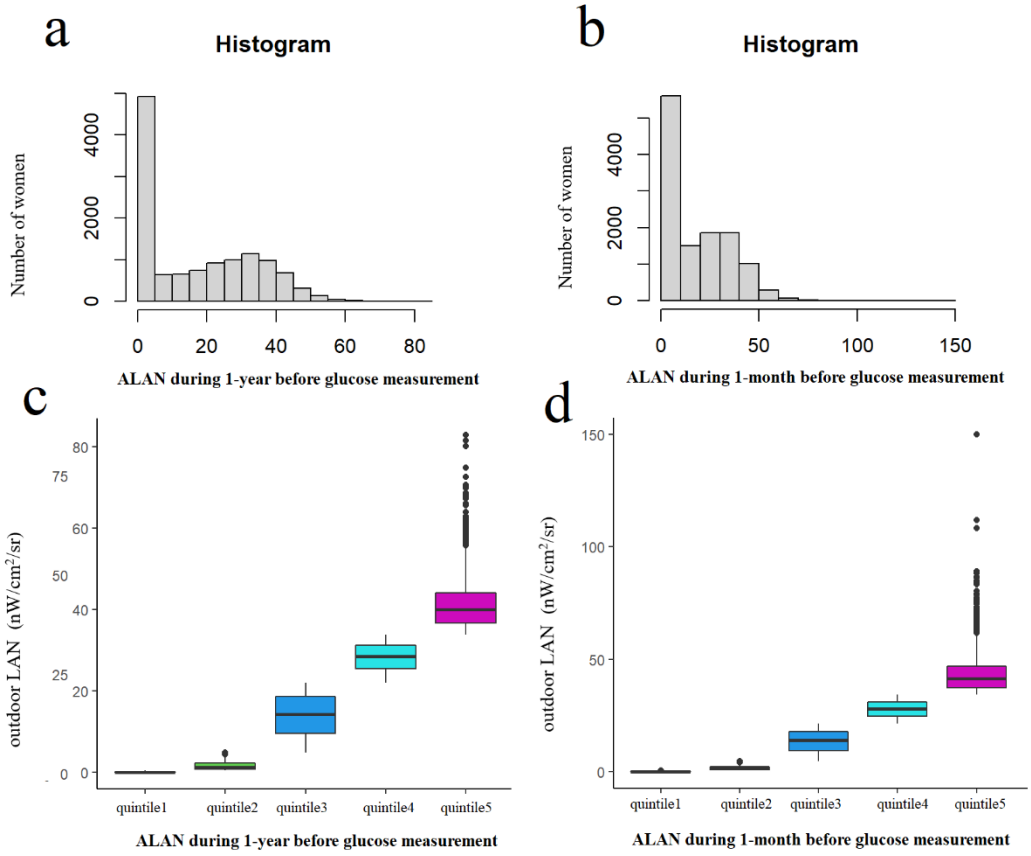

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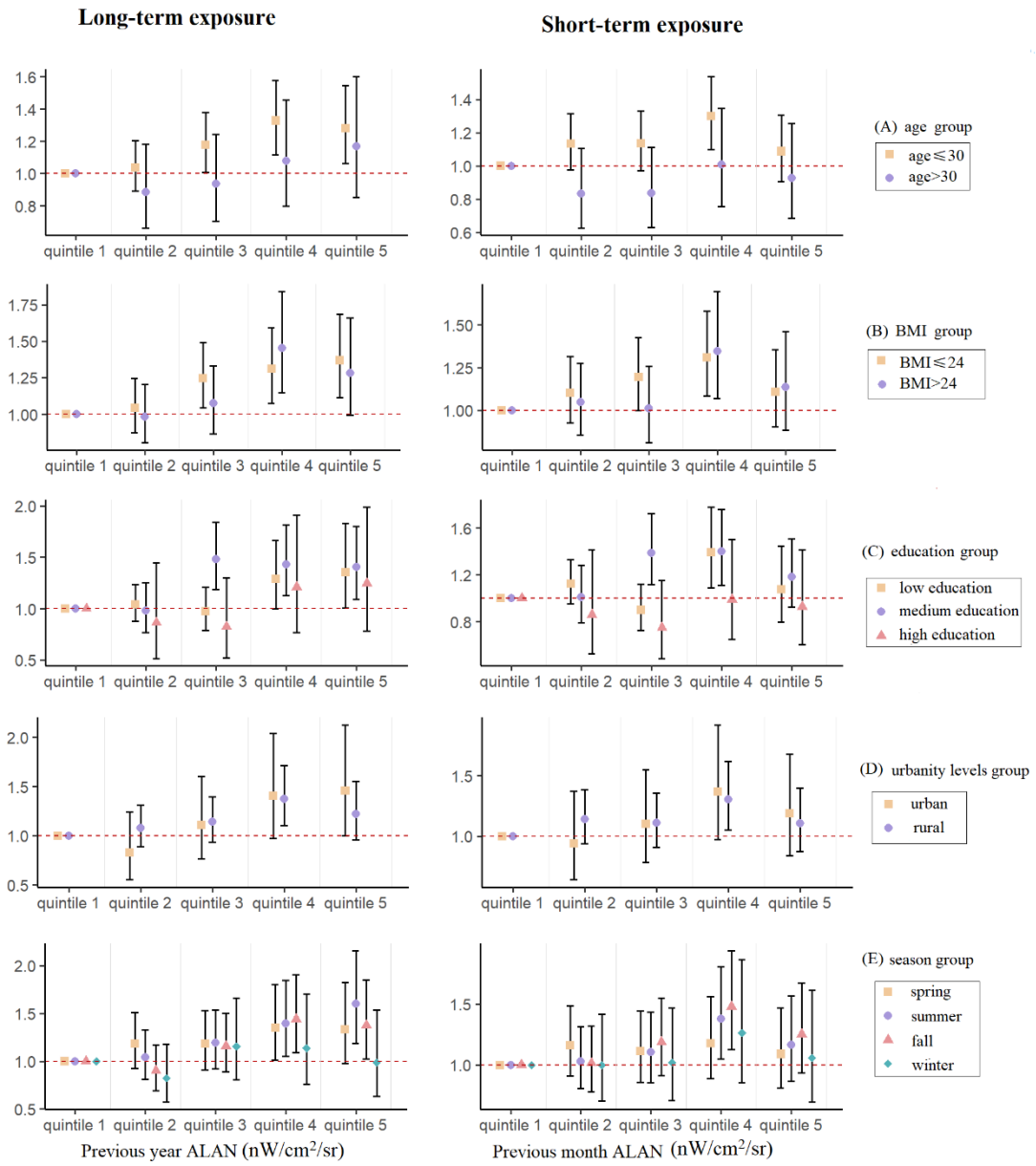

