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Cross-sectional study of the association between long working hours and the risk of pre-diabetes: 2013-2017 Korea National Health and Nutrition Examination Survey

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4 **Cross-sectional study of the association between long working hours and the risk**
5 **of pre-diabetes: 2013-2017 Korea National Health and Nutrition Examination**
6 **Survey**
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ABSTRACT

OBJECTIVE: Long working hours have been associated with type 2 diabetes (T2DM). However, the relationship with pre-diabetes in the general population remains unexplored. We aimed to investigate whether long working hours were linked with an increased risk of pre-diabetes as determined by glycated hemoglobin (HbA1c) level.

DESIGN: Cross-sectional survey

PARTICIPANTS: This study included 5,536 men and 5,147 women without diabetes from the 2013-2017 Korean National Health and Nutrition Examination Survey (KNHANES).

PRIMARY OUTCOME MEASURES: The study outcome of interest was pre-diabetes, defined as HbA1c values 5.7-6.4%

RESULTS: Logistic regression was performed to obtain the odds ratios (OR) for pre-diabetes according to categories of work hour (≤ 40 hours/week, 41-52 hours/week, >52 hours/week), after adjusting for relevant covariates. Of the 10,683 eligible participants, 1,977 (35.7%) men and 1,713 (33.3%) women had pre-diabetes. After adjusting for age, educational attainment, monthly household income, life-style related factors, perceived stress, family history of diabetes, hypertension, hypercholesterolemia and other covariates, a multiple logistic regression analysis found that extended working hours (>52 hours per week) was associated with an increased likelihood of pre-diabetes in men (adjusted OR=1.40; 95%CI=1.19-1.65). In the subgroup analysis by occupational categories, the association was only apparent in green- and blue-collar worker groups.

CONCLUSION: Extended working hours were significant related to the increased risk of pre-diabetes, independent of conventional risk factors. Our results suggest prolonged working hours are associated with glucose metabolism among non-diabetic male workers in Korea.

Keywords: Pre-diabetes, Hba1c, working hours, Glucose metabolism

Strengths and limitations of this study

- As far as we are aware, this is the first report of an association between long working hours and pre-diabetes among individuals without diabetes using a nationally representative sample of Korean adults. We further compared associations by occupational categories.
- This study controlled for a range of factors that are known to affect HbA1c levels.
- Our analyses are based on cross-sectional data and, as such, preclude direct causal inference.

INTRODUCTION

Pre-diabetes, defined as an intermediate state of hyperglycemia with glycemic parameters above normal but below the diagnostic threshold for diabetes is considered an important risk factor for β -cell dysfunction¹ and the development of type 2 diabetes mellitus (T2DM).^{2,3} According to the 2012 projection estimates, prevalence of pre-diabetes will continue to rise, and it is estimated that by 2030 over 470 million people will have pre-diabetes globally.⁴ Approximately 70% of individuals diagnosed with pre-diabetes are expected to progress to T2DM within 10 years.⁵ Given the high incidence rate of diabetes among pre-diabetic adults, identification of the modifiable risk factors of pre-diabetes in the general population is thus essential to effectively prevent or delay the onset of diabetes and its associated complications.

South Korea has one of the longest work hours among member states of the Organization for Economic Cooperation and Development (OECD), with people spending on average 2,069 hours at work annually compared to the OECD average of 1,764 hours.⁶ There is increasing epidemiological evidence that working long hours raise the risk of various health outcomes, including coronary heart disease^{7, 8}, cognitive function⁹, type 2 diabetes^{2,10}, as well as a high prevalence of anxiety¹¹, depressive symptoms^{12, 13}, and sleeping disturbances.¹⁴ In a meta-analysis of epidemiological studies conducted in USA, Europe, Japan, and Australia, Kivimäki et al. reported a prospective association between long working hours and the incidence of diabetes, but only among employees with a low socioeconomic position.¹⁵ Similarly, one study of Chinese male workers found that the risk of developing diabetes increased with longer hours of overtime work per week.¹⁶ However, the relationship between long working hours and pre-diabetes in populations without diabetes remains unexplored. To fill this evidence gap, we investigated the relationship between weekly working hours and the risk of pre-diabetes using a cross-sectional survey of 10,683 workers in South Korea.

METHODS

Study population

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3 Data were drawn from the 2013-2017 Korean National Health and Nutrition Examination
4 Survey (KNHANES). KNHANES is an ongoing population based, cross-sectional study which
5 is designed to assess the health and nutritional status of people residing in South Korea.¹⁷
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7 The survey's sampling strategy was designed to be representative of the non-institutionalized
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9 civilian population aged 1 year or over which was selected using a complex, multistage,
10 stratified sampling design. Of the 39,225 participants (Men : 17,842, Women : 21,383) who
11 participated in the 2013-2017 survey, 16,131 reported as being economically active and
12 therefore were eligible to be asked job-related modules and 16,091 provided valid responses
13 concerning weekly work hours. KNHANES participants under 30 or >70 years old and
14 pregnant women were excluded from the analysis. We also excluded those who reported a
15 previous clinical diagnosis of diabetes made by a physician or taking insulin or anti-diabetic
16 medication or missing data on Hba1c, or Hba1c values greater than 6.5% (N=1,840). Finally,
17 we excluded participants with missing covariate data (N=473), yielding a final sample of
18 10,683 participants (Men : 5,536 , Women : 5,147) (See Figure 1).
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35 **Patient and Public Involvement (PPI)**

36 No patients were included in the design and planning of the study. Including PPI statements
37 aligns closely with BMJ Open's values of transparency and inclusiveness. We hope that
38 including PPI statements in all articles is the first step of many for BMJ Open in encouraging
39 patient involvement.
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48 **Measures**

49 **Definition of Pre-diabetes**

50 The main study outcome was glycated hemoglobin (HbA1c). HbA1c is a form of
51 hemoglobin in which glucose is attached to its β -chain after exposure to high plasma levels of
52 glucose. As such, it is used as an integrated index of long-term serum glucose regulation.¹⁸
53 Fasting bloods samples were collected during a medical examination and HbA1c levels were
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3 measured via high performance liquid chromatography (HLC-723G7; Tosoh, Tokyo, Japan).
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5 Participants were identified as being normoglycemic if they had a HbA1c level below 5.7%;
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7 HbA1c level between 5.7 and 6.4 percent were indicative of pre-diabetes according to the
8
9 2018 American Diabetes Association (ADA) standards of care in diabetes.¹⁹
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13 **Working hours**

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15 In the KNHANES, participants were asked about their working hours using the following
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17 question: “During the last month, how many hours on average in a week did you work,
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19 including unpaid overtime work (excluding meal time)?” In Korea, statutory weekly work hours
20
21 based on the Labor Standards Act (LSA) are 40 hours per week and 8 hours per day. The
22
23 working hours stipulated in LSA Article 50 may be extended up to additional 12 hours by
24
25 agreement between the parties. Therefore, in the current study we defined long working hours
26
27 as working beyond the legal threshold of 52 hours. Participants reported their working hours
28
29 as a continuous variable, and this was further categorized as follows: ≤ 40 hours, 41-52 hours,
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31 or >52 hours per week.
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37 **Covariates**

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39 Data on socio-demographic characteristics, lifestyle- and health-related factors were
40
41 collected using interviewer-administered standardized questionnaires. Age was categorized
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43 into 30–39, 40–49, 50–59, and ≥ 60 years. Participants were categorized by educational
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45 attainment (elementary school, middle school, high school, and university degree or above),
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47 monthly household income quartiles, and occupational categories (white collar (managers,
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49 professionals), pink collar (clerks, service, and sales workers), green collar (agricultural,
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51 fishery or forestry workers) and blue collar (craft/trades workers, machine operators and
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53 assemblers, and elementary manual workers). Work schedules were assessed using the
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55 following question: “Do you work mostly during the day time, or do you work at a different time
56
57 period?” Respondent who usually worked during the daytime (06:00-18:00), evening hours
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59 (14:00-24:00), or night-time (21:00-08:00) were categorized as fixed schedule workers, while
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3 those who worked 24-hours rotating shifts, split shifts, or irregular shifts were classified as shift
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5 schedule workers.

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7 Health-related behaviours included smoking status (Never smoker, former smoker, and
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9 current smoker) alcohol consumption (Yes or no), muscle strengthening activity at least twice
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11 a week (yes/no), and sleep duration (< 6, 6-8, ≥9 hours). Body mass index (BMI [kg/m²]) was
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13 used to determine obesity status and calculated based on respondent's self-reported height
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15 and weight. A BMI of <18.5 was considered underweight, a BMI > 18.5 and <23.0 was
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17 considered normal weight, a BMI greater than or equal to 23.0 and <25.0 was considered
18
19 overweight, and a BMI ≥ 25 was considered obese. The level of perceived stress was
20
21 measured using the following question: "How stressed are you on a daily basis?" with possible
22
23 answers ranging from 'None' coded 0 to 'High' coded 4. Respondents were reclassified into
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25 low (none/low) and high perceived stress (moderate/high). Hypercholesterolemia (yes/no) was
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27 defined as a serum total cholesterol level ≥240 mg/dL or the use of lipid-lowering medications.
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29 Hypertension (yes/no) was defined as a systolic blood pressure of 140 mmHg or higher,
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31 diastolic blood pressure of 90 mmHg or higher or on antihypertensive treatment. A family
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33 history of diabetes was ascertained by asking participants whether their first-degree relatives
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35 (parents or siblings) had ever been told they have diabetes (yes/no).
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43 **STATISTICAL ANALYSES**

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45 Statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC,
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47 USA). The SAS survey procedure was applied to reflect the stratification and clustering of the
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49 complex sampling design and sampling weights of the KNHANES and to ensure nationally
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51 representative prevalence estimates. Baseline characteristics of the study sample were
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53 described using frequency and weighted percentages. Chi-square test was used to compare
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55 the characteristics between normoglycemic and pre-diabetic subjects. Multivariable logistic
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57 regression analysis was used to evaluate the association between working hours and pre-
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59 diabetes status, and odds ratios (ORs) and 95% CI were calculated after adjusting for socio-
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3 demographic and health-related behavioural variables that showed significant association
4 in univariate analysis and based on clinical relevance. Additionally, we evaluated whether the
5 association between long working hours and pre-diabetes was dependent on age or work-
6 related characteristics by testing interaction effects and conducting subgroup analyses. A
7 multiplicative interaction term (working hour×effect modifier variable) was included in the
8 multivariable logistic regression model along with the main effects. All analyses were
9 performed separately for men and women and statistical significance set at $p < 0.05$.

21 22 **RESULTS**

23 24 **General characteristics of the study population**

25
26 Table 1 presents participants' general characteristics by Hba1c status in men and women.
27 A total of 1,977 (34.42%) men and 1,713 (30.97%) women had pre-diabetes. Men who worked
28 40 hours or less had the lowest pre-diabetes prevalence (32.09%), followed by those working
29 41–52 hours (32.99%) and >52 hours (38.79%). Male workers with pre-diabetes were also
30 more likely to be older, have a lower level of education, to be working in a blue-collar
31 occupation, obese, current smokers; sleep less than 6 hours and to have a diagnosis of
32 hypertension, hypercholesteremia and a family history of diabetes compared with
33 normoglycemic subjects. The proportion of subjects who participated in muscle strengthening
34 activity least twice a week was lower in the group with pre-diabetes. For women, we observed
35 statistically significant differences in prevalence of pre-diabetes for most characteristics,
36 except for smoking status, muscle strengthening activity, family history of diabetes and work
37 schedule.

