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1 *Supplementary files*

2 **Different exposure metrics of rotating night shift work and**

3 **hyperhomocysteinemia among Chinese steelworkers: a cross-**

4 **sectional study**

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14 *Assessment of covariates*

15 Smoking and drinking status were divided into "never", "ever" and "current". Dietary patterns were

16 assessed based on the DASH diet score.[1] The level of education was divided into three categories:

17 "primary or illiterate," "middle or high school," and "university or college." The calculation of

18 metabolic equivalents was based on the International Physical Activity Questionnaire (IPAQ).[2] The

19 sleep quality assessment was estimated using the Athens Insomnia Scale (AIS).[3] Sedentary

20 behaviour (hours/day) was assessed using a set of open-ended questions on the average working

21 days and rest days time spent over the last four weeks on: television viewing (including DVDs and

22 videos) and any other sitting during leisure time (including reading, studying, using a computer, and

23 playing video games).[4] The durations of sleep and sedentary behaviour were the weighted averages

24 of sleep and sedentary behaviour on working days and rest days, respectively.

25 Standard study protocols were used to train qualified physicians and nurses prior to this survey.

26 Height and weight were measured three times each. The participants stood upright and barefoot in

27 light clothes. The height and weight data that were ultimately used for analysis were accurate to 0.1

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28 cm and 0.1 kg. Body mass index (BMI) was defined as body weight (kg) divided by the square of

29 the body height (m^2). Blood pressure measurements were performed three times at five-minute

30 intervals using an electronic sphygmomanometer (OMRON, HBP-1100, China), and the

31 participants were required to rest for more than ten minutes. Finally, the mean was obtained for

32 analysis. Elevated blood pressure was defined as current systolic blood pressure ≥140 mmHg,

33 diastolic blood pressure ≥90 mmHg, or if the patient was receiving antihypertensive therapy.

34 Participants were required to fast overnight before the abdominal ultrasound examination and blood

35 collection. Participants' anterior elbow vein blood was collected and centrifuged at room

36 temperature (3000 r/min, 15 minutes) immediately. All blood samples were tested in the central

37 laboratory of Tangshan Hongci Hospital Laboratory using automatic biochemical analysers

38 (mindrary, BS-800, China) within four hours. Total cholesterol (TC) ≥6.22 mmol/L, low-density

39 lipoprotein (LDL-C) ≥4.11 mmol/L, or high-density lipoprotein (HDL-C) ≤1.04 mmol/L or

40 triglycerides (TG) ≥2.32 mmol/L, or patients undergoing lipid-lowering therapy were considered to

41 demonstrate dyslipidaemia.[5] Alanine aminotransferase (ALT) >40 U/L, aspartate aminotransferase

42 (AST) >40 U/L or glutamyl transpeptidase (γ-GT) >58 U/L was defined as abnormal liver enzymes.

43 Diabetes was defined as fasting blood glucose ≥7.0 mmol/L or if the patient was receiving

44 hypoglycaemic therapy. Assessment of estimated glomerular filtration rate (eGFR) was based on

45 the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[6] The CKD-EPI

46 formula is as follows: eGFR (mL/min/1.73 m^2) = $141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times$

47 $0.993^{Age} \times (1.018$ if female$) \times (1.159$ if black$)$. Scr indicates serum creatinine (μmol/L), $\kappa = 0.7$ for

48 females and 0.9 for males, $\alpha = -0.329$ for females and -0.411 for males, min and max indicate the

49 minimum of Scr/κ or 1, the maximum of Scr/κ or 1, respectively. According to the Kidney Disease

50 Improving Global Outcomes 2012 recommendations, the range of GFR (mL/min/1.73 m^2) was

51 classed into five categories: normal or high (GFR ≥90, G1), mildly decreased (GFR: 60–89, G2),

52 mildly to moderately decreased (GFR: 45–59, G3a), moderately to severely decreased (GFR: 30–

53 44, G3b), severely decreased (GFR: 15–29, G4), and kidney failure (GFR <15, G5).[7] Based on these

54 classification criteria, only 22 (0.3%) participants had eGFR<60 mL/min/1.73 m^2 (G3a-G5), so we

55 combined these categories into G2 in the subsequent analysis and defined them as "decreased eGFR"

56 (<90 mL/min/1.73 m^2).

57   Exposure to dust was defined as workers who may be exposed to productive dust (inorganic

58 dust, organic dust or mixed dust) during production (GBZ/T 229.1–2010).[8] The total dust in the air

59 of the workplace was collected at the breathing zone with a filter membrane, and its concentration

60 was calculated based on the increased weight of the filter membrane and the amount of gas collected.

61 When the dust concentration in the air was ≤ 50 mg/m^3, a filter membrane with a diameter of 37 mm

62 or 40 mm was used; otherwise, a filter membrane with a diameter of 75 mm was used (GBZ/T

63 192.1–2007).[9] Exposure to heat stress work was defined as the average wet-bulb globe temperature

64 (WBGT) index of the workplace being equal to or greater than 25°C in the process of production

65 (GBZ 2.2–2007).[10] The WBGT index was measured by a black-wet bulb globe thermometer. If there

66 was no productive heat source in the workplace, three measuring points were selected to take the

67 average value of the WBGT index; if where there was a productive heat source, 3 to 5 measuring

68 points were selected to take the average value of the WBGT index. If the workplace was isolated

69 into different thermal or ventilated environments, 2 measuring points were selected to take the