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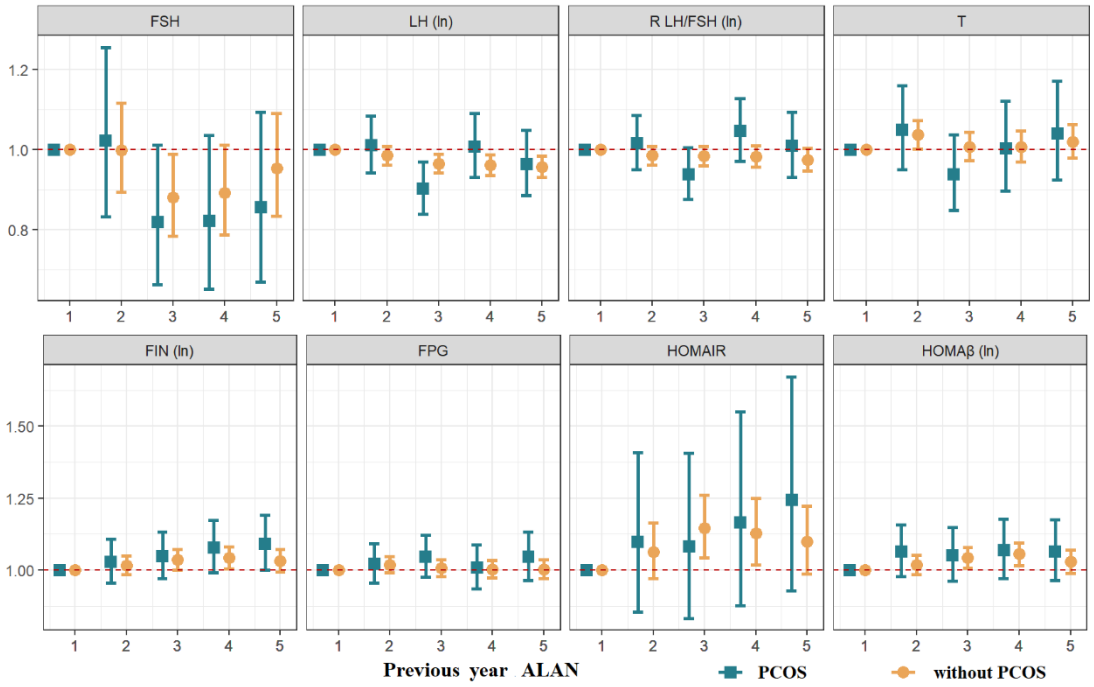