Table 1. General characteristics of the study population by HbA1c status, KNHANES 2013-2017

	Men (N=5,536)				Women (N=5,147)			
	Total	Pre-diabetes N (%)	Normoglycemia N (%)	p-value	Total	Pre-diabetes N (%)	Normoglycemia N (%)	p-value
Working hours per week (hours)				0.0003				0.003
40 or less	2,139 (37.3)	736 (32.1)	1,403 (67.9)		3,131 (60.9)	1,049 (31.0)	2,082 (68.99)	
41-52	1,762 (32.2)	598 (33.0)	1,164 (67.0)		1,133 (22.0)	392 (27.4)	801 (72.57)	
>52	1,635 (30.5)	643 (38.8)	992 (61.2)		883 (17.1)	322 (35.4)	551 (64.59)	
Age (years)				<.0001				<.0001
30-39	1,533 (31.7)	373 (23.7)	1,160 (76.3)		1,187 (24.9)	405 (13.7)	1,022 (86.3)	
40-49	1,654 (32.6)	563 (34.8)	1,091 (65.2)		1,592 (34.0)	509 (23.0)	1,213 (77.0)	
50-59	1,450 (25.8)	613 (41.8)	837 (58.2)		1,524 (29.2)	565 (45.3)	819 (54.7)	
≥60	899 (9.9)	428 (48.1)	471 (51.9)		844 (11.9)	404 (54.9)	380 (45.1)	
Education				<.0001				<.0001
Elementary School	467 (6.5)	216 (45.5)	251 (54.5)		859 (13.4)	408 (51.2)	411 (48.8)	
Middle school	517 (8.1)	229 (43.6)	288 (56.4)		575 (10.7)	244 (42.1)	321 (57.9)	
High school	1,785 (32.7)	704 (39.0)	1,081 (61.0)		1,837 (38.0)	702 (31.7)	1,225 (68.3)	
University degree or above	2,767 (52.7)	828 (28.8)	1,939 (71.2)		1,876 (37.9)	639 (20.0)	1,477 (80.0)	
Total household income				0.106				<.0001
Low	314 (4.6)	126 (39.9)	188 (60.1)		500 (8.6)	208 (40.8)	282 (59.2)	
Middle-low	1,240 (21.8)	476 (36.3)	764 (63.7)		1,234 (22.7)	449 (34.1)	785 (65.9)	
Middle-high	1,889 (35.1)	660 (34.2)	1,229 (65.8)		1,625 (33.1)	500 (29.7)	1,105 (70.3)	
High	2,093 (38.5)	715 (32.9)	1,378 (67.1)		1,788 (35.6)	506 (27.8)	1,262 (72.2)	
Smoking status				0.0001				0.083
Never smoker	1,135 (20.8)	337 (29.6)	798 (70.4)		4,655 (89.8)	1,575 (31.5)	3,080 (68.5)	
Former smoker	2,144 (36.7)	764 (33.6)	1,380 (66.4)		234 (4.9)	80 (24.7)	172 (75.3)	
Current smoker	2,257 (42.5)	876 (37.5)	1,381 (62.5)		258 (5.3)	96 (27.7)	182 (72.3)	
Alcohol consumption				0.333				<.0001
No	175 (2.9)	66 (38.5)	109 (61.5)		615 (11.0)	209 (43.2)	326 (56.8)	
Yes	5,361 (97.1)	1,911 (34.3)	3,450 (65.7)		4,532 (89.0)	1,424 (29.5)	3,108 (70.5)	
Muscle strengthening activity				0.053				0.556
No	4,088 (74.0)	1,495 (35.3)	2,593 (64.7)		4,483 (87.2)	1,491 (31.1)	2,992 (68.9)	
Yes	1,448 (26.0)	482 (32.1)	966 (67.9)		664 (12.8)	222 (29.9)	442 (70.1)	
BMI				<.0001				<.0001
Underweight	91 (1.7)	17 (18.4)	74 (81.6)		211 (4.4)	33 (15.9)	172 (84.1)	
Normal	1,627 (29.5)	468 (27.9)	1,159 (72.1)		2,429 (48.3)	622 (22.1)	1,847 (77.9)	
Overweight	1,548 (27.9)	534 (32.4)	1,014 (67.6)		1,138 (21.7)	333 (35.7)	705 (64.3)	
Obese	2,270 (40.9)	958 (41.2)	1,312 (58.8)		1,369 (25.6)	469 (46.3)	710 (53.7)	

Table 1 Continued

Hypertension				<.0001			<.0001
No	3,976 (73.25)	1,333 (32.37)	2,643(67.63)		4,180 (83.17)	1,239 (27.73)	2,941 (72.27)
Yes	1,560 (26.75)	644 (40.05)	916 (59.95)		967 (16.83)	474 (47.00)	493 (53.00)
Hypercholesterolemia				<.0001			<.0001
No	4,690 (85.63)	1,580 (32.43)	3,110 (67.57)		4,266 (84.08)	1,258 (27.52)	3,008 (72.48)
Yes	846 (14.37)	397 (42.27)	449 (53.73)		881 (15.92)	475 (49.20)	426 (50.80)
Family history of diabetes				<.0001			0.5349
No	4,356 (78.19)	1,505 (32.67)	2,851 (67.33)		3,878 (74.80)	1,275 (30.72)	2,604 (69.28)
Yes	1,180 (21.81)	472 (40.71)	708 (59.29)		1,268 (25.20)	478 (31.71)	830 (68.29)
Sleep duration (hours)				0.0203			<.0001
< 6	673 (12.06)	265 (38.15)	408 (61.85)		724 (14.42)	277 (39.11)	427 (60.89)
6-8	4,394 (80.14)	1,563 (34.37)	2,831 (65.63)		3,824 (74.05)	1,259 (30.53)	2,565 (69.47)
≥9	469 (8.00)	149 (29.15)	320 (70.85)		599 (11.52)	177 (23.61)	442 (76.39)
Perceived stress				0.8854			0.020
None/Low	4,063 (72.01)	1,463 (34.48)	2,600 (65.52)		3,715 (71.71)	1,281 (32.00)	2,434 (67.99)
Moderate/High	1,473 (27.99)	514 (34.26)	959 (65.74)		1,432 (28.29)	472 (28.36)	1,000 (71.64)
Occupation				<.0001			<.0001
White collar	2,366 (44.45)	723 (29.39)	1,643 (70.61)		2,059 (41.36)	722 (20.32)	1,607 (78.68)
Pink collar	721 (13.38)	259 (36.21)	462 (63.79)		1,521 (30.12)	574 (37.03)	927 (62.98)
Green collar	375 (4.79)	166 (44.02)	209 (55.98)		305 (4.31)	176 (49.00)	149 (51.00)
Blue collar	2,074 (37.38)	829 (38.53)	1,245 (61.47)		1,262 (24.21)	511 (38.43)	751 (61.57)
Work schedule				0.896			0.392
Fixed	5,161 (93.44)	1,835 (34.40)	3,326 (65.60)		4,970 (96.33)	1,651 (30.85)	3,319 (69.15)
Shift	375 (6.56)	142 (34.78)	233 (65.22)		177 (3.67)	63 (34.14)	115 (65.86)
Participants		1,977 (34.42%)	3,559 (65.58%)			664 (30.97%)	3,434 (69.03)

*Unless otherwise stated, unweighted frequency (weighted %) are shown.

†P value comparing prediabetes with normoglycemia

Association between long working hours and pre-diabetes

Adjusted odds ratios (ORs) from the multiple logistic regression analysis are shown in Table 2. We found no statistically significant associations between long working hours and pre-diabetes in women (adjusted OR: 0.86; 95% CI: 0.70-1.05; $P = 0.137$). In the case of men, those who worked >52 hours were 1.40 times more likely to have pre-diabetes after adjusting for covariates (adjusted Odds Ratio (OR): 1.40; 95% Confidence Interval (CI): 1.19-1.65; $P < 0.0001$). Age, smoking status, hypercholesteremia, family history of diabetes and sleep duration were also found to considerably increase the risk of pre-diabetes in men, but there were no statistically significant differences based on educational level, monthly household income, alcohol consumption, muscle strengthening activity, hypertension, perceived stress, occupation and work schedule.

Table 3 presents the ORs for subgroup analyses by age and work-related characteristics. We did not observe a significant interaction between the number of hours worked per week and age (P for interaction = 0.413) nor between work schedule and working hours ($P = 0.708$). A tendency towards a more pronounced effect of long working hours on pre-diabetes among shift workers (41-52 hrs: aOR= 1.19, 95% CI: 0.57-2.52; >52 hrs: aOR= 1.56, 95% CI: 0.78-3.12; p for trend=0.186). However, this effect did not reach statistical significance. In the subgroup analysis by occupational categories, male workers who worked in green-collar occupation were likely to have pre-diabetes as their average weekly working hours increased, after adjustment for all covariates. The adjusted ORs were 1.03 (95% CI 0.56-1.88) and 1.91 (95% CI 1.05-3.48) for the 41-52 hrs and >52 hrs categories, respectively (p for trend= 0.041). Similar results were observed for blue-collar workers (41-52 hrs: aOR= 1.22, 95% CI: 0.93-1.61; >52 hrs: aOR= 1.82, 95% CI: 1.40-2.36; p for trend= <0.0001). The interaction effect by occupational categories was only marginally significant (p for interaction=0.063).

Table 2. Results of the multiple logistic regression analysis for the association between long working hours and pre-diabetes (HbA1c 5.7-6.4%)

Characteristics	Prediabetes (HbA1c 5.7-6.4%)					
	Men			Women		
	OR	95% CI	P-value	OR	95% CI	P-value
Working hours per week (hours)						
40 or less	1.00			1.00		
41-52	1.17	0.99-1.38	0.011	0.89	0.74-1.07	0.207
>52	1.40	1.19-1.65	<0.0001	0.86	0.70-1.05	0.137
Age (years)						
30-39	1.00			1.00		
40-49	1.70	1.43-2.03	<0.0001	1.48	1.16-1.89	0.0015
50-59	2.40	1.98-2.92	<0.0001	3.53	2.76-4.57	<0.0001
≥60	3.30	2.59-4.22	<0.0001	4.84	3.52-6.66	<0.0001
Education						
Elementary School	1.00			1.00		
Middle school	1.06	0.79-1.42	0.719	0.89	0.68-1.18	0.435
High school	1.09	0.83-1.44	0.526	1.07	0.83-1.39	0.588
University degree or above	0.85	0.63-1.16	0.311	0.95	0.69-1.30	0.750
Total household income						
Low	1.00			1.00		
Middle-low	1.03	0.75-1.40	0.82	1.07	0.81-1.41	0.627
Middle-high	0.99	0.73-1.34	0.935	1.11	0.84-1.47	0.483
High	0.96	0.70-1.31	0.802	1.12	0.84-1.49	0.451
Smoking status						
Never smoker	1.00			1.00		
Former smoker	0.98	0.82-1.18	0.858	1.04	0.71-1.52	0.858
Current smoker	1.38	1.15-1.66	0.001	1.06	0.76-1.47	0.733
Alcohol consumption						
No	1.00			1.00		
Yes	0.97	0.67-1.42	0.889	0.89	0.71-1.10	0.274
Muscle strengthening activity						
No	1.00			1.00		
Yes	0.91	0.78-1.06	0.174	0.96	0.78-1.19	0.727
BMI						
Underweight	1.00			1.00		
Normal	1.76	0.91-3.40	0.094	1.04	0.69-1.57	0.846
Overweight	2.19	1.13-4.28	0.021	1.60	1.04-2.46	0.031
Obese	3.33	1.72-6.43	0.003	2.50	1.64-3.83	<0.0001