70 average value of the WBGT index (GBZ/T 189.7–2007).[11] Exposure to industrial toxicants was

71 defined as workers who may be exposed to a variety of harmful chemicals (the toxicant specifically

72 refers to carbon monoxide in this population) during production (GBZ/T 229.2–2010).[12] Carbon

73 monoxide or carbon dioxide in the air of the workplace was pumped into a non-dispersive infrared-

74 ray (NDIR) analyzer and selectively absorbed its infrared rays. The concentration of carbon

75 monoxide was determined according to the absorption value (GBZ/T 160.28–2004).[13] Exposure to

76 noise was defined as workers who were exposed to a noisy environment where the 8-h/d or 40-

77 h/week equivalent A-weighted sound pressure level was ≥ 80 dB, which may be harmful to health

78 and hearing (GBZ/T 229.4–2012).[14] The workplace production noise was measured by a sound level

79 meter. If the distribution of the sound field in the workplace was uniform (between-field difference

80 of A-sound levels were less than 3 dB(A)), three measuring points were selected to take the average

81 value; otherwise, the workplace was divided into several sound level areas. In each sound field, two

82 measuring points were selected to take the average value (GBZ/T 189.8–2007).[15]

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100   of night shifts.

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102 **Table S1** Basic characteristics of participants according to sex

Variables	Total	Female	Male	
	N=6846	n=585	n=6261	*P* value
Current shift status, n (%)				<0.001
Never	1027 (15.0)	118 (20.2)	909 (14.5)	
Ever	1493 (21.8)	140 (23.9)	1353 (21.6)	
Current	4326 (63.2)	327 (55.9)	3999 (63.9)	
Duration of night shifts (years), n (%)				<0.001
Never	1027 (15.0)	118 (20.2)	909 (14.5)	
Q1 (1–12)	1467 (21.4)	122 (20.9)	1345 (21.5)	
Q2 (13–20)	1491 (21.8)	130 (22.2)	1361 (21.7)	
Q3 (21–27)	1308 (19.1)	129 (22.1)	1179 (18.8)	
Q4 (28–43)	1553 (22.7)	86 (14.7)	1467 (23.4)	
Cumulative number of night shifts (nights), n (%)				<0.001
Never	1027 (15.0)	118 (20.2)	909 (14.5)	
Q1 (43–1131)	1455 (21.3)	117 (20.0)	1338 (21.4)	
Q2 (1132–1848)	1455 (21.3)	131 (22.4)	1324 (21.2)	
Q3 (1854–2584)	1456 (21.3)	139 (23.8)	1317 (21.0)	
Q4 (2585–5239)	1453 (21.2)	80 (13.7)	1373 (21.9)	
Cumulative length of night shifts (hours), n (%)				<0.001
Never	1027 (15.0)	118 (20.2)	909 (14.5)	
Q1 (344–9488)	1452 (21.2)	118 (20.2)	1334 (21.3)	
Q2 (9490–15259)	1458 (21.3)	131 (22.4)	1327 (21.2)	
Q3 (15265–21293)	1456 (21.3)	134 (22.9)	1322 (21.1)	
Q4 (21295–53541)	1453 (21.2)	84 (14.4)	1369 (21.9)	
Average frequency of night shifts, n (%)				<0.001
Never	1027 (15.0)	118 (20.2)	909 (14.5)	
<3 nights/month	1576 (23.0)	152 (26.0)	1424 (22.7)	
3–7 nights/month	901 (13.2)	78 (13.3)	823 (13.1)	
>7 nights/month	3342 (48.8)	237 (40.5)	3105 (49.6)	
Average length of night shifts, n (%)				0.002
Never	1027 (15.0)	118 (20.2)	909 (14.5)	
≤8 hours/night	4442 (64.9)	365 (62.4)	4077 (65.1)	
8–9 hours/night	810 (11.8)	57 (9.7)	753 (12.0)	
>9 hours/night	567 (8.3)	45 (7.7)	522 (8.3)	
Percentage of hours on night shifts, n (%)				<0.001
Never	1027 (15.0)	118 (20.2)	909 (14.5)	
<20%	819 (12.0)	86 (14.7)	733 (11.7)	
20%–30%	1056 (15.4)	86 (14.7)	970 (15.5)	
>30%	3944 (57.6)	295 (50.4)	3649 (58.3)	
Age (years), mean ± SD	44.2 ± 8.0	44.0 ± 5.1	44.3 ± 8.3	0.406
Age (years), n (%)				<0.001
22–29	399 (5.8)	3 (0.5)	396 (6.3)	