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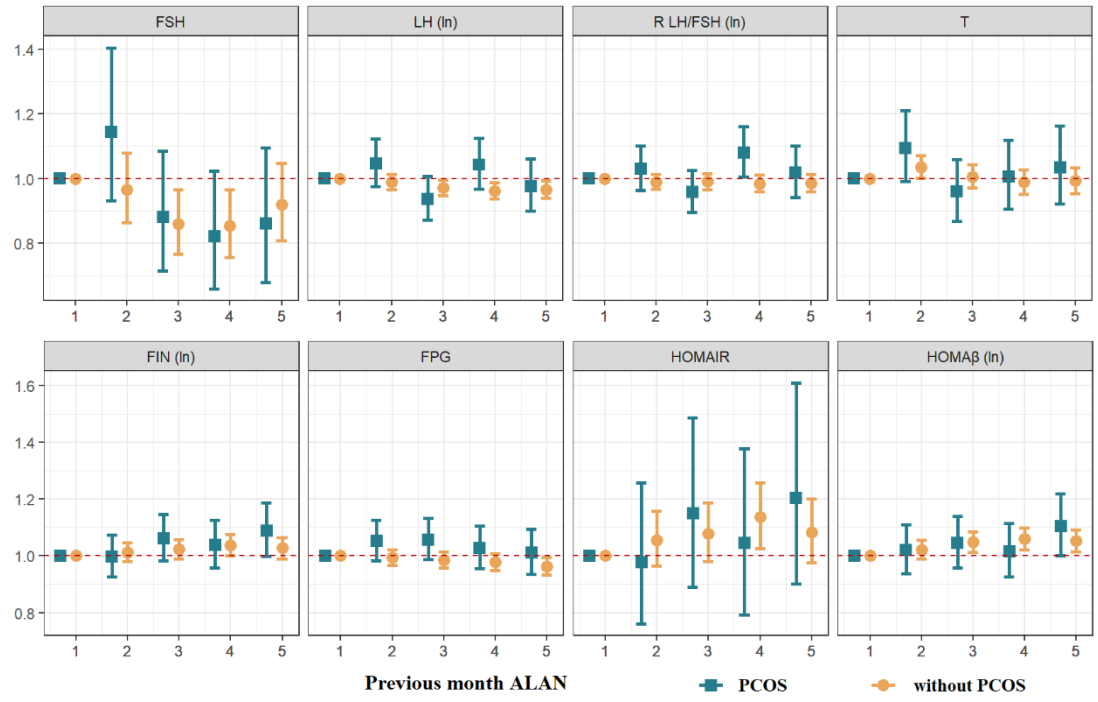

e Figure. 7. The short-term effects of ALAN on sex hormones and glucose homeostasis markers in participants with and without PCOS.

e Table 1. Serum hormones, glucose homeostasis markers, as well as seasons at disease diagnosis and hormones and glucose homeostasis testing in the study population.