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Table 2 Continued

Hypertension						
No	1.00				1.00	
Yes	0.99	0.85-1.15	0.796		1.08	0.90-1.30 0.423
Hypercholesterolemia						
No	1.00				1.00	
Yes	1.61	1.35-1.92	<0.001		1.42	1.18-1.71 0.001
Family history of diabetes						
No	1.00				1.00	
Yes	1.48	1.27-1.73	<0.001		1.21	1.03-1.43 0.022
Sleep duration (hours)						
< 6	1.01	0.84-1.22	0.95		1.20	0.98-1.48 0.080
6-8	1.00				1.00	
≥9	0.75	0.59-0.97	0.027		0.75	0.59-0.94 0.013
Perceived stress						
None/Low	1.00				1.00	
Moderate/High	1.06	0.92-1.23	0.45		0.91	0.78-1.08 0.284
Occupation						
White collar	1.00				1.00	
Pink collar	1.15	0.91-1.44	0.22		1.34	1.08-1.66 0.007
Green collar	1.17	0.86-1.58	0.24		1.41	0.99-2.01 0.060
Blue collar	1.12	0.93-1.34	0.24		1.17	0.93-1.48 0.182
Work schedule						
Fixed	1.00				1.00	
Shift	0.99	0.75-1.30	0.27		1.19	0.81-1.76 0.367

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Table 3. Results of subgroup analysis of association between hba1c and working hours by age and work characteristics

Characteristics	Men			p for trend	p for interaction	Women			p for trend	p for interaction
	Odds ratio (95% CI)					Odds ratio (95% CI)				
	≤40 hrs	41-52 hrs	>52 hrs			≤40 hrs	41-52 hrs	>52 hrs		
Occupational categories					0.063					0.297
White collar	1.00	1.14 (0.90-1.44)	1.11 (0.84-1.48)	0.369		1.00	0.95 (0.70-1.28)	0.60 (0.36-1.00)	0.099	
Pink collar	1.00	1.29 (0.79-2.10)	1.11 (0.71-1.73)	0.728		1.00	0.76 (0.55-1.05)	0.81 (0.61-1.09)	0.133	
Green collar	1.00	1.03 (0.56-1.88)	1.91 (1.05-3.48)	0.041		1.00	1.38 (0.74-2.58)	0.41 (0.69-2.90)	0.306	
Blue collar	1.00	1.22 (0.93-1.61)	1.82 (1.40-2.36)	<.0001		1.00	0.89 (0.60-1.32)	0.89 (0.61-1.30)	0.473	
Work schedule					0.708					0.080
Fixed	1.00	1.16 (0.98-1.38)	1.37 (1.15-1.63)	0.0003		1.00	0.85 (0.71-1.03)	0.88 (0.71-1.08)	0.119	
Shift	1.00	1.19 (0.57-2.52)	1.56 (0.78-3.12)	0.186		1.00	2.86 (1.12-7.33)	0.73 (0.25-2.12)	0.895	
Age (years)					0.413					0.822
30-39	1.00	1.51 (1.07-2.14)	1.73 (1.22-2.47)	0.002		1.00	0.93 (0.60-1.44)	0.73 (0.36-1.49)	0.380	
40-49	1.00	0.92 (0.69-1.23)	1.22 (0.91-1.62)	0.218		1.00	0.79 (0.57-1.09)	0.74 (0.49-1.11)	0.084	
50-59	1.00	1.20 (0.89-1.60)	1.36 (0.99-1.86)	0.052		1.00	1.03 (0.76-1.40)	0.98 (0.73-1.33)	0.938	
≥60	1.00	1.61 (1.07-2.44)	1.75 (1.18-2.60)	0.004		1.00	0.78 (0.49-1.23)	0.69 (0.46-1.04)	0.061	

DISCUSSION

In this population-based study of Korean working adults without diabetes, we found that men who worked over 52 hours per week exhibited 40% increased risk of pre-diabetes than did those who worked ≤ 40 hours per week. This association was robust to adjustments for socio-demographic variables and lifestyle factors, such as obesity, participation in muscle strengthening activity, smoking, and alcohol consumption and other covariates. Importantly, the excess risk of pre-diabetes associated with long working hours was more marked in the case of the workers in manual occupations.

In the present study, the prevalence of pre-diabetes in the Korean working population was 34.4% and 30.9% for men and women, respectively. These prevalence estimates are comparable to general population estimates reported in the U.S.²⁰, U.K.²¹, and those of other Asian countries.²² Several previous studies have yielded prevalence estimates for pre-diabetes in Korea. Using the HbA1c cutoff, pre-diabetes prevalence in 2011 was reported to be 38.3% (Men: 41%; women: 35.7%) in a community-based cross-sectional study of Korean adults aged 30 years or over.²³ Another Korean study reported a pre-diabetes prevalence of 26.1% in men and 20.5% according to American diabetes association criteria.²⁴ However, this study was based on a sample from rural areas. Pre-diabetes is a well-recognized risk factors for future diabetes, that gives rise to micro- and macrovascular complications and have enormous social and economic burden^{25, 26}; increased attention needs to be paid to the high prevalence of pre-diabetes in Korea.

We are not aware of other studies that has reported a relationship between long working hours and pre-diabetes, although our findings are comparable with a meta-analysis showing that long working hours is associated with the incidence of type 2 diabetes, only in individuals from low socioeconomic status groups.¹⁵ Other studies also reported a similar finding, indicating that prevalence of pre-diabetes is positively correlated with longer working hours.^{3, 14, 16} However, conflicting findings have also been reported in other studies where relative risks of T2DM significantly decreased with an increase in hours of work per day.²⁷

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3 The mechanisms underlying the association between long working hours and pre-diabetes
4 are yet unknown. It is likely that a similar mechanism to that of diabetes could be responsible
5 for the observed findings. Plausible explanations are that longer working hours impacts pre-
6 diabetes risk via their association with behavioural risk factors. Prior research has indicated
7 that working longer than recommended hours is linked to many behavioural risk factors, such
8 as binge drinking ^{28,29} and low physical activity ³⁰, possibly because individuals feel that they
9 lack the time to engage in leisure-time physical activity due to demands and responsibilities at
10 work. In the present study, working hour–pre-diabetes association attenuated but remained
11 statistically significant after adjustment for behaviour risk factors. As such, conventional risk
12 factors for pre-diabetes are likely to explain only part of the association between long working
13 hours and pre-diabetes.
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26 Meanwhile, there has been a proposition that extended working hours are related to
27 cortisol secretion ³¹, a known risk factor for impaired glucose metabolism.³² Cortisol induces
28 the formation of glucose in the liver and have insulin-antagonistic effects in the peripheral
29 tissues; both processes have the potential to contribute to risk of hyperglycemia. Furthermore,
30 individuals work longer hours are more often exposed to harmful psychological factors in the
31 work environment, such as job strain ^{33, 34} and effort-reward imbalance ³⁵, which are known to
32 be associated with subsequent elevation of Hba1c.³⁶ As such, stress-related mechanisms that
33 trigger dysregulation of neuroendocrine pathways, might be a potentially promising areas for
34 future research studying the differences in risk of pre-diabetes according to work hours.
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45 The present study has several strengths. First, this study is based on a nationally
46 representative survey, and to the best of our knowledge, this is the first report of an association
47 between long working hours and pre-diabetes among individuals without diabetes. Second,
48 blood samples were collected using standardized laboratory procedures, ensuring an accurate
49 estimate of HbA1c. Finally, we were able to control for several important confounding variables,
50 such as sleep duration and perceived control. However, this study is not without limitations.
51 Our analyses are based on data from observational studies and, as such, preclude direct
52 causal inference. Information on working hours and other covariates were self-reported and
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3 thus subject to recall bias. Moreover, we cannot exclude the possibility that the results were
4 affected by residual confounding caused by imprecisely measured covariates or some other
5 unmeasured occupational factors, such as job strain and job satisfaction. Working hours was
6 measured at a single point in time that might not represent long-term exposure. In future
7 studies, use of repeated measurements is needed to characterize longitudinal relation
8 between long working hours and pre-diabetes.
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18 CONCLUSIONS

19 In conclusion, long working hours was significantly correlated with pre-diabetes
20 independent of conventional risk factors. Our results suggest prolonged working hours are
21 related to glucose metabolism among non-diabetic male workers in Korea. Additional large-
22 scale longitudinal studies are needed to verify these findings.
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32 **Ethical statement:** The survey protocols for the KNHANES were approved by the Institutional Review
33 Board of the Korea Centers for Disease Control and Prevention (IRB No. 2013-07CON-03-4C, 2013-
34 12EXP-03-5C, and 2015-01-02-6C), and informed consent was obtained from all participants.
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40 **Conflict of interest:** The authors have no conflict of interest to declare.
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44 **Funding:** This research did not receive any specific grant from funding agencies in the public,
45 commercial, or not-for-profit sectors.
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50 **Data sharing statement:** Data used in this study are available from the KNHANES official website
51 (<http://knhanes.cdc.go.kr/>).
52
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54

55 **Author contributions:** BYS, MK, GRK contributed to the conception and design of the study. BYS,
56 MK, GRK, ECP contributed to analyses and interpretation of the data, BYS, MK, GRK drafted the
57 manuscript. All authors read and approved the final manuscript.
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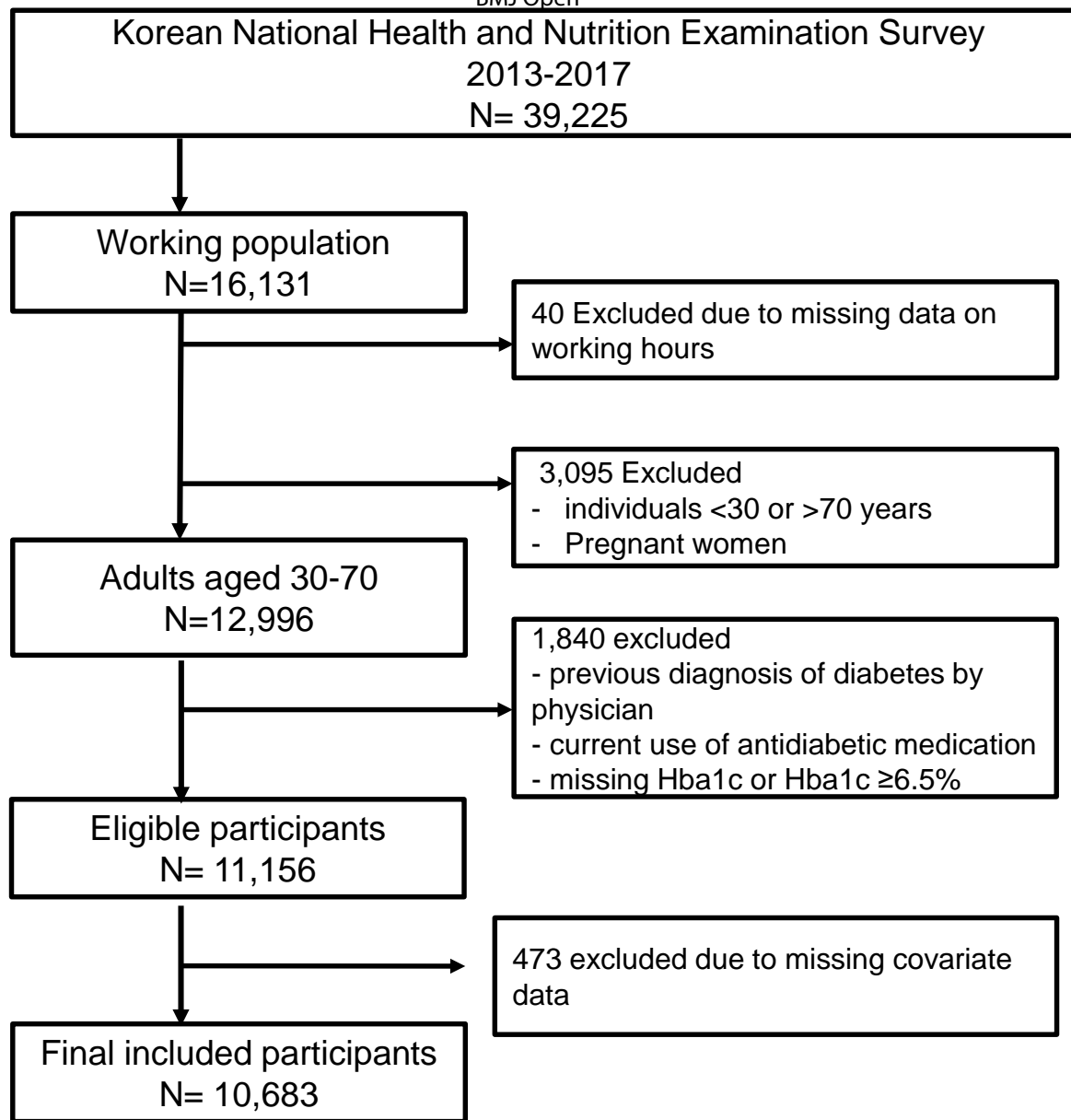