30–39	1745 (25.5)	131 (22.4)	1614 (25.8)	
40–49	2979 (43.5)	426 (72.8)	2553 (40.8)	
50–60	1723 (25.2)	25 (4.3)	1698 (27.1)	
BMI (kg/m^2), n (%)				<0.001
<25	3466 (50.6)	414 (70.8)	3052 (48.75)	
25–30	2830 (41.3)	143 (24.4)	2687 (42.9)	
≥30	550 (8.0)	28 (4.8)	522 (8.3)	
Smoking status, n (%)				<0.001
Never	2809 (41.0)	513 (87.7)	2296 (36.7)	
Ever	547 (8.0)	20 (3.4)	527 (8.4)	
Current	3490 (51.0)	52 (8.9)	3438 (54.9)	
Drinking status, n (%)				<0.001
Never	3926 (57.4)	526 (89.9)	3400 (54.3)	
Ever	392 (5.7)	23 (3.9)	369 (5.9)	
Current	2528 (36.9)	36 (6.2)	2492 (39.8)	
Education level, n (%)				0.656
Primary or illiterate	86 (1.3)	5 (0.9)	81 (1.3)	
Middle or high school	5304 (77.5)	454 (77.6)	4850 (77.5)	
University or college	1456 (21.3)	126 (21.5)	1330 (21.2)	
Physical activity (MET-h/week), median (IQR)	121.8 (84.0–150.7)	103.8 (80.8–124.5)	121.8 (84.0–153.3)	<0.001
DASH score	21.7 ± 2.2	23.0 ± 2.2	21.5 ± 2.2	<0.001
Sedentary behavior (h), median (IQR)	2.6 (1.3–4.3)	4.0 (2.1–5.4)	2.5 (1.3–4.0)	<0.001
Sleep duration (h), mean ± SD	6.8 ± 1.2	6.8 ± 1.2	6.8 ± 1.2	0.247
Insomnia, n (%)	2675 (39.1)	218 (37.3)	2457 (39.2)	0.348
Diabetes, n (%)	719 (10.5)	31 (5.3)	688 (11.0)	<0.001
Dyslipidemia, n (%)	2781 (40.6)	138 (23.6)	2643 (42.2)	<0.001
Hypertension, n (%)	1755 (25.6)	72 (12.3)	1683 (26.9)	<0.001
Liver enzyme abnormality, n (%)	1384 (20.2)	32 (5.5)	1352 (21.6)	<0.001
eGFR (mL/min/1.73 m^2), mean ± SD	101.7 ± 11.4	102.3 ± 12.5	101.6 ± 11.3	0.207
tHcy (μmol/L), mean ± SD	12.2 (10.1–16.8)	9.2 (7.9–11.2)	12.5 (10.4–17.4)	<0.001
Hyperhomocysteinemia, n (%)	2093 (30.6)	63 (10.8)	2030 (32.4)	<0.001

103   BMI, body mass index; MET, metabolic equivalent units; IQR, interquartile range; DASH, dietary approaches to stop hypertension.

104   Values are expressed as the mean ± SD or median (IQR) or number (%); P-values were from Pearson's chi-square test for categorical

105   variables and Student's t test or Wilcoxon Scores (Rank Sums) for continuous variables. The cut-off points of the duration of night shifts

106   (range: 1 to 43 years), cumulative number of night shifts (range: 43 to 5239 nights), and cumulative length of night shifts (range: 344 to

107   53541 hours) were quarters of the corresponding continuous variables. The cut-off points of average frequency of night shifts (range: 0.1

108   to 10.3 nights/month), average length of night shifts (range: 8.0 to 12.0 hours/night), and percentage of hours on night shifts (range:0.1%

109   to 46.2%) were chosen to secure a reasonable number of observations in each category.

110   **Table S2** Basic characteristics of participants according to duration of night shifts

Variables	Total	Duration of night shifts (years)					P value
		Never	Q1 (1–12)	Q2 (13–20)	Q3 (21–28)	Q4 (29–43)	
	N=6846	n=1027	n=1454	n=1469	n=1439	n=1457	
Duration of employment (years), median (IQR)	26.4 (18.5–29.6)	27.4 (17.3–30.4)	15.4 (9.4–27.8)	19.2 (15.9–23.7)	24.8 (23.4–27.4)	30.3 (29.4–34.4)	<0.001
Age (years), mean±SD	44.2±8.0	44.±9.1	39.5±9.1	41.2±6.9	45.5±5.2	50.6±3.8	<0.001
Sex (male), n (%)	6261 (91.5)	909 (88.5)	1336 (91.9)	1340 (91.2)	1296 (90.1)	1380 (94.7)	<0.001
BMI (kg/m^2), mean±SD	25.2±3.4	24.8±3.3	25.3±3.6	25.4±3.6	25.2±3.3	25.2±3.1	<0.001
BMI (kg/m^2), n (%)							<0.001
<25	3466 (50.6)	570 (55.5)	748 (51.4)	702 (47.8)	712 (49.5)	734 (50.4)	
25–30	2830 (41.3)	393 (38.3)	565 (38.9)	617 (42.0)	624 (43.4)	631 (43.3)	
≥30	550 (8.0)	64 (6.2)	141 (9.7)	150 (10.2)	103 (7.2)	92 (6.3)	
Smoking status, n (%)							<0.001
Never	2809 (41.0)	460 (44.8)	623 (42.9)	622 (42.3)	578 (40.2)	526 (36.1)	
Ever	547 (8.0)	53 (5.2)	115 (7.9)	124 (8.4)	146 (10.2)	109 (7.5)	
Current	3490 (51.0)	514 (50.1)	716 (49.2)	723 (49.2)	715 (49.7)	822 (56.4)	
Alcohol consumption, n (%)							<0.001
Never	3926 (57.4)	630 (61.3)	908 (62.5)	870 (59.2)	789 (54.8)	729 (50.0)	
Ever	392 (5.7)	26 (2.5)	87 (6.0)	110 (7.5)	115 (8.0)	54 (3.7)	
Current	2528 (36.9)	371 (36.1)	459 (31.6)	489 (33.3)	535 (37.2)	674 (46.3)	
Education level, n (%)							<0.001
Primary or illiterate	86 (1.3)	9 (0.9)	10 (0.7)	5 (0.3)	26 (1.8)	36 (2.5)	
Middle or high school	5304 (77.5)	710 (69.1)	920 (63.3)	1073 (73.0)	1240 (86.2)	1361 (93.4)	
University or college	1456 (21.3)	308 (30.0)	524 (36.0)	391 (26.6)	173 (12.0)	60 (4.12)	
Physical activity (MET-h/week), median (IQR)	121.8 (84.0–150.7)	116.3 (84.0–152.5)	121.8 (84.0–152.2)	121.8 (84.0–142.0)	121.8 (84.0–150.2)	121.8 (84.0–155.6)	0.06