Characteristic	Overall (n= 20,633)	Non-PCOS (n = 17,822)	PCOS (n = 2,811)	*P* value
Sex hormones				
FSH, mIU/mL, Mean ± SD	7.4±2.4	7.5±2.4	6.4±1.7	<0.001
Missing	706	581	125	
LH, Median (IQR)	4.6 (3.0)	4.3 (2.6)	7.6 (6.1)	<0.001
Missing	652	430	222	
LH/ FSH, Median (IQR)	0.6 (0.5)	0.6 (0.4)	1.2 (1)	<0.001
Missing	993	734	259	
T, nmol/L, Mean ± SD	1.4±0.7	1.4±0.7	1.7±0.8	<0.001
Missing	2,385	2,016	369	
Glucose homeostasis markers				
FI, mU/L, Median (IQR)	9.4 (6.6)	9.1 (6.2)	11.7 (8.6)	<0.001
Missing	8,785	7,766	1,019	
FPG, mmol/L, Mean ± SD	5.3±0.4	5.3±0.4	5.3±0.5	0.026
Missing	8,944	7,882	1,062	
HOMA-IR, Mean ± SD	2.6±1.5	2.5±1.4	3.2±1.7	<0.001
Missing	11,880	10,466	1,414	
HOMA-β, Median (IQR)	106.7 (72.1)	103.1 (67.4)	130.9 (94.2)	<0.001
Missing	11,880	10,476	1,404	
Season at disease diagnosis, n (%)				<0.001
Spring (March-May)	6,218 (30.1)	5,464 (30.7)	754 (26.8)	
Summer (June-August)	6,041 (29.3)	5,194 (29.1)	847 (30.1)	
Autumn (September-November)	5,460 (26.5)	4,666 (26.2)	794 (28.2)	
Winter (December-February)	2,914 (14.1)	2,498 (14)	416 (14.8)	
Season at hormones measurement, n (%)				0.5
Spring (March-May)	7,353 (36.0)	6,370 (36.1)	983 (35.0)	
Summer (June-August)	5,514 (27.0)	4,758 (27.0)	756 (26.9)	
Autumn (September-November)	4,575 (22.4)	3,918 (22.2)	657 (23.4)	
Winter (December-February)	3,010 (14.7)	2,596 (14.7)	414 (14.7)	
Missing	181	180	1	
Season at glucose measurement, n (%)				>0.9
Spring (March-May)	4,048 (33.0)	3,411 (33.0)	637 (32.9)	
Summer (June-August)	3,307 (27.0)	2,781 (26.9)	526 (27.2)	
Autumn (September-November)	3,198 (26.1)	2,690 (26.1)	508 (26.2)	
Winter (December-February)	1,705 (13.9)	1,440 (14)	265 (13.7)	
Missing	8,375	7,500	875	

Categorical variables were presented as n (%). n, numbers of subjects; %, percentage. Normally distributed continuous variables were expressed as mean ± SD; non-normally distributed continuous

variables were expressed as median (IQR).

e Table 2 Descriptive data of exposure level of ALAN during the 1 year or month exposure windows.

	Exposure windows	Mean ± SD	P_0	P_{25}	P_{50}	P_{75}	P_{100}
PCOS	During 1-year before disease diagnosis	16.9±16.2	0.00	0.78	14.03	30.94	86.38
	During 1-month before disease diagnosis	17.1±16.9	0.00	0.84	13.73	30.96	107.79
Sex hormones	During 1-year before hormones measurement	16.7±16.1	0.00	0.75	13.74	30.71	86.38
	During 1-month before hormones measurement	16.9±16.8	0.00	0.80	13.36	30.54	111.83
Glucose homeostasis markers	During 1-year before glucose measurement	17.1±16.3	0.00	0.84	14.27	31.27	82.84
	During 1-month before glucose measurement	17.3±17.1	0.00	0.89	14.97	31.01	149.88

e Table 3 Demographic characteristics of 20633 women by ALAN quintiles during 1 year before disease diagnosis.