Figure 1 Flow chart of participant selection

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STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up and data collection	4,5,6
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	4,5,6
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Data sources/measurement	8*	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4,5,6
Bias	9	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4,5,6
Study size	10	Describe any efforts to address potential sources of bias	6,7
Quantitative variables	11	Explain how the study size was arrived at	4
Statistical methods	12	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5,6,7
		(a) Describe all statistical methods, including those used to control for confounding	6,7
		(b) Describe any methods used to examine subgroups and interactions	6,7
		(c) Explain how missing data were addressed	4
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8,9
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10, 11, 12
		(b) Report category boundaries when continuous variables were categorized	4
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15, 16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14, 15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Cross-sectional study of the association between long working hours and pre-diabetes: 2010-2017 Korea National Health and Nutrition Examination Survey

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Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	pre-diabetes, Hba1c, working hours, glucose metabolism

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4 **1 Cross-sectional study of the association between long working hours and pre-**
5 **2 diabetes: 2010-2017 Korea National Health and Nutrition Examination Survey**

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53 39 **Word counts**

54 40 **Abstract:** 260 words

55 41 **Manuscript:** 3,057 words

56 42 **Tables:** 4

57 43 **Figures:** 1
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1 ABSTRACT

2 **OBJECTIVE:** Long working hours have been shown to raise the risk of various health outcomes.
3 However, epidemiological evidence has shown inconsistent result in relation to type 2 diabetes (T2DM)
4 and the association between long working hours and pre-diabetes among non-diabetic adults remains
5 largely unexplored. We thus aimed to investigate whether long working hours were linked with pre-
6 diabetes as determined by glycated hemoglobin (HbA1c) level.

7
8 **DESIGN:** Cross-sectional survey

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10 **PARTICIPANTS:** This study included 6,324 men and 4,001 women without diabetes from the 2010-
11 2017 Korean National Health and Nutrition Examination Survey (KNHANES).

12
13 **PRIMARY OUTCOME MEASURES:** The study outcome of interest was pre-diabetes, defined as
14 HbA1c values 5.7-6.4%

15
16 **RESULTS:** Logistic regression was performed to obtain the odds ratios (OR) for pre-diabetes according
17 to categories of work hour (40 hours/week, 41-52 hours/week, >52 hours/week), after adjusting for
18 relevant covariates. Of the 10,325 eligible participants, 2,261 (34.4%) men and 1,317 (31.0%) women
19 had pre-diabetes. No statistically significant relationship was found for women. In men,
20 extended working hours (>52 hours per week) was associated with an increased likelihood of pre-
21 diabetes, after adjustment for age, educational attainment, monthly household income, life-style related
22 factors, perceived stress, family history of diabetes, hypertension, hypercholesterolemia and other
23 covariates (adjusted OR=1.22; 95% confidence interval=1.03-1.46). In the subgroup analysis by
24 occupational categories, the association was only apparent among men in blue-collar worker groups.

25
26 **CONCLUSION:** Extended working hours were significant related to the increased risk of pre-diabetes
27 in men, with no statistically significant association observed for women. Our results suggest prolonged
28 working hours are associated with glucose metabolism among non-diabetic male workers in Korea.

29
30 **Keywords:** Pre-diabetes, Hba1c, working hours, Glucose metabolism

31 32 33 34 35 36 37 38 39 **Strengths and limitations of this study**

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- As far as we are aware, this is the first report of an association between long working hours and pre-diabetes among individuals without diabetes using a nationally representative sample of Korean adults. We further compared associations by occupational categories.
 - This study controlled for a range of factors that are known to affect HbA1c levels.
 - Our analyses are based on cross-sectional data and, as such, preclude direct causal inference.

1 INTRODUCTION

2 Pre-diabetes, defined as an intermediate state of hyperglycemia with glycemic parameters
3 above normal but below the diagnostic threshold for diabetes is considered an important risk
4 factor for β -cell dysfunction¹ and the development of type 2 diabetes mellitus (T2DM).²
5 According to the 2012 projection estimates, prevalence of pre-diabetes will continue to rise,
6 and it is estimated that by 2030 over 470 million people will have pre-diabetes globally.³
7 Approximately 70% of individuals diagnosed with pre-diabetes are expected to progress to
8 T2DM within 10 years.⁴ Given the high incidence rate of diabetes among pre-diabetic adults,
9 identification of the modifiable risk factors of pre-diabetes in the general population is thus
10 essential to effectively prevent or delay the onset of diabetes and its associated complications.

11 South Korea has one of the longest work hours among member states of the Organization
12 for Economic Cooperation and Development (OECD), with people spending on average 2,069
13 hours at work annually compared to the OECD average of 1,764 hours.⁵

14 Several studies have assessed long working hours in relationship with the risk of various
15 health outcomes, including coronary heart disease^{6,7}, cognitive function⁸, as well as a high
16 prevalence of anxiety⁹ and sleeping disturbances.¹⁰ However, epidemiological evidence have
17 shown inconsistent result in relation to diabetes¹¹⁻¹⁴ and the association between long working
18 hours and pre-diabetes in populations without diabetes remains largely unexplored. In a
19 meta-analysis of epidemiological studies conducted in USA, Europe, Japan, and Australia,
20 Kivimäki et al. reported a prospective association between long working hours and the
21 incidence of diabetes, but only among employees with a low socioeconomic position.¹²
22 Similarly, one study of Chinese male workers found that the risk of developing diabetes
23 increased with longer hours of overtime work per week.¹³ In contrast, in a study of Japanese
24 male workers, the relative risk of type 2 diabetes significantly decreased among those who
25 worked over 10 hours a day compared with those who worked 7 to 8 hours.¹⁴ To fill this
26 evidence gap, we investigated the relationship between weekly working hours and the pre-
27 diabetes using a cross-sectional survey of 10,325 workers in South Korea.

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2 **METHODS**

3 **Study population**

4 Data were drawn from the 2010-2017 Korean National Health and Nutrition Examination
5 Survey (KNHANES). KNHANES is an ongoing population based, cross-sectional study which
6 is designed to assess the health and nutritional status of people residing in South Korea.¹⁵
7 The survey's sampling strategy was designed to be representative of the non-institutionalized
8 civilian population aged 1 year or over which was selected using a complex, multistage,
9 stratified sampling design. Of the 64,759 participants (Men : 29,458, Women : 35,301) who
10 participated in the 2010-2017 survey, 26,750 reported as being economically active and
11 therefore were eligible to be asked job-related modules and 26,696 provided valid responses
12 concerning weekly work hours. We restricted analyses to individuals working 40
13 hours or more per week, as participants who worked for less than 40 hours are likely to do so
14 due to health reasons (N=17,298). Additionally, KNHANES participants under 30 or >70 years
15 old and pregnant women were excluded from the analysis (N=2,649). We also excluded those
16 who reported a previous clinical diagnosis of diabetes made by a physician or taking insulin
17 or anti-diabetic medication or missing data on Hba1c, or Hba1c values greater than 6.5%
18 (N=3,800). Finally, we excluded participants with missing covariate data (N=524), yielding a
19 final sample of 10,325 participants (Men : 6,324 , Women : 4,001) (See Figure 1).

20

21 **Patient and Public Involvement (PPI)**

22 No patients were included in the design and planning of the study. Including PPI statements
23 aligns closely with BMJ Open's values of transparency and inclusiveness. We hope that
24 including PPI statements in all articles is the first step of many for BMJ Open in encouraging
25 patient involvement.

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27 **Measures**

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1 **Definition of Pre-diabetes**

2 The main study outcome was glycated hemoglobin (HbA1c). HbA1c is a form of hemoglobin
3 in which glucose is attached to its β -chain after exposure to high plasma levels of glucose. As
4 such, it is used as an integrated index of long-term serum glucose regulation.¹⁶ Fasting bloods
5 samples were collected during a medical examination and HbA1c levels were measured via
6 high performance liquid chromatography (HLC-723G7; Tosoh, Tokyo, Japan). Participants
7 were identified as being normoglycemic if they had a HbA1c level below 5.7%; HbA1c level
8 between 5.7 and 6.4 percent were indicative of pre-diabetes according to the 2018 American
9 Diabetes Association (ADA) standards of care in diabetes.¹⁷ Previous research has indicated
10 that HbA1c and fasting plasma glucose (FPG) are equally in the detection of Type 2 diabetes.¹⁸
11 Also, HbA1c has several advantages to the FPG, including the ability to use non-fasting blood
12 samples, greater pre-analytical stability, and less day-to-day perturbations during periods of
13 stress and illness.¹⁹

16 **Working hours**

17 In the KNHANES, participants were asked about their working hours using the following
18 question: "During the last month, how many hours on average in a week did you work,
19 including unpaid overtime work (excluding meal time)?" In Korea, statutory weekly work hours
20 based on the Labor Standards Act (LSA) are 40 hours per week and 8 hours per day. The
21 working hours stipulated in LSA Article 50 may be extended up to additional 12 hours by
22 agreement between the parties. Therefore, in the current study we defined long working hours
23 as working beyond the legal threshold of 52 hours. Participants reported their working hours
24 as a continuous variable, and this was further categorized as follows: 40 hours, 41-52 hours,
25 or >52 hours per week.

27 **Covariates**

1 Data on socio-demographic characteristics, lifestyle- and health-related factors were
2 collected using interviewer-administered standardized questionnaires. Age was categorized
3 into 30–39, 40–49, 50–59, and ≥ 60 years. Participants were categorized by educational
4 attainment (elementary school, middle school, high school, and university degree or above),
5 monthly household income quartiles, and occupational categories (white collar (managers,
6 professionals), pink collar (clerks, service, and sales workers), green collar (agricultural,
7 fishery or forestry workers) and blue collar (craft/trades workers, machine operators and
8 assemblers, and elementary manual workers)^{20 21}. Work schedules were assessed using the
9 following question: “Do you work mostly during the day time, or do you work at a different time
10 period?” Respondent who usually worked during the daytime (06:00-18:00), evening hours
11 (14:00-24:00), or night-time (21:00-08:00) were categorized as fixed schedule workers, while
12 those who worked 24-hours rotating shifts, split shifts, or irregular shifts were classified as shift
13 schedule workers.