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DASH score, mean±SD	21.7±2.2	21.7±2.1	21.6±2.2	21.5±2.2	21.8±2.2	21.7±2.2	0.592
Sedentary behaviour (hours), median (IQR)	2.6 (1.3–4.3)	2.3 (1.3–3.7)	2.6 (1.3–4.0)	2.5 (1.1–4.5)	2.6 (1.2–4.3)	3.0 (1.5–4.5)	<0.001
Sleep duration (hour), mean±SD	6.8±1.2	7.1±1.3	6.9±1.2	6.9±1.1	6.7±1.1	6.6±1.2	0.001
Insomnia, n (%)	2675 (39.1)	353 (34.4)	560 (38.5)	592 (40.3)	575 (40.0)	595 (40.8)	0.011
Diabetes, n (%)	719 (10.5)	102 (9.9)	119 (8.2)	118 (8.0)	149 (10.4)	231 (15.9)	<0.001
Dyslipidemia, n (%)	2781 (40.6)	388 (37.8)	558 (38.4)	640 (43.6)	586 (40.7)	609 (41.8)	0.013
Hypertension, n (%)	1755 (25.6)	255 (24.8)	294 (20.2)	319 (21.7)	388 (27.0)	499 (34.3)	<0.001
Liver enzyme abnormality, n (%)	1384 (20.2)	171 (16.7)	299 (20.6)	360 (24.5)	276 (19.2)	278 (19.1)	<0.001
eGFR (mL/min/1.73 m^2), mean ± SD	101.7 ± 11.4	102.1 ± 11.3	104.1 ± 12.4	103.8 ± 10.4	100.8 ±10.7	97.8 ± 10.9	<0.001
tHcy (μmol/L), median (IQR)	12.2 (10.1–16.8)	11.7 (9.8–15.8)	12.1 (10.1–16.8)	12.0 (10.0–16.1)	12.1 (10.1–17.0)	12.9 (10.6–17.7)	<0.001
HHcy, n (%)	2093 (30.6)	280 (27.3)	441 (30.3)	418 (28.5)	442 (30.7)	512 (35.1)	<0.001

111   BMI, body mass index; MET, metabolic equivalent units; IQR, interquartile range; DASH, dietary approaches to stop hypertension; tHcy, total homocysteine; HHcy, hyperhomocysteinemia; eGFR, estimated glomerular filtration rate.

112   Values are expressed as the mean ± SD or median (IQR) or number (%); P-values were from Pearson's chi-square test for categorical variables and analysis of variance (ANOVA) or Kruskal-Wallis test for continuous variables.

113   **Table S3** Distribution of plasma total homocysteine levels according to age group

Variables	Age group (years)				P value
	22–29	30–39	40–49	50–60	
HHcy, n (%)					0.001
No	269 (67.4)	1242 (71.2)	2111 (70.9)	1131 (65.6)	
Yes	130 (32.6)	503 (28.8)	868 (29.1)	592 (34.4)	
tHcy (μmol/L), median (IQR)	12.1 (10.2–17.3)	11.8 (9.9–16.7)	12.0 (9.9–16.4)	12.9 (10.6–17.3)	<0.001

114   tHcy, total homocysteine; HHcy, hyperhomocysteinemia.

115

116 **Table S4** Independent effects of different exposure metrics of night shift work on HHcy among

117 night shift workers (ever or current)

Exposure metrics	OR (95% CI)		
	Model 1[a]	Model 2[b]	Model 3[c]
Current shift status			
Ever	1.00	1.00	1.00
Current	1.08 (0.92–1.26)	1.08 (0.92–1.27)	1.07 (0.92–1.27)
Duration of night shifts			
≤20 years	1.00	1.00	1.00
>20 years	1.14 (1.01–1.29)	1.10 (0.94–1.28)	1.07 (0.91–1.25)
Average frequency of night shifts			
≤7 nights/month	1.00	1.00	1.00
>7 nights/month	1.06 (0.92–1.23)	1.07 (0.92–1.24)	1.07 (0.91–1.24)
Average length of night shifts			
≤8 hours/night	1.00	1.00	1.00
>8 hours/night	1.11 (0.97–1.27)	1.08 (0.94–1.24)	1.08 (0.94–1.24)

118 OR, odds ratio; CI, confidence intervals.

119 [a] Model 1, adjusted for current shift status, duration of night shifts, average frequency of night shifts, and average length of night shifts.

120 [b] Model 2, adjusted for current shift status, duration of night shifts, average frequency of night shifts, average length of night shifts, age,

121 and sex.

122 [c] Model 3, adjusted for current shift status, duration of night shifts, average frequency of night shifts, average length of night shifts, age,

123 sex, BMI, smoking status, dyslipidaemia, hypertension, and decreased eGFR.