Characteristic	Quintile 1 N = 4,127	Quintile 2 N = 4,125	Quintile 3 N = 4,128	Quintile 4 N = 4,126	Quintile 5 N = 4,127
age, Mean ± SD	29.8 ± 5.2	30.0 ± 5.2	30.9 ± 4.9	31.2 ± 4.8	31.5 ± 4.7
BMI, kg/m^2, Mean ± SD	22.8 ± 3.2	22.8 ± 3.3	22.4 ± 3.0	22.2 ± 3.0	22.0 ± 2.9
Education, n (%)					
≤middle school	2,718.0 (65.9)	2,469.0 (59.9)	1,261.0 (30.5)	819.0 (19.8)	589.0 (14.3)
High/technical school	1,180.0 (28.6)	1,273.0 (30.9)	1,913.0 (46.3)	1,874.0 (45.4)	1,811.0 (43.9)
≥college	229.0 (5.5)	383.0 (9.3)	954.0 (23.1)	1,433.0 (34.7)	1,727.0 (41.8)
Occupation, n (%)					
Unemployment	2,032.0 (49.2)	1,907.0 (46.2)	1,373.0 (33.3)	1,111.0 (26.9)	898.0 (21.8)
Manual worker	1,017.0 (24.6)	1,048.0 (25.4)	1,009.0 (24.4)	900.0 (21.8)	912.0 (22.1)
Technical personnel	193.0 (4.7)	353.0 (8.6)	602.0 (14.6)	769.0 (18.6)	755.0 (18.3)
Businessman/service staff	170.0 (4.1)	179.0 (4.3)	414.0	523.0	655.0

			(10.0)	(12.7)	(15.9)
Government staff	715.0 (17.3)	638.0 (15.5)	730.0 (17.7)	823.0 (19.9)	907.0 (22.0)
Season at disease diagnosis, n (%)					
Spring (March-May)	1,355.0 (32.8)	1,267.0 (30.7)	1,216.0 (29.5)	1,166.0 (28.3)	1,214.0 (29.4)
Summer (June-August)	1,180.0 (28.6)	1,218.0 (29.5)	1,215.0 (29.4)	1,205.0 (29.2)	1,223.0 (29.6)
Autumn (September-November)	1,036.0 (25.1)	1,092.0 (26.5)	1,112.0 (26.9)	1,122.0 (27.2)	1,098.0 (26.6)
Winter (December-February)	556.0 (13.5)	548.0 (13.3)	585.0 (14.2)	633.0 (15.3)	592.0 (14.3)
Infertile type, n (%)					
Primary infertility	2,355.0 (57.1)	2,227.0 (54.0)	2,205.0 (53.4)	2,262.0 (54.8)	2,287.0 (55.4)
Secondary infertility	1,772.0 (42.9)	1,898.0 (46.0)	1,923.0 (46.6)	1,864.0 (45.2)	1,840.0 (44.6)
Infertile factors, n ()					
Non-female factor	1,553.0 (37.6)	1,719.0 (41.7)	1,451.0 (35.2)	1,596.0 (38.7)	1,740.0 (42.2)
Female factor	2,574.0 (62.4)	2,406.0 (58.3)	2,677.0 (64.8)	2,530.0 (61.3)	2,387.0 (57.8)
Previous year $PM_{2.5}$, Mean ± SD	49.5 ± 10.7	50.9 ± 9.5	51.5 ± 9.5	51.8 ± 9.0	50.3 ± 9.6
City-GDP, ￥per capita, n (%)					
16121-33370	1,354.0 (32.8)	1,361.0 (33.0)	1,166.0 (28.2)	590.0 (14.3)	289.0 (7.0)
33370-52249	1,512.0 (36.6)	1,537.0 (37.3)	1,463.0 (35.4)	612.0 (14.8)	219.0 (5.3)
52249-116300	878.0 (21.3)	786.0 (19.1)	984.0 (23.8)	1,365.0 (33.1)	1,275.0 (30.9)
116300-122673	383.0 (9.3)	441.0 (10.7)	515.0 (12.5)	1,559.0 (37.8)	2,344.0 (56.8)

The mean values and percentages in different quintiles were compared using ANOVA analysis and χ 2 tests; the distributions of the characteristics by quintiles were significantly different (all $p<0.05$).

e Table 4 Demographic characteristics of 20633 women by ALAN quintiles during 1 month before

disease diagnosis.