14 Health-related behaviours included smoking status (Never smoker, former smoker, and
15 current smoker) alcohol consumption (Yes or no), muscle strengthening activity at least twice
16 a week (yes/no), participation in aerobic activity, defined as walking at least 10 minutes at a
17 time, for 30 minutes or more per day, on 5 or more per days during the 7 days preceding the
18 survey, and sleep duration (< 6, 6-8, ≥ 9 hours). Body mass index (BMI [kg/m²]) was used to
19 determine obesity status and calculated based on respondent's self-reported height and
20 weight. A BMI of <18.5 was considered underweight, a BMI > 18.5 and <23.0 was considered
21 normal weight, a BMI greater than or equal to 23.0 and <25.0 was considered overweight, and
22 a BMI ≥ 25 was considered obese. The level of perceived stress was measured using the
23 following question: “How stressed are you on a daily basis?” with possible answers ranging
24 from ‘None’ coded 0 to ‘High’ coded 4. Respondents were reclassified into low (none/low) and
25 high perceived stress (moderate/high). Hypercholesterolemia (yes/no) was defined as a
26 serum total cholesterol level ≥ 240 mg/dL or the use of lipid-lowering medications.
27 Hypertension (yes/no) was defined as a systolic blood pressure of 140 mmHg or higher,
28 diastolic blood pressure of 90 mmHg or higher or on antihypertensive treatment. A family

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3 1 history of diabetes was ascertained by asking participants whether their first-degree relatives
4
5 2 (parents or siblings) had ever been told they have diabetes (yes/no).
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4 **STATISTICAL ANALYSES**

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6 Statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC,
7 USA). The SAS survey procedure was applied to reflect the stratification and clustering of the
8 complex sampling design and sampling weights of the KNHANES and to ensure nationally
9 representative prevalence estimates. Baseline characteristics of the study sample were
10 described using frequency and weighted percentages. Chi-square test was used to compare
11 participant characteristics across working hours and between normoglycemic and pre-diabetic
12 subjects. Multivariable logistic regression analysis was used to evaluate the association
13 between working hours and pre-diabetes status, and odds ratios (ORs) and 95% confidence
14 interval (CI) were calculated after adjusting for socio-demographic and health-related
15 behavioural variables that showed significant association in univariate analysis and based on
16 clinical relevance. Additionally, we evaluated whether the association between long working
17 hours and pre-diabetes was dependent on age or work-related characteristics by testing
18 interaction effects and conducting subgroup analyses. Interaction was assessed by including
19 a cross-product interaction term (working hour×effect modifier variable) was in the logistic
20 regression model along with the main effect. All analyses were performed separately for men
21 and women. All reported P values were based on 2-sided tests; statistical significance was set
22 at $p < 0.05$.
23

24 **RESULTS**

25 **General characteristics of the study population**

26 Table 1 presents participants' general characteristics by HbA1c status in men and women.
27 A total of 2,261 (34.43%) men and 1,317 (31.04%) women had pre-diabetes. Men who worked
28 40 hours per week had the lowest pre-diabetes prevalence (30.92%), followed by those
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1 working 41–52 hours (32.88%) and >52 hours (38.00%). Male workers with pre-diabetes were
2 also more likely to be older, work over 52 hours/week, have a lower level of education, to be
3 working in a manual occupations, obese, current smokers, sleep less than 6 hours and to have
4 a diagnosis of hypertension, hypercholesteremia and a family history of diabetes compared
5 with normoglycemic subjects. For women, we observed statistically significant differences in
6 prevalence of pre-diabetes for most characteristics, except for participation in aerobic activity,
7 muscle strengthening activity, family history of diabetes and work schedule.

8 Table 2 shows characteristics of study participants according to categories of working
9 hours. A total of 1,399 (22.08%) male participants reported 40 hours of work per week, 2,483
10 (39.03%) reported 41–52 hours, and 2,442 (38.89%) reported more than 52 hours of work per
11 week; the corresponding values for women were 1,086 (27.49%), 1,574 (39.19%), and 1,341
12 (33.32%), respectively. Compared with men working 40 hours per week, a higher proportion
13 of those who worked more than 52 hours were older, had a lower education, lower household
14 income, higher self perceived stress, in blue-collar occupation, and have shift work schedule.
15 As regard health-related related variables, subjects who worked more than 52 hours tended
16 to be current smoker, non-drinker, physically inactive, have shorter sleep. Among women, no
17 appreciable differences in smoking status, muscle strengthening activity, and work schedule
18 were apparent across working hours per week.

Table 1. General characteristics of the study population by HbA1c status, KNHANES 2010-2017

	Men (N=6,324)				Women (N=4,001)			
	Total	Pre-diabetes N (%)	Normoglycemia N (%)	p-value	Total	Pre-diabetes N (%)	Normoglycemia N (%)	p-value
Working hours per week (hours)				0.0001				<.0001
40	1,399 (22.08)	447 (30.92)	952 (69.08)		1,086 (27.49)	288 (27.15)	788 (72.85)	
41-52	2,483 (39.03)	867 (32.88)	1,616 (67.12)		1,574 (39.19)	422 (29.21)	1,082 (70.79)	
>52	2,442 (38.89)	947 (38.00)	1,495 (62.00)		1,341 (33.32)	527 (36.40)	814 (63.60)	
Age group (years)				<.0001				<.0001
30-39	1,966 (34.77)	497 (24.41)	1,469 (75.59)		994 (26.69)	333 (14.97)	851 (85.03)	
40-49	2,016 (34.82)	687 (34.75)	1,329 (65.25)		1,241 (34.82)	333 (24.39)	928 (75.61)	
50-59	1,569 (23.31)	685 (43.40)	884 (56.59)		1,220 (28.79)	524 (46.11)	656 (53.89)	
≥60	773 (7.10)	392 (52.54)	381 (47.46)		546 (9.70)	307 (54.31)	249 (45.69)	
Education				<.0001				<.0001
Elementary School	480 (5.94)	227 (49.18)	253 (50.82)		698 (14.10)	339 (51.00)	339 (49.00)	
Middle school	540 (7.75)	239 (42.72)	301 (57.28)		477 (12.07)	211 (40.56)	266 (59.44)	
High school	2,083 (33.96)	816 (37.42)	1,267 (62.58)		1,508 (40.55)	525 (31.69)	1,013 (68.31)	
University degree or above	3,221 (52.35)	979 (29.60)	2,242 (70.40)		1,318 (33.28)	322 (18.33)	1,066 (81.67)	
Total household income				0.016				<.0001
Low	265 (3.59)	113 (44.21)	152 (55.79)		319 (7.07)	140 (42.38)	179 (57.62)	
Middle-low	1,444 (22.78)	549 (35.74)	895 (64.26)		942 (22.85)	344 (33.56)	598 (66.44)	
Middle-high	2,172 (35.26)	765 (34.22)	1,407 (65.78)		1,308 (34.11)	420 (30.06)	888 (69.94)	
High	2,443 (38.37)	834 (32.94)	1,609 (67.06)		1,432 (35.97)	413 (28.12)	1,019 (71.88)	
Smoking status				<.0001				0.019
Never smoker	1,250 (20.05)	365 (28.66)	885 (71.34)		3,624 (89.27)	1,229 (31.90)	2,395 (68.10)	
Former smoker	2,373 (35.12)	830 (33.37)	1,543 (66.63)		163 (4.76)	24 (22.21)	129 (77.79)	
Current smoker	2,701 (44.83)	1,066 (37.85)	1,635 (62.15)		214 (5.97)	24 (25.21)	160 (74.79)	
Alcohol consumption				0.263				<.0001
No	201 (2.95)	79 (38.77)	122 (61.22)		464 (10.18)	212 (43.03)	252 (56.97)	
Yes	6,123 (97.05)	2,182 (34.30)	3,941 (65.70)		3,537 (89.82)	1,005 (29.68)	2,432 (70.32)	
Aerobic activity				0.223				0.254
No	4,008 (63.30)	1,451 (35.08)	2,557 (64.92)		2,643 (65.73)	888 (30.34)	1,775 (69.66)	
Yes	2,316 (36.70)	810 (33.33)	1,506 (66.67)		1,358 (34.27)	429 (32.36)	909 (67.64)	
Muscle strengthening activity				0.242				0.969
No	4,651 (73.63)	1,681 (34.92)	2,970 (65.08)		3,528 (87.71)	1,167 (31.05)	2,361 (68.95)	

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Table 1 continued

Yes	1,673 (26.37)	580 (33.08)	1,093 (66.92)		473 (12.29)	160 (30.95)	323 (69.05)	
BMI				<.0001				<.0001
Underweight	113 (1.93)	23 (19.02)	90 (80.98)		166 (4.22)	10 (14.14)	137 (85.86)	
Normal	1,934 (29.94)	557 (27.12)	1,377 (72.88)		1,869 (47.18)	438 (21.87)	1,431 (78.13)	
Overweight	1,733 (27.61)	602 (33.77)	1,131 (66.23)		890 (22.09)	164 (35.11)	566 (64.89)	
Obese	2,544 (40.52)	1,079 (41.02)	1,465 (58.98)		1,076 (26.51)	166 (46.64)	550 (53.36)	
Hypertension				<.0001				<.0001
No	4,639 (74.63)	1,531 (31.96)	3,108 (68.04)		3,252 (82.90)	168 (28.05)	2,294 (71.95)	
Yes	1,685 (25.37)	730 (41.70)	955 (58.30)		749 (17.10)	169 (45.53)	390 (54.47)	
Hypercholesterolemia				<.0001				<.0001
No	5,469 (87.19)	1,852 (32.59)	3,617 (67.41)		3,423 (86.67)	117 (28.18)	2,406 (71.82)	
Yes	855 (12.81)	409 (46.96)	446 (53.04)		578 (13.33)	160 (49.58)	278 (50.42)	
Family history of diabetes				<.0001				0.579
No	5,045 (79.35)	1,739 (32.70)	3,306 (67.30)		3,086 (76.91)	103 (30.79)	2,083 (69.21)	
Yes	1,279 (20.65)	522 (41.09)	757 (58.91)		915 (23.09)	114 (31.87)	601 (68.13)	
Sleep duration (hours)				0.069				0.0002
< 6	738 (11.62)	282 (36.32)	456 (63.68)		562 (14.49)	123 (39.68)	339 (60.32)	
6-8	5,167 (82.16)	1,850 (34.59)	3,317 (65.41)		3,083 (76.56)	106 (29.91)	2,087 (70.09)	
≥9	419 (6.22)	129 (28.90)	290 (71.10)		356 (8.95)	118 (26.69)	258 (73.31)	
Perceived stress				0.553				0.008
None/Low	4,513 (70.82)	1,633 (34.68)	2,880 (65.32)		2,743 (67.68)	115 (32.51)	1,798 (67.49)	
Moderate/High	1,811 (29.18)	628 (33.83)	1,183 (66.17)		1,258 (32.32)	112 (27.94)	886 (72.06)	
Occupation				<.0001				<.0001
White collar	2,774 (44.48)	845 (29.50)	1,929 (70.50)		1,527 (38.26)	111 (19.16)	1,216 (80.84)	
Pink collar	859 (14.05)	317 (36.50)	542 (63.50)		1,263 (32.68)	103 (36.87)	770 (63.13)	
Green collar	356 (4.20)	163 (44.57)	193 (55.43)		309 (5.45)	119 (52.94)	140 (47.06)	
Blue collar	2,335 (37.27)	936 (38.40)	1,399 (61.60)		902 (23.61)	114 (37.15)	558 (62.85)	
Work schedule				0.998				0.290
Fixed	5,801 (92.25)	2,060 (34.43)	3,741 (65.57)		3,826 (32.11)	115 (30.83)	2,571 (69.17)	
Shift	523 (7.75)	201 (34.44)	322 (65.56)		175 (22.05)	112 (35.09)	113 (64.91)	
Participants		2,261 (34.43)	4,063 (65.57)			1,617 (31.04)	2,684 (68.96)	

*Unless otherwise stated, unweighted frequency (weighted %) are shown.