124 **Table S5** Interaction between duration and average frequency of night shifts on odds of HHcy

	All	Male	Female
Main effects, OR (95% CI)			
Duration of night shifts (>20 years vs ≤20 years)	1.01 (0.83–1.23)	1.03 (0.84–1.26)	1.77 (0.45–6.91)
Average frequency of night shifts (>7nights/month vs ≤7 nights/month)	1.00 (0.83–1.22)	0.99 (0.81–1.20)	1.71 (0.64–4.59)
Joint effect, OR (95% CI)	1.20 (1.03–1.39)	1.20 (1.03–1.40)	1.12 (0.54–2.36)
Multiplicative interaction, OR (95% CI)	1.18 (0.90–1.55)	1.19 (0.90–1.56)	1.08 (0.21–5.58)
Additive interaction [a]			
Relative excess risk due to interaction, RERI (95% CI)	0.18 (-0.09–0.46)	0.19 (-0.09–0.47)	-1.36 (-4.27–1.56)
Attributable proportion due to interaction, AP (95% CI)	0.15 (-0.08–0.38)	0.16 (-0.07–0.39)	-1.21 (-3.91–1.49)

125 **OR,** odds ratio**; CI, c**onfidence intervals; RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction;

126 [a] If there is no biological interaction, RERI and AP are equal to 0.

127 Adjusted for age, sex, BMI, smoking status, dyslipidaemia, hypertension, and decreased eGFR.

128

129   **Table S6** Multivariate-adjusted ORs between HHcy and different exposure metrics of night shift work according to sex

Exposure metrics	Male			Female		
	HHcy		OR (95% CI)	HHcy		OR (95% CI)
	No, [n (%)]	Yes, [n (%)]		No, [n (%)]	Yes, [n (%)]	
Current shift status, n (%)						
Never	641 (15.2)	268 (13.2)	1.00	106 (20.3)	12 (19.1)	1.00
Ever	938 (22.2)	415 (20.4)	1.08 (0.89–1.29)	124 (23.8)	16 (25.4)	1.05 (0.46–2.39)
Current	2652 (62.7)	1347 (66.4)	1.24 (1.06–1.46)	292 (55.9)	35 (55.6)	0.94 (0.46–1.92)
Duration of night shifts (years)						
Never	641 (15.2)	268 (13.2)	1.00	106 (20.3)	12 (19.1)	1.00
Q1 (1–12)	918 (21.7)	427 (21.0)	1.14 (0.94–1.38)	104 (19.9)	18 (28.6)	1.29 (0.57–2.91)
Q2 (13–20)	954 (22.6)	407 (20.1)	1.07 (0.88–1.30)	118 (22.6)	12 (19.1)	0.78 (0.32–1.86)
Q3 (21–27)	792 (18.7)	387 (19.1)	1.20 (0.99–1.46)	118 (22.6)	11 (17.5)	0.84 (0.35–2.04)
Q4 (28–43)	926 (21.9)	541 (26.7)	1.36 (1.13–1.64)	76 (14.6)	10 (15.9))	1.04 (0.41–2.65)
P trend			0.002			0.629
Cumulative number of night shifts (nights)						
Never	641 (15.2)	268 (13.2)	1.00	106 (20.3)	12 (19.1)	1.00
Q1 (43–1131)	911 (21.5)	427 (21.0)	1.15 (0.95–1.39)	101 (19.4)	16 (25.4)	1.22 (0.53–2.80)
Q2 (1132–1848)	932 (22.0)	392 (19.3)	1.05 (0.87–1.28)	118 (22.6)	13 (20.6)	0.79 (0.34–1.88)
Q3 (1854–2584)	879 (20.8)	438 (21.6)	1.23 (1.02–1.48)	127 (24.3)	12 (19.1)	0.86 (0.36–2.05)
Q4 (2585–5239)	868 (20.5)	505 (24.9)	1.35 (1.12–1.63)	70 (13.4)	10 (15.9)	1.14 (0.45–2.91)
P trend			0.003			0.799
Cumulative length of night shifts (hours)						
Never	641 (15.2)	268 (13.2)	1.00	106 (20.3)	12 (19.1)	1.00

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Q1 (344–9488)	904 (21.4)	430 (21.2)	1.16 (0.96–1.40)	102 (19.5)	16 (25.4)	1.20 (0.52–2.74)
Q2 (9490–15259)	937 (22.2)	390 (19.2)	1.04 (0.86–1.27)	117 (22.4)	14 (22.2)	0.91 (0.39–2.13)
Q3 (15265–21293)	881 (20.8)	441 (21.7)	1.24 (1.02–1.50)	126 (24.1)	8 (12.7)	0.57 (0.22–1.48)
Q4 (21295–53541)	868 (20.5)	501 (24.7)	1.33 (1.11–1.61)	71 (13.6)	13 (20.6)	1.43 (0.59–3.46)
P trend			0.005			0.942
Average frequency of night shifts						
Never	641 (15.2)	268 (13.2)	1.00	106 (20.3)	12 (19.1)	1.00
<3 nights/month	976 (23.1)	448 (2.1)	1.11 (0.93–1.34)	134 (25.7)	18 (28.6)	1.04 (0.46–2.32)
3–7 nights/month	562 (13.3)	261 (12.9)	1.14 (0.93–1.40)	74 (14.2)	4 (6.4)	0.40 (0.12–1.34)
>7 nights/month	2052 (48.5)	1053 (51.9)	1.26 (1.07–1.48)	208 (39.9)	29 (46.0)	1.11 (0.54–2.30)
P trend			0.003			0.861
Average length of night shifts						
Never	641 (15.2)	268 (13.2)	1.00	106 (20.3)	12 (19.1)	1.00
≤8 hours/night	2754 (65.1)	1323 (65.2)	1.18 (1.01–1.39)	328 (62.8)	37 (58.7)	0.89 (0.44–1.79)
8–9 hours/night	497 (11.8)	256 (12.6)	1.27 (1.03–1.57)	54 (10.3)	3 (4.8)	0.43 (0.11–1.77)
>9 hours/night	339 (8.0)	183 (9.0)	1.22 (0.96–1.54)	34 (6.5)	11 (17.5)	2.48 (0.96–6.43)
P trend			0.058			0.149
Percentage of hours on night shifts						
Never	641 (15.2)	268 (13.2)	1.00	106 (20.3)	12 (19.1)	1.00
<20%	499 (11.8)	234 (11.5)	1.14 (0.92–1.41)	74 (14.2)	12 (19.1)	1.21 (0.50–2.94)
20%–30%	670 (15.8)	300 (14.8)	1.09 (0.89–1.34)	77 (14.8)	9 (14.3)	0.88 (0.33–2.34)
>30%	2421 (57.2)	1228 (60.5)	1.24 (1.06–1.46)	265 (50.8)	30 (47.6)	0.93 (0.45–1.91)
P trend			0.008			0.677