Characteristic	Quintile 1 N = 4,127	Quintile 2 N = 4,126	Quintile 3 N = 4,127	Quintile 4 N = 4,126	Quintile 5 N = 4,127
age, Mean ± SD	29.8 ± 5.2	30.1 ± 5.2	30.9 ± 4.9	31.1 ± 4.7	31.5 ± 4.8
BMI, kg/m^2, Mean ± SD	22.7 ± 3.2	22.8 ± 3.3	22.4 ± 3.1	22.2 ± 3.0	22.1 ± 2.9
Education, n (%)					
≤middle school	2,678.0 (64.9)	2,486.0 (60.3)	1,248.0 (30.2)	817.0 (19.8)	627.0 (15.2)
High/technical school	1,193.0 (28.9)	1,282.0 (31.1)	1,895.0 (45.9)	1,883.0 (45.6)	1,798.0 (43.6)
≥college	256.0 (6.2)	358.0 (8.7)	984.0 (23.8)	1,426.0 (34.6)	1,702.0 (41.2)
Occupation, n (%)					
Unemployment	2,004.0 (48.6)	1,924.0 (46.6)	1,361.0 (33.0)	1,087.0 (26.3)	945.0 (22.9)
Manual worker	1,030.0 (25.0)	1,039.0 (25.2)	1,006.0 (24.4)	938.0 (22.7)	873.0 (21.2)
Technical personnel	212.0 (5.1)	336.0 (8.1)	608.0 (14.7)	756.0 (18.3)	760.0 (18.4)
Businessman/service staff	171.0 (4.1)	183.0 (4.4)	402.0 (9.7)	529.0 (12.8)	656.0 (15.9)
Government staff	710.0 (17.2)	644.0 (15.6)	750.0 (18.2)	816.0 (19.8)	893.0 (21.6)
Season at disease diagnosis, n (%)					
Spring (March-May)	1,315.0 (31.9)	1,262.0 (30.6)	1,251.0 (30.3)	1,186.0 (28.7)	1,204.0 (29.2)
Summer (June-August)	1,132.0 (27.4)	1,273.0 (30.9)	1,194.0 (28.9)	1,263.0 (30.6)	1,179.0 (28.6)
Autumn (September-November)	1,082.0 (26.2)	1,047.0 (25.4)	1,053.0 (25.5)	1,109.0 (26.9)	1,169.0 (28.3)
Winter (December-February)	598.0 (14.5)	544.0 (13.2)	629.0 (15.2)	568.0 (13.8)	575.0 (13.9)
Infertile type, n (%)					
Primary infertility	2,362.0 (57.2)	2,229.0 (54.0)	2,176.0 (52.7)	2,294.0 (55.6)	2,275.0 (55.1)
Secondary infertility	1,765.0 (42.8)	1,897.0 (46.0)	1,951.0 (47.3)	1,832.0 (44.4)	1,852.0 (44.9)
Infertile factors, n ()					

Non-female factor	1,547.0 (37.5)	1,732.0 (42.0)	1,430.0 (34.6)	1,623.0 (39.3)	1,727.0 (41.8)
Female factor	2,580.0 (62.5)	2,394.0 (58.0)	2,697.0 (65.4)	2,503.0 (60.7)	2,400.0 (58.2)
Previous month $PM_{2.5}$, Mean ± SD	44.4 ± 18.4	44.5 ± 19.2	46.9 ± 19.9	45.5 ± 20.0	43.1 ± 17.4
Missing	12	4	6	0	0
City-GDP, ¥ per capita, n (%)					
16121-33370	1,341.0 (32.5)	1,375.0 (33.3)	1,117.0 (27.1)	610.0 (14.8)	317.0 (7.7)
33370-52249	1,505.0 (36.5)	1,538.0 (37.3)	1,382.0 (33.5)	654.0 (15.9)	264.0 (6.4)
52249-116300	908.0 (22.0)	769.0 (18.6)	974.0 (23.6)	1,374.0 (33.3)	1,263.0 (30.6)
116300-122673	373.0 (9.0)	444.0 (10.8)	654.0 (15.8)	1,488.0 (36.1)	2,283.0 (55.3)

The mean values and percentages in different quintiles were compared using ANOVA analysis and χ 2 tests; the distributions of the characteristics by quintiles were significantly different (all $p<0.05$).

e Table 5. Sensitivity analysis of effects of ALAN exposure on PCOS further adjusted for urbanity levels in the fully adjusted model.