†P value comparing prediabetes with normoglycemia

Table 2. General characteristics of the study population according to working hours per week , KNHANES 2010-2017

	Men (N=6,324)				Women (N=4,001)				p-value
	40 hrs	41-52 hrs	>52 hrs	p-value	40 hrs	41-52 hrs	>52 hrs	p-value	
	N (%)	N (%)	N (%)		N (%)	N (%)	N (%)		
Age (years)				<.0001				<.0001	
30-39	444 (22.67)	820 (41.31)	702 (36.02)		372 (35.53)	446 (44.41)	176 (20.06)		
40-49	481 (22.78)	804 (38.88)	731 (38.34)		401 (30.75)	490 (39.41)	350 (29.84)		
50-59	351 (22.13)	592 (36.99)	626 (40.88)		242 (20.61)	334 (35.34)	544 (44.05)		
≥60	123 (15.66)	267 (35.32)	383 (49.02)		71 (14.14)	104 (35.47)	271 (50.39)		
Education				<.0001				<.0001	
Elementary School	48 (10.13)	169 (33.71)	263 (56.16)		84 (12.00)	156 (37.23)	358 (50.77)		
Middle school	64 (12.65)	201 (36.98)	275 (50.37)		62 (14.79)	166 (32.69)	249 (52.52)		
High school	396 (18.74)	780 (37.96)	907 (43.30)		413 (26.86)	775 (38.06)	520 (35.08)		
University degree or above	891 (27.00)	1,333 (40.64)	997 (32.36)		527 (39.44)	777 (43.76)	214 (16.80)		
Total household income				<.0001				<.0001	
Low	38 (16.03)	97 (36.36)	130 (47.61)		56 (21.14)	133 (38.21)	130 (40.65)		
Middle-low	234 (16.57)	539 (36.83)	671 (46.60)		201 (22.13)	459 (38.21)	382 (39.66)		
Middle-high	454 (21.04)	888 (41.13)	830 (37.83)		373 (28.63)	492 (37.81)	444 (33.56)		
High	673 (26.88)	959 (38.67)	811 (34.45)		457 (31.06)	490 (41.32)	385 (27.62)		
Smoking status				0.0003				0.207	
Never smoker	288 (23.71)	512 (41.10)	450 (35.19)		997 (27.99)	1,416 (39.05)	1,211 (32.96)		
Former smoker	578 (24.17)	908 (38.77)	887 (37.06)		41 (24.07)	44 (44.36)	48 (31.57)		
Current smoker	533 (19.72)	1,063 (38.31)	1,105 (41.97)		48 (22.70)	44 (37.19)	82 (40.11)		
Alcohol consumption				0.009				0.002	
No	24 (13.30)	76 (37.13)	101 (49.57)		95 (20.48)	178 (39.32)	191 (40.20)		
Yes	1,375 (22.35)	2,407 (39.09)	2,341 (38.56)		991 (28.29)	1,396 (39.18)	1,150 (32.53)		
Aerobic activity				0.104					
No	866 (21.83)	1,547 (38.19)	1,595 (39.98)		662 (25.15)	1,042 (39.47)	939 (35.38)	0.0001	
Yes	533 (22.52)	936 (40.50)	847 (36.98)		424 (31.99)	432 (38.65)	402 (29.36)		
Muscle strengthening activity				0.005				0.385	
No	980 (21.21)	1,809 (38.70)	1,862 (40.09)		948 (27.34)	1,375 (38.89)	1,205 (33.77)		
Yes	419 (24.54)	674 (39.96)	580 (35.50)		138 (28.56)	199 (41.32)	136 (30.12)		
BMI				0.548				<.0001	
Underweight	22 (19.73)	41 (37.30)	50 (42.97)		50 (28.13)	66 (46.74)	40 (25.13)		
Normal	405 (21.00)	760 (38.59)	769 (40.41)		578 (31.10)	748 (39.54)	543 (29.36)		
Overweight	415 (23.76)	655 (38.80)	663 (37.44)		217 (24.53)	344 (39.30)	329 (36.17)		
Obese	557 (21.86)	1,027 (39.60)	960 (38.54)		241 (23.43)	306 (37.28)	429 (39.29)		

Table 2 Continued

Hypertension				0.163			<.0001	
No	1,024 (22.07)	1,844 (39.75)	1,771 (38.18)		947 (29.03)	1,290 (39.70)	1,015 (31.27)	
Yes	375 (22.13)	639 (36.93)	671 (40.94)		139 (20.06)	184 (36.75)	326 (43.19)	
Hypercholesterolemia				0.027				0.005
No	1,187 (21.52)	2,149 (39.13)	2,133 (39.35)		967 (28.28)	1,353 (39.34)	1,103 (32.38)	
Yes	212 (25.93)	334 (38.36)	309 (35.71)		119 (22.34)	121 (38.25)	238 (39.41)	
Family history of diabetes				0.549				0.033
No	1,103 (21.75)	1,991 (39.18)	1,951 (39.07)		799 (26.53)	1,211 (39.04)	1,076 (34.43)	
Yes	296 (23.38)	492 (38.47)	491 (38.15)		287 (30.69)	363 (39.68)	265 (29.63)	
Sleep duration (hours)				<.0001				0.004
< 6	120 (16.41)	256 (36.01)	362 (47.58)		128 (22.88)	109 (38.82)	225 (38.30)	
6-8	1,182 (22.74)	2,070 (39.52)	1,915 (37.74)		836 (27.65)	1,223 (39.06)	1,024 (33.29)	
≥9	97 (24.00)	157 (38.20)	165 (37.80)		122 (33.60)	142 (40.91)	92 (25.49)	
Perceived stress				<.0001				0.005
None/Low	1,083 (23.75)	1,785 (39.25)	1,645 (37.00)		788 (29.16)	1,076 (39.03)	879 (31.81)	
Moderate/High	316 (18.04)	698 (38.51)	797 (43.45)		298 (24.00)	398 (39.53)	462 (36.47)	
Occupation				<.0001				<.0001
White collar	873 (30.54)	1,200 (43.04)	701 (26.42)		665 (43.28)	1,072 (43.74)	190 (12.98)	
Pink collar	130 (16.12)	252 (28.51)	477 (55.37)		168 (13.42)	119 (33.54)	676 (53.04)	
Green collar	25 (6.30)	132 (34.54)	199 (59.16)		17 (4.22)	124 (41.57)	168 (54.21)	
Blue collar	371 (16.02)	899 (38.73)	1,065 (45.25)		236 ()	159 ()	307 ()	
Work schedule				<.0001				0.283
Fixed	1,334 (22.84)	2,297 (39.09)	2,170 (38.07)		1,034 (27.20)	1,507 (39.42)	1,285 (33.38)	
Shift	65 (13.09)	186 (38.39)	272 (48.52)		52 (33.35)	107 (34.66)	56 (31.99)	
Participants	1,399 (22.08)	2,483 (39.03)	2,442 (38.89)		1,086 (27.49)	1,574 (39.19)	1,341 (33.32)	

*Unless otherwise stated, unweighted frequency (weighted %) are shown.

Association between long working hours and pre-diabetes

Results from the logistic regression analysis are shown in Table 3. In univariate logistic regression analyses, long working hours was significantly associated with increased odds of having pre-diabetes in both men and women. Compared with the individuals who worked 40 hours, the ORs of pre-diabetes for the those who belong to the >52 hours category were 1.37 (95% CI 1.17-1.61; p for trend <0.0001) and 1.54 (95% CI 1.25-1.88; p for trend <0.0001) for men and women, respectively. For women, the positive association between the working hours and pre-diabetes was no longer significant after controlling for age, with OR of 1.06 (95% CI 0.84-1.32). In the case of men, those who worked >52 hours were 1.22 times more likely to have pre-diabetes after adjusting for covariates (multivariable-adjusted Odds Ratio (OR): 1.40; 95% Confidence Interval (CI): 1.03-1.46; P for trend 0.017). Age, smoking status, hypercholesteremia, family history of diabetes and sleep duration were also found to considerably increase the risk of pre-diabetes in men, but there were no statistically significant differences based on educational level, monthly household income, alcohol consumption, muscle strengthening activity, hypertension, perceived stress, occupation and work schedule.

Table 4 presents the ORs for subgroup analyses by age and work-related characteristics. We did not observe a significant interaction between the number of hours worked per week and age (Men:P for interaction =0.309) nor between work schedule and working hours (Men: P for interaction 0.864). The relationship between long working hours and pre-diabetes was more pronounced among male shift workers, albeit not statistically significantly, (41-52 hrs: aOR= 1.64, 95% CI: 0.77-3.47; >52 hrs: aOR= 1.64, 95% CI: 0.78-3.44; p for interaction=0.864). In the subgroup analysis by occupational categories, male workers who worked in blue-collar occupation were likely to have pre-diabetes as their average weekly working hours increased, after adjustment for all covariates. The adjusted ORs were 1.13 (95% CI 0.84-1.53) and 1.54 (95% CI 1.15-2.06) for the 41-52 hrs and >52 hrs categories, respectively (p for trend= 0.041). However, the interaction effect by occupational categories was not statistically significant (p for interaction=0.146).

Table 3. Results of the logistic regression analysis for the association between long working hours and pre-diabetes (HbA1c 5.7-6.4%)

	Case	Participants	Crude			Model 1			Model 2		
			OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Men (N=5,536)											
Working hours per week (hours)											
40	447	1,399	1.00			1.00			1.00		
41-52	867	2,483	1.09	0.93-1.29	0.278	1.10	0.93-1.29	0.279	1.07	0.90-1.27	0.477
>52	947	2,442	1.37	1.17-1.61	0.0001	1.31	1.11-1.55	0.001	1.22	1.03-1.46	0.026
P for trend				<0.0001			0.001			0.017	
Women (N=5,147)											
Working hours per week (hours)											
40	298	1,086	1.00			1.00			1.00		
41-52	492	1,574	1.11	0.91-1.35	0.307	0.98	0.80-1.20	0.84	0.89	0.72-1.12	0.338
>52	527	1,341	1.54	1.25-1.88	<0.0001	1.06	0.84-1.32	0.64	0.90	0.70-1.15	0.405
P for trend				<0.0001			0.601			0.436	

Note: OR, Odds ratio; CI, confidence interval;

Model 1 adjusted for age

Model 2 adjusted for age, educational attainment, total household income, obesity, smoking status, alcohol consumption, participation in aerobic activity, muscle strengthening activity, hypertension, hypercholesterolemia, family history of diabetes, sleep duration, perceived stress, occupation, work schedule

Table 4. Results of subgroup analysis of association between hba1c and working hours by age and work characteristics