130 HHcy, hyperhomocysteinemia; OR, odds ratio; CI, confidence intervals.

131 Adjusted for age, sex, BMI, smoking status, dyslipidaemia, hypertension, and decreased eGFR.

Table S7 Multivariate-adjusted ORs between HHcy and different exposure metrics of night shift work after further adjustment for the main occupational hazards

Exposure metrics	OR (95% CI)		
	All	Male	Female
Current shift status			
Never	1.00	1.00	1.00
Ever	1.08 (0.90–1.30)	1.08 (0.90–1.30)	0.99 (0.43–2.27)
Current	1.25 (1.07–1.47)	1.27 (1.08–1.49)	0.89 (0.43–1.85)
Duration of night shifts (years)			
Never	1.00	1.00	1.00
Q1 (1–12)	1.16 (0.96–1.39)	1.15 (0.95–1.39)	1.20 (0.52–2.73)
Q2 (13–20)	1.06 (0.88–1.29)	1.08 (0.89–1.32)	0.73 (0.30–1.78)
Q3 (21–27)	1.20 (0.99–1.45)	1.22 (1.00–1.49)	0.82 (0.33–2.04)
Q4 (28–43)	1.36 (1.13–1.64)	1.38 (1.14–1.66)	0.97 (0.38–2.49)
P trend	0.003	0.001	0.576
Cumulative number of night shifts (nights)			
Never	1.00	1.00	1.00
Q1 (43–1131)	1.16 (0.97–1.40)	1.16 (0.96–1.40)	1.13 (0.49–2.63)
Q2 (1132–1848)	1.06 (0.87–1.28)	1.07 (0.88–1.30)	0.75 (0.31–1.81)
Q3 (1854–2584)	1.22 (1.01–1.47)	1.24 (1.03–1.51)	0.85 (0.35–2.05)
Q4 (2585–5239)	1.35 (1.12–1.63)	1.36 (1.13–1.65)	1.05 (0.41–2.71)
P trend	0.003	0.002	0.737
Cumulative length of night shifts (hours)			
Never	1.00	1.00	1.00
Q1 (344–9488)	1.17 (0.97–1.41)	1.17 (0.97–1.41)	1.12 (0.48–2.59)
Q2 (9490–15259)	1.05 (0.87–1.27)	1.06 (0.87–1.29)	0.86 (0.36–2.03)
Q3 (15265–21293)	1.21 (1.01–1.47)	1.25 (1.03–1.52)	0.54 (0.20–1.43)
Q4 (21295–53541)	1.35 (1.12–1.63)	1.35 (1.11–1.64)	1.32 (0.54–3.22)
P trend	0.005	0.004	0.854
Average frequency of night shifts (nights/month)			
Never	1.00	1.00	1.00
<3	1.12 (0.94–1.34)	1.12 (0.93–1.35)	0.95 (0.42–2.16)
3–7	1.12 (0.91–1.38)	1.16 (0.94–1.43)	0.37 (0.11–1.28)
>7	1.27 (1.08–1.50)	1.28 (1.08–1.51)	1.07 (0.50–2.45)
P trend	0.002	0.002	0.880
Average length of night shifts (hours/night)			
Never	1.00	1.00	1.00
≤8	1.18 (1.01–1.38)	1.19 (1.02–1.41)	0.82 (0.40–1.68)
8–9	1.25 (1.01–1.54)	1.28 (1.04–1.59)	0.38 (0.90–1.63)
>9	1.28 (1.02–1.61)	1.23 (0.97–1.56)	2.37 (0.91–6.21)
P trend	0.028	0.052	0.169
Percentage of hours on night shifts, n (%)			

Never	1.00	1.00	1.00
<20%	1.16 (0.94–1.43)	1.15 (0.93–1.43)	1.12 (0.45–2.78)
20%–30%	1.10 (0.90–1.34)	1.11 (0.90–1.35)	0.82 (0.31–2.20)
>30%	1.24 (1.06–1.46)	1.26 (1.07–1.49)	0.89 (0.43–1.86)
P trend	0.010	0.006	0.628

OR, odds ratio; CI, confidence intervals.