Long-term exposure [a]	
Prior year ALAN exposure	OR (95%CI)
Continuous (per IQR increased [b])	1.34 (1.19,1.51)
Quintile 1 (median 0.1 $nW/cm^2/sr$)	Reference [c]
Quintile 2 (median 1.2 $nW/cm^2/sr$)	1.04 (0.91, 1.19)
Quintile 3 (median 14.0 $nW/cm^2/sr$)	1.21 (1.12, 1.53)
Quintile 4 (median 28.2 $nW/cm^2/sr$)	1.57 (1.31, 1.87)
Quintile 5 (median 39.7 $nW/cm^2/sr$)	1.59 (1.32, 1.91)
Short-term exposure [a]	
Prior month ALAN exposure	
Continuous (per IQR increased [b])	1.17 (1.05,1.30)
Quintile 1 (median 0.0 $nW/cm^2/sr$)	Reference
Quintile 2 (median 1.2 $nW/cm^2/sr$)	1.09 (0.96, 1.25)
Quintile 3 (median 13.7 $nW/cm^2/sr$)	1.21 (1.04, 1.40)
Quintile 4 (median 27.8 $nW/cm^2/sr$)	1.47 (1.24, 1.74)
Quintile 5 (median 41.4 $nW/cm^2/sr$)	1.26 (1.06, 1.51)

[a]: The model was adjusted for age, BMI, education, occupation, season, $PM_{2.5}$ at the residential

address, GDP per capita (quartiles), infertile type, infertile factors, and urbanity levels;

[b]: An IQR increase in outdoor ALAN during 1-year or month is 30.2 or 30.1 nW/cm^2/sr;

[c]: *P* for trend<0.05.

e Table 6. Sensitivity analysis of effects of ALAN exposure on PCOS in the fully adjusted models excluding $PM_{2.5}$.

Long-term exposure [a]	
Prior year ALAN exposure	OR (95%CI)
Continuous (per IQR increased [b])	1.12 (1.01,1.24)
Quintile 1 (median 0.1 nW/cm^2/sr)	Reference [c]
Quintile 2 (median 1.2 nW/cm^2/sr)	0.96(0.84,1.10)
Quintile 3 (median 14.0 nW/cm^2/sr)	1.08(0.95,1.24)
Quintile 4 (median 28.2 nW/cm^2/sr)	1.16(1.00,1.34)
Quintile 5 (median 39.7 nW/cm^2/sr)	1.16(0.99,1.36)
Short-term exposure [a]	
Prior month ALAN exposure	
Continuous (per IQR increased [b])	1.10 (1.00,1.20)
Quintile 1 (median 0.0 nW/cm^2/sr)	Reference
Quintile 2 (median 1.2 nW/cm^2/sr)	1.06 (0.93, 1.21)
Quintile 3 (median 13.7 nW/cm^2/sr)	1.08 (0.94, 1.24)
Quintile 4 (median 27.8 nW/cm^2/sr)	1.27 (1.10, 1.46)
Quintile 5 (median 41.4 nW/cm^2/sr)	1.10 (0.94, 1.28)

[a]: The model was adjusted for age, BMI, education, occupation, season, $PM_{2.5}$ at the residential address, GDP per capita (quartiles), infertile type, and infertile factors;

[b]: An IQR increase in outdoor ALAN during 1-year or month is 30.2 or 30.1 nW/cm^2/sr;

[c]: *P* for trend<0.05.

e Table 7. The joint effects of ALAN at the residential address and $PM_{2.5}$ on PCOS.