Characteristics	Men				Women					
	40 hrs	Odds ratio (95% CI)		p for trend	p for interaction	40 hrs	Odds ratio (95% CI)		p for trend	P for interaction
		41-52 hrs	>52 hrs				41-52 hrs	>52 hrs		
Occupational categories					0.146					0.442
White collar	1.00	1.04 (0.83-1.30)	1.06 (0.82-1.38)	0.664		1.00	1.14 (0.82-1.60)	0.78 (0.48-1.27)	0.619	
Pink collar	1.00	1.22 (0.72-2.06)	0.99 (0.60-1.65)	0.714		1.00	0.62 (0.39-0.98)	0.77 (0.50-1.19)	0.706	
Green collar	1.00	0.52 (0.16-1.65)	0.90 (0.32-2.55)	0.247		1.00	1.42 (0.45-4.45)	0.94 (0.30-2.93)	0.309	
Blue collar	1.00	1.13 (0.84-1.53)	1.54 (1.15-2.06)	0.001		1.00	0.89 (0.58-1.35)	0.93 (0.59-1.45)	0.769	
Work schedule					0.864					0.202
Fixed	1.00	1.04 (0.87-1.25)	1.21 (1.01-1.45)	0.031		1.00	0.85 (0.68-1.06)	0.87 (0.68-1.11)	0.302	
Shift	1.00	1.64 (0.77-3.47)	1.64 (0.78-3.44)	0.317		1.00	2.71 (0.88-8.30)	2.57 (0.80-8.25)	0.121	
Age (years)					0.309					0.978
30-39	1.00	1.31 (0.94 to 1.83)	1.44 (1.01 to 2.06)	0.047		1.00	0.79 (0.48 to 1.29)	0.79 (0.39-1.58)	0.451	
40-49	1.00	0.89 (0.67 to 1.19)	1.20 (0.89 to 1.61)	0.124		1.00	0.89 (0.62-1.31)	0.81 (0.54-1.23)	0.327	
50-59	1.00	1.05 (0.76 to 1.47)	1.11 (0.80 to 1.55)	0.529		1.00	0.95 (0.64-1.39)	1.02 (0.69-1.52)	0.828	
≥60	1.00	1.29 (0.77 to 2.17)	1.12 (0.68 to 1.87)	0.079		1.00	0.94 (0.46-1.92)	0.82 (0.42-1.62)	0.485	

1 DISCUSSION

2 In this population-based study of Korean working adults without diabetes, we found that men
3 who worked over 52 hours per week exhibited 22% increased risk of pre-diabetes than did
4 those who worked 40 hours per week. This association was robust to adjustments for socio-
5 demographic variables and lifestyle factors, such as obesity, participation in aerobic and
6 muscle strengthening activity, smoking, and alcohol consumption and other covariates.
7 Importantly, we found that the increased odds of pre-diabetes associated with long working
8 hours was – albeit not statistically significant – more pronounced among workers of blue collar
9 occupations and shift workers. These findings are in line with the evidence from a prospective
10 study conducted in Japan which found that long working hours are related to the risk of incident
11 diabetes among shift workers.²² Further studies with larger sample sizes are warranted to
12 explore whether the lack of statistical significance observed is a results of sample size, or
13 reflects a true lack of association. Additionally, assessment of additive interaction between
14 long working hours and lifestyle factors would be a fruitful venue for further research for more
15 in depth understanding of the impacts of such interaction.

16 In the present study, the prevalence of pre-diabetes in the Korean working population was
17 34.4% and 31.0% for men and women, respectively. These prevalence estimates are
18 comparable to general population estimates reported in the U.S²³, U.K²⁴ and those of other
19 Asian countries.²⁵ Several previous studies have yielded prevalence estimates for pre-
20 diabetes in Korea. Using the HbA1c cutoff, pre-diabetes prevalence in 2011 was reported to
21 be 38.3% (Men: 41%; women: 35.7%) in a community-based cross-sectional study of Korean
22 adults aged 30 years or over.²⁶ Another Korean study reported a pre-diabetes prevalence of
23 26.1% in men and 20.5% according to American diabetes association criteria.²⁷ However, this
24 study was based on a sample from rural areas. Pre-diabetes is a well-recognized risk factors
25 for future diabetes, that gives rise to micro- and macrovascular complications and have
26 enormous social and economic burden^{28, 29}; increased attention needs to be paid to the high
27 prevalence of pre-diabetes in Korea.

1 We are not aware of other studies that has reported a relationship between long working
2 hours and pre-diabetes, although our findings are comparable with a meta-analysis showing
3 that long working hours is associated with the incidence of type 2 diabetes among individuals
4 from low socioeconomic status groups.¹² Another study have also reported a similar finding,
5 indicating that extended working hours is positively correlated with non-insulin dependent
6 diabetes mellitus in men.³⁰ However, our results conflict with a previous study that found
7 relative risks of T2DM significantly decreased with an increase in hours of work per day.¹⁴

8 The mechanisms underlying the association between long working hours and pre-diabetes
9 are yet unknown. It is likely that a similar mechanism to that of diabetes could be responsible
10 for the observed findings. Plausible explanations are that longer working hours impacts pre-
11 diabetes risk via their association with behavioural risk factors. As shown in this study, prior
12 research has indicated that working longer than recommended hours is linked to many
13 behavioural risk factors, such as binge drinking ^{31, 32} and low physical activity ³³, possibly
14 because individuals feel that they lack the time to engage in leisure-time physical activity due
15 to demands and responsibilities at work. In the present study, working hour–pre-diabetes
16 association attenuated but remained statistically significant in men after adjustment for
17 behavioural risk factors. As such, conventional risk factors for pre-diabetes are likely to explain
18 only part of the association between long working hours and pre-diabetes.

19 Meanwhile, there has been a proposition that extended working hours are related to
20 cortisol secretion ³⁴, a known risk factor for impaired glucose metabolism.³⁵ Cortisol induces
21 the formation of glucose in the liver and have insulin-antagonistic effects in the peripheral
22 tissues; both processes have the potential to contribute to risk of hyperglycemia. Furthermore,
23 individuals work longer hours are more often exposed to harmful psychological factors in the
24 work environment, such as job strain ^{36, 37} and effort-reward imbalance ³⁸, which are known to
25 be associated with subsequent elevation of Hba1c.³⁹ As such, stress-related mechanisms that
26 trigger dysregulation of neuroendocrine pathways, might be a potentially promising areas for
27 future research studying the differences in risk of pre-diabetes according to work hours.

28 The present study has several strengths. First, this study is based on a nationally

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3 1 representative survey, and to the best of our knowledge, this is the first report of an association
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5 2 between long working hours and pre-diabetes among individuals without diabetes. Second,
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7 3 blood samples were collected using standardized laboratory procedures, ensuring an accurate
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9 4 estimate of HbA1c. Finally, we were able to control for several important confounding variables,
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11 5 such as sleep duration and perceived control. However, this study is not without limitations.
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13 6 Our analyses are based on data from observational studies and, as such, preclude direct
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15 7 causal inference. Information on working hours and other covariates were self-reported and
16
17 8 thus subject to recall bias. Moreover, we cannot exclude the possibility that the results were
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19 9 affected by residual confounding caused by imprecisely measured covariates or some other
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21 10 unmeasured occupational factors, such as job strain and job satisfaction. Working hours was
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23 11 measured at a single point in time that might not represent long-term exposure. In future
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25 12 studies, use of repeated measurements is needed to characterize longitudinal relation
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27 13 between long working hours and pre-diabetes.
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33 **CONCLUSIONS**

34 16 In conclusion, extended working hours in men was significantly correlated with the odds
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36 17 of pre-diabetes, independent of conventional risk factors. No statistically
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38 18 significant relationship was found for women. Our results suggest prolonged working hours
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40 19 are related to glucose metabolism among non-diabetic male workers in Korea. Additional
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42 20 large-scale longitudinal studies are needed to verify these findings.
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50 23 **Ethical statement:** The survey protocols for the KNHANES were approved by the Institutional Review
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52 24 Board of the Korea Centers for Disease Control and Prevention (IRB No. 2013-07CON-03-4C, 2013-
53
54 25 12EXP-03-5C, and 2015-01-02-6C), and informed consent was obtained from all participants.
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56 27 **Conflict of interest:** The authors have no conflict of interest to declare.
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4 commercial, or not-for-profit sectors.
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9 **Data sharing statement:** Data used in this study are available from the KNHANES official website
10 (<http://knhanes.cdc.go.kr/>).
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15 **Author contributions:** BYS, MK, GRK contributed to the conception and design of the study. BYS,
16 MK, GRK, ECP contributed to analyses and interpretation of the data, BYS, MK, GRK drafted the
17 manuscript. All authors read and approved the final manuscript.
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17 15 effort–reward imbalance model. *International journal of environmental research and*
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22 18 **Figure legends**

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24 19 Figure 1 Flowchart of participant selection
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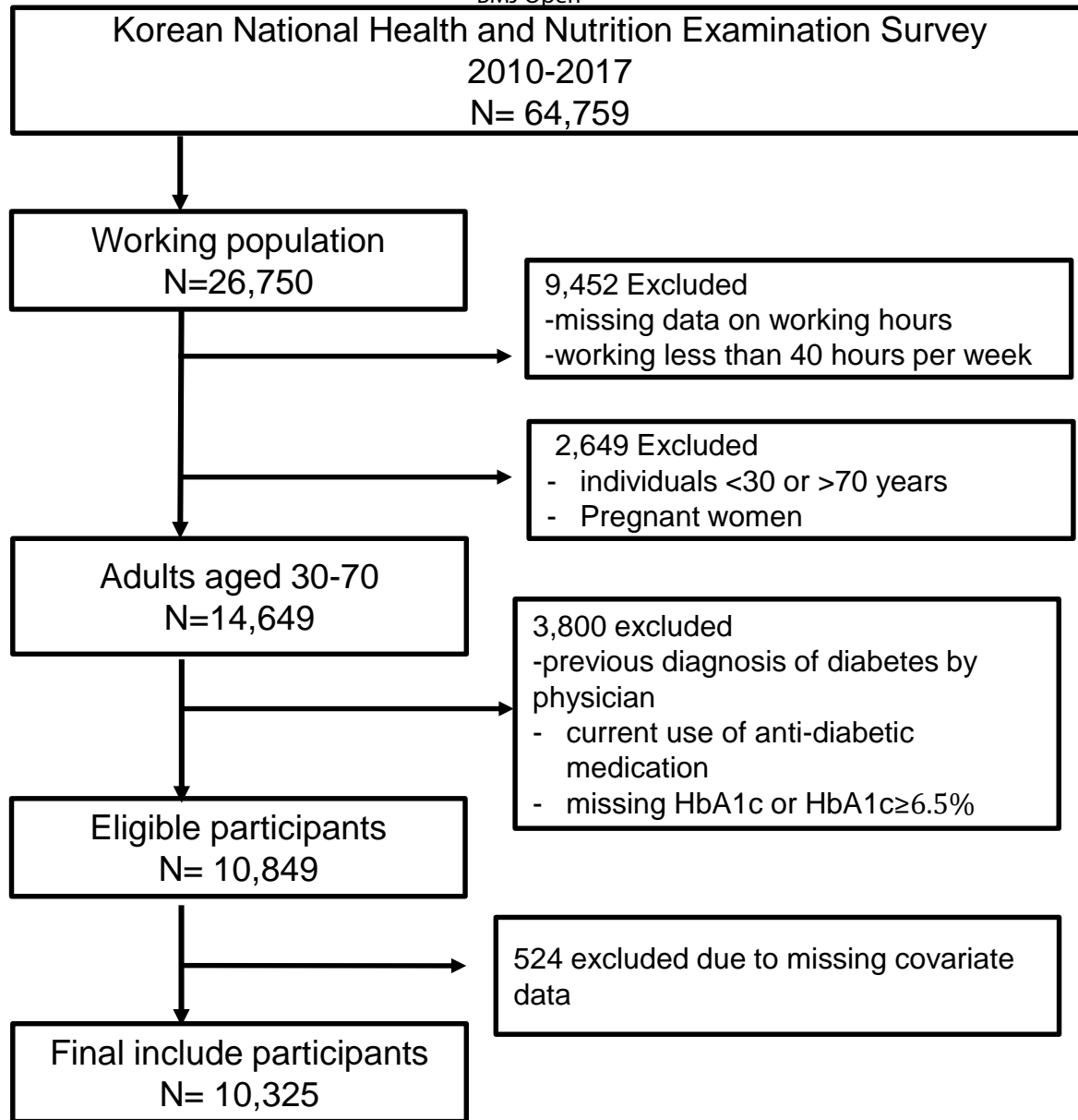


Figure 1 Flow chart of participant selection

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STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up and data collection	4,5,6
		(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	
Participants	6	<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	4
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	4,5,6
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Data sources/measurement	8*	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4,5,6
		For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	6,7
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5,6,7
		(a) Describe all statistical methods, including those used to control for confounding	
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	
Statistical methods	12	<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	6,7
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8,9,10,11,12
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	7,14
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13,14
		(b) Report category boundaries when continuous variables were categorized	5,6
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13,15
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17,18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16, 17
Generalisability	21	Discuss the generalisability (external validity) of the study results	16,17
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Cross-sectional study of the association between long working hours and pre-diabetes: 2010-2017 Korea National Health and Nutrition Examination Survey

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4 **1 Cross-sectional study of the association between long working hours and pre-**
5 **2 diabetes: 2010-2017 Korea National Health and Nutrition Examination Survey**

6
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51 38 **Word counts**

52 39 **Abstract:** 273 words

53 40 **Manuscript:** 3,065 words

54 41 **Tables:** 4

55 42 **Figures:** 1
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1 ABSTRACT

2 **OBJECTIVE:** Long working hours have been shown to raise the risk of various health outcomes.
3 However, epidemiological evidence has shown inconsistent result in relation to type 2 diabetes (T2DM)
4 and the association between long working hours and pre-diabetes among non-diabetic adults remains
5 largely unexplored. We thus aimed to investigate whether long working hours were linked with pre-
6 diabetes as determined by glycated hemoglobin (HbA1c) level.