Adjusted for age, sex (except for gender stratification), BMI, smoking status, dyslipidaemia, hypertension, decreased eGFR, dust exposure

(No or Yes), heat stress exposure (No or Yes), noise exposure (No or Yes), and carbon monoxide exposure (No or Yes)

Exposure metrics	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Current shift status			
Never	1.00	1.00	1.00
Ever	1.08 (0.91–1.29)	1.07 (0.89–1.28)	1.08 (0.90–1.29)
Current	1.25 (1.08–1.46)	1.23 (1.05–1.44)	1.23 (1.06–1.44)
Duration of night shifts (years)			
Never	1.00	1.00	1.00
Q1 (1–12)	1.16 (0.97–1.39)	1.13 (0.95–1.36)	1.15 (0.96–1.38)
Q2 (13–20)	1.04 (0.87–1.25)	1.04 (0.86–1.25)	1.05 (0.87–1.27)
Q3 (21–27)	1.17 (0.97–1.40)	1.17 (0.97–1.41)	1.19 (0.98–1.43)
Q4 (28–43)	1.47 (1.24–1.74)	1.38 (1.15–1.65)	1.35 (1.12–1.61)
P trend	<0.001	0.001	0.003
Cumulative number of night shifts (nights)			
Never	1.00	1.00	1.00
Q1 (43–1131)	1.17 (0.98–1.39)	1.14 (0.95–1.36)	1.15 (0.96–1.38)
Q2 (1132–1848)	1.03 (0.86–1.23)	1.03 (0.85–1.24)	1.04 (0.86–1.26)
Q3 (1854–2584)	1.19 (1.00–1.42)	1.20 (1.00–1.44)	1.21 (1.01–1.45)
Q4 (2585–5239)	1.47 (1.23–1.74)	1.37 (1.14–1.65)	1.34 (1.11–1.61)
P trend	<0.001	0.001	0.004
Cumulative length of night shifts (hours)			
Never	1.00	1.00	1.00
Q1 (344–9488)	1.18 (0.99–1.41)	1.15 (0.96–1.39)	1.16 (0.97–1.40)
Q2 (9490–15259)	1.02 (0.86–1.22)	1.02 (0.84–1.23)	1.04 (0.86–1.25)
Q3 (15265–21293)	1.19 (1.00–1.42)	1.18 (0.99–1.42)	1.20 (1.00–1.45)
Q4 (21295–53541)	1.46 (1.23–1.74)	1.37 (1.14–1.65)	1.33 (1.11–1.61)
P trend	<0.001	0.003	0.006
Average frequency of night shifts (nights/month)			
Never	1.00	1.00	1.00
<3	1.12 (0.94–1.33)	1.11 (0.93–1.32)	1.11 (0.93–1.33)
3–7	1.11 (0.91–1.36)	1.09 (0.89–1.34)	1.10 (0.91–1.35)
>7	1.28 (1.09–1.49)	1.25 (1.07–1.47)	1.25 (1.07–1.47)
P trend	0.001	0.003	0.004
Average length of night shifts (hours/night)			
Never	1.00	1.00	1.00
≤8	1.18 (1.01–1.37)	1.16 (1.00–1.36)	1.17 (1.01–1.37)
8–9	1.25 (1.03–1.53)	1.21 (0.99–1.48)	1.23 (1.00–1.52)
>9	1.39 (1.11–1.73)	1.30 (1.04–1.63)	1.27 (1.01–1.60)
P trend	0.003	0.022	0.031
Percentage of hours on night shifts			
Never	1.00	1.00	1.00
<20%	1.15 (0.94–1.40)	1.14 (0.93–1.40)	1.15 (0.94–1.42)
20%–30%	1.10 (0.91–1.34)	1.08 (0.89–1.31)	1.09 (0.90–1.32)
>30%	1.25 (1.07–1.46)	1.23 (1.05–1.44)	1.23 (1.05–1.43)
P trend	0.004	0.009	0.010