Long-term effect	OR (95%CI)	$P_{\text{interaction term}}$
Prior year ALAN	1.16 (1.02, 1.32)	
Prior year $PM_{2.5}$	0.75 (0.65, 0.86)	
Prior year ALAN * $PM_{2.5}$	1.03 (0.87, 1.23)	0.714
Short-term effect		
Prior month ALAN	1.15 (1.02, 1.29)	
Prior month $PM_{2.5}$	0.72 (0.63, 0.83)	
Prior month ALAN * $PM_{2.5}$	0.95 (0.81, 1.10)	0.471

The model was adjusted for age, BMI, education, occupation, season, $PM_{2.5}$ at the residential address, GDP per capita (quartiles), infertile type, and infertile factors.

e Table 8. Sensitivity analysis of long-term and short-term effects of ALAN exposure on female LH/FSH≥2, T≥2 nmol/L, and HOMA-IR≥2.6 in the fully adjusted model.

Prior year ALAN		Prior month ALAN	
Indicators	OR (95%CI)	Indicators	OR (95%CI)
		LH/FSH≥2	
quintile 1	Reference	quintile 1	Reference
quintile 2	0.98(0.78,1.24)	quintile 2	0.94(0.75,1.19)
quintile 3	1.04(0.81,1.32)	quintile 3	1.04(0.81,1.32)
quintile 4	1.25(0.96,1.62)	quintile 4	1.27(0.99,1.64)
quintile 5	1.16(0.87,1.55)	quintile 5	1.30(0.99,1.71)
		T≥2 nmol/L	
quintile 1	Reference	quintile 1	Reference
quintile 2	1.15(1.02,1.29)	quintile 2	1.15(1.03,1.29)
quintile 3	1.12(0.99,1.26)	quintile 3	1.09(0.97,1.24)
quintile 4	1.19(1.04,1.36)	quintile 4	1.11(0.98,1.26)
quintile 5	1.22(1.06,1.40)	quintile 5	1.13(0.99,1.30)
		HOMA-IR≥2.6	
quintile 1	Reference	quintile 1	Reference
quintile 2	1.01(0.87,1.18)	quintile 2	1.02(0.87,1.18)
quintile 3	1.20(1.03,1.41)	quintile 3	1.17(1.00,1.37)
quintile 4	1.11(0.94,1.32)	quintile 4	1.12(0.95,1.33)
quintile 5	1.14(0.96,1.37)	quintile 5	1.12(0.94,1.33)

The model was adjusted for age, BMI, education, occupation, season, $PM_{2.5}$ at the residential address, GDP per capita (quartiles), infertile type, and infertile factors.

e Table 9. Sensitivity analysis of effects of ALAN exposure on PCOS in participants who excluded women with infertility.

Long-term exposure [a]	
Prior year ALAN exposure	OR (95%CI)
Continuous (per IQR increased [b])	1.26(1.05,1.53)
Quintile 1 (median 0.1 nW/cm^2/sr)	Reference
Quintile 2 (median 1.2 nW/cm^2/sr)	1.42(1.10,1.84)
Quintile 3 (median 14.0 nW/cm^2/sr)	1.51(1.14,2.00)
Quintile 4 (median 28.2 nW/cm^2/sr)	1.57(1.16,2.12)
Quintile 5 (median 39.7 nW/cm^2/sr)	1.69(1.24,2.32)
Short-term exposure [a]	
Prior month ALAN exposure	

Continuous (per IQR increased [b])	1.10 (0.92,1.31)
Quintile 1 (median 0.0 nW/cm^2/sr)	Reference
Quintile 2 (median 1.2 nW/cm^2/sr)	1.33(1.03,1.72)
Quintile 3 (median 13.7 nW/cm^2/sr)	1.29(0.97,1.71)
Quintile 4 (median 27.8 nW/cm^2/sr)	1.35(1.01,1.80)
Quintile 5 (median 41.4 nW/cm^2/sr)	1.34(0.99,1.82)

[a]: The model was adjusted for age, BMI, education, occupation, season, $PM_{2.5}$ at the residential address, GDP per capita (quartiles), and infertile type;

[b]: An IQR increase in outdoor ALAN during 1-year or month is 30.2 or 30.1 nW/cm^2/sr.