7
8 **DESIGN:** Cross-sectional survey

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10 **PARTICIPANTS:** This study included 6,324 men and 4,001 women without diabetes from the 2010-
11 2017 Korean National Health and Nutrition Examination Survey (KNHANES).

12
13 **PRIMARY OUTCOME MEASURES:** The study outcome of interest was pre-diabetes, defined as
14 HbA1c values 5.7-6.4%

15
16 **RESULTS:** Logistic regression was performed to obtain the odds ratios (OR) for pre-diabetes according
17 to categories of work hour (40 hours/week, 41-52 hours/week, >52 hours/week), after adjusting for
18 relevant covariates. Of the 10,325 eligible participants, 2,261 (34.4%) men and 1,317 (31.0%) women
19 had pre-diabetes. No statistically significant relationship was found for women. In men,
20 extended working hours (>52 hours per week) was associated with an increased likelihood of pre-
21 diabetes, after adjustment for age, educational attainment, monthly household income, life-style related
22 factors, perceived stress, family history of diabetes, hypertension, hypercholesterolemia and other
23 covariates (adjusted OR=1.22; 95% confidence interval=1.03-1.46). In the subgroup analysis by
24 occupational categories, the association was only apparent among men in blue-collar worker groups.

25
26 **CONCLUSION:** Extended working hours were significant related to the increased risk of pre-diabetes
27 in men, with no statistically significant association observed for women. Further subgroup analysis by
28 occupational categories revealed that the increased odds of pre-diabetes associated with long working
29 hours was only apparent among male workers of blue collar occupations and shift workers.

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31 **Keywords:** Pre-diabetes, Hba1c, working hours, Glucose metabolism

32 33 34 35 36 37 38 39 40 **Strengths and limitations of this study**

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- As far as we are aware, this is the first report of an association between long working hours and pre-diabetes among individuals without diabetes using a nationally representative sample of Korean adults. We further compared associations by occupational categories.
 - This study controlled for a range of factors that are known to affect HbA1c levels.
 - Our analyses are based on cross-sectional data and, as such, preclude direct causal inference.

1 INTRODUCTION

2 Pre-diabetes, defined as an intermediate state of hyperglycemia with glycemic parameters
3 above normal but below the diagnostic threshold for diabetes is considered an important risk
4 factor for β -cell dysfunction¹ and the development of type 2 diabetes mellitus (T2DM).²
5 According to the 2012 projection estimates, prevalence of pre-diabetes will continue to rise,
6 and it is estimated that by 2030 over 470 million people will have pre-diabetes globally.³
7 Approximately 70% of individuals diagnosed with pre-diabetes are expected to progress to
8 T2DM within 10 years.⁴ Given the high incidence rate of diabetes among pre-diabetic adults,
9 identification of the modifiable risk factors of pre-diabetes in the general population is thus
10 essential to effectively prevent or delay the onset of diabetes and its associated complications.

11 South Korea has one of the longest work hours among member states of the Organization
12 for Economic Cooperation and Development (OECD), with people spending on average 2,069
13 hours at work annually compared to the OECD average of 1,764 hours.⁵

14 Several studies have assessed long working hours in relationship with the risk of various
15 health outcomes, including coronary heart disease^{6,7}, cognitive function⁸, as well as a high
16 prevalence of anxiety⁹ and sleeping disturbances.¹⁰ However, epidemiological evidence have
17 shown inconsistent result in relation to diabetes¹¹⁻¹⁴ and the association between long working
18 hours and pre-diabetes in populations without diabetes remains largely unexplored. In a
19 meta-analysis of epidemiological studies conducted in USA, Europe, Japan, and Australia,
20 Kivimäki et al. reported a prospective association between long working hours and the
21 incidence of diabetes, but only among employees with a low socioeconomic position.¹²
22 Similarly, one study of Chinese male workers found that the risk of developing diabetes
23 increased with longer hours of overtime work per week.¹³ In contrast, in a study of Japanese
24 male workers, the relative risk of type 2 diabetes significantly decreased among those who
25 worked over 10 hours a day compared with those who worked 7 to 8 hours.¹⁴ To fill this
26 evidence gap, we investigated the relationship between weekly working hours and the pre-
27 diabetes using a cross-sectional survey of 10,325 workers in South Korea.

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2 **METHODS**

3 **Study population**

4 Data were drawn from the 2010-2017 Korean National Health and Nutrition Examination
5 Survey (KNHANES). KNHANES is an ongoing population based, cross-sectional study which
6 is designed to assess the health and nutritional status of people residing in South Korea.¹⁵
7 The survey's sampling strategy was designed to be representative of the non-institutionalized
8 civilian population aged 1 year or over which was selected using a complex, multistage,
9 stratified sampling design. Of the 64,759 participants (Men : 29,458, Women : 35,301) who
10 participated in the 2010-2017 survey, 26,750 reported as being economically active and
11 therefore were eligible to be asked job-related modules and 26,696 provided valid responses
12 concerning weekly work hours. We restricted analyses to individuals working 40
13 hours or more per week, as participants who worked for less than 40 hours are likely to do so
14 due to health reasons (N=17,298). Additionally, KNHANES participants under 30 or >70 years
15 old and pregnant women were excluded from the analysis (N=2,649). We also excluded those
16 who reported a previous clinical diagnosis of diabetes made by a physician or taking insulin
17 or anti-diabetic medication or missing data on Hba1c, or Hba1c values greater than 6.5%
18 (N=3,800). Finally, we excluded participants with missing covariate data (N=524), yielding a
19 final sample of 10,325 participants (Men : 6,324 , Women : 4,001) (See Figure 1).

20

21 **Patient and Public Involvement (PPI)**

22 No patients were included in the design and planning of the study. Including PPI statements
23 aligns closely with BMJ Open's values of transparency and inclusiveness. We hope that
24 including PPI statements in all articles is the first step of many for BMJ Open in encouraging
25 patient involvement.

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1 **Measures**

2 **Definition of Pre-diabetes**

3 The main study outcome was glycated hemoglobin (HbA1c). HbA1c is a form of hemoglobin
4 in which glucose is attached to its β -chain after exposure to high plasma levels of glucose. As
5 such, it is used as an integrated index of long-term serum glucose regulation.¹⁶ Fasting bloods
6 samples were collected during a medical examination and HbA1c levels were measured via
7 high performance liquid chromatography (HLC-723G7; Tosoh, Tokyo, Japan). Participants
8 were identified as being normoglycemic if they had a HbA1c level below 5.7%; HbA1c level
9 between 5.7 and 6.4 percent were indicative of pre-diabetes according to the 2018 American
10 Diabetes Association (ADA) standards of care in diabetes.¹⁷ Previous research has indicated
11 that HbA1c and fasting blood glucose (FBG) are equally in the detection of Type 2 diabetes.¹⁸
12 Also, HbA1c has several advantages to the FBS, including the ability to use non-fasting blood
13 samples, greater pre-analytical stability, and less day-to-day perturbations during periods of
14 stress and illness.¹⁹

17 **Working hours**

18 In the KNHANES, participants were asked about their working hours using the following
19 question: "During the last month, how many hours on average in a week did you work,
20 including unpaid overtime work (excluding meal time)?" In Korea, statutory weekly work hours
21 based on the Labor Standards Act (LSA) are 40 hours per week and 8 hours per day. The
22 working hours stipulated in LSA Article 50 may be extended up to additional 12 hours by
23 agreement between the parties. Therefore, in the current study we defined long working hours
24 as working beyond the legal threshold of 52 hours. Participants reported their working hours
25 as a continuous variable, and this was further categorized as follows: 40 hours, 41-52 hours,
26 or >52 hours per week.

1 **Covariates**

2 Data on socio-demographic characteristics, lifestyle- and health-related factors were collected
3 using interviewer-administered standardized questionnaires. Age was categorized into 30–39,
4 40–49, 50–59, and ≥ 60 years. Participants were categorized by educational attainment
5 (elementary school, middle school, high school, and university degree or above), monthly
6 household income quartiles, and occupational categories (white collar (managers,
7 professionals), pink collar (clerks, service, and sales workers), green collar (agricultural,
8 fishery or forestry workers) and blue collar (craft/trades workers, machine operators and
9 assemblers, and elementary manual workers)^{20 21}. Work schedules were assessed using the
10 following question: “Do you work mostly during the day time, or do you work at a different time
11 period?” Respondent who usually worked during the daytime (06:00-18:00), evening hours
12 (14:00-24:00), or night-time (21:00-08:00) were categorized as fixed schedule workers, while
13 those who worked 24-hours rotating shifts, split shifts, or irregular shifts were classified as shift
14 schedule workers.

15 Health-related behaviours included smoking status (Never smoker, former smoker, and
16 current smoker) alcohol consumption (Yes or no), muscle strengthening activity at least twice
17 a week (yes/no), participation in aerobic activity, defined as walking at least 10 minutes at a
18 time, for 30 minutes or more per day, on 5 or more per days during the 7 days preceding the
19 survey, and sleep duration (< 6 , 6-8, ≥ 9 hours). Body mass index (BMI [kg/m²]) was used to
20 determine obesity status and calculated based on respondent's self-reported height and
21 weight. A BMI of < 18.5 was considered underweight, a BMI > 18.5 and < 23.0 was considered
22 normal weight, a BMI greater than or equal to 23.0 and < 25.0 was considered overweight, and
23 a BMI ≥ 25 was considered obese. The level of perceived stress was measured using the
24 following question: “How stressed are you on a daily basis?” with possible answers ranging
25 from ‘None’ coded 0 to ‘High’ coded 4. Respondents were reclassified into low (none/low) and
26 high perceived stress (moderate/high). Hypercholesterolemia (yes/no) was defined as a
27 serum total cholesterol level ≥ 240 mg/dL or the use of lipid-lowering medications.
28 Hypertension (yes/no) was defined as a systolic blood pressure of 140 mmHg or higher,

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3 1 diastolic blood pressure of 90 mmHg or higher or