Figure S1 Associations of different exposure metrics of night shift work with HHcy odds. HHcy, hyperhomocysteinemia; OR, odds ratio; CI, confidence intervals. Model 1: unadjusted; Model 2: adjusted for age and sex; Model 3: adjusted for age, sex, BMI, smoking status, dyslipidaemia, hypertension, and decreased eGFR.
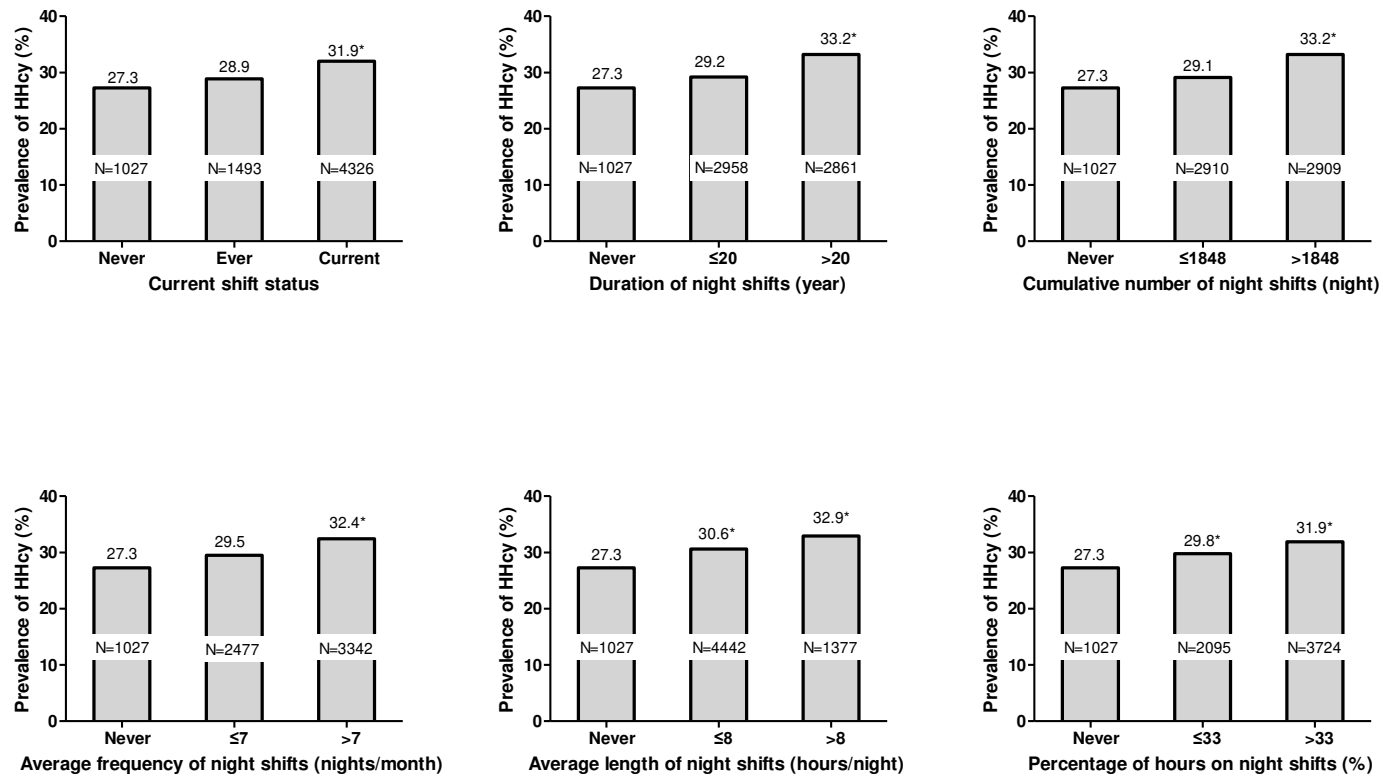
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Figure S2 Prevalence of HHcy according to different exposure metrics of night shift work. The number in the middle of each column indicates the number of subjects included in the category. $^{*}P < 0.05$ (vs. the "Never" group).

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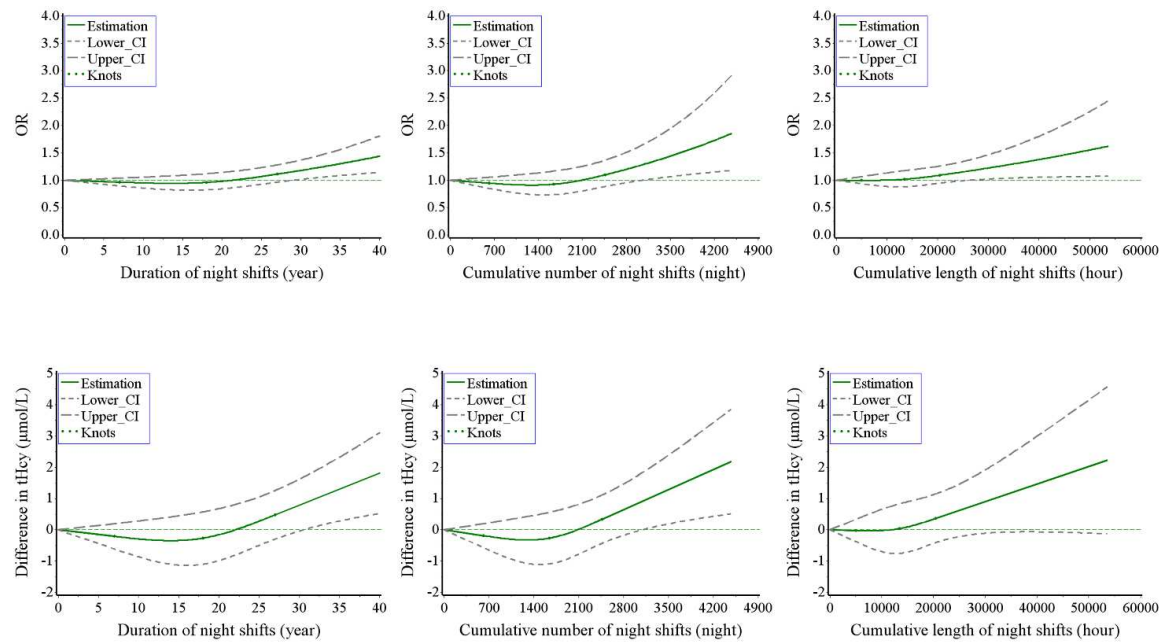
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Figure S3 Associations of duration, cumulative number and cumulative length of night shifts with tHcy (as a continuous or a binary variable) from restricted cubic spline models after deleting the last 1% quantile of the duration of night shifts, cumulative number of night shifts and cumulative length of night shifts. "Difference in tHcy" indicates difference of tHcy (µmol/L) levels in the serum where the reference values for duration, cumulative number and cumulative length of night shifts are all 0 (never worked night shifts); Adjusted for age, sex, BMI, smoking status, dyslipidaemia, hypertension, and decreased eGFR. OR, odds ratio; CI, confidence interval; tHcy, total homocysteine; HHcy, hyperhomocysteinemia.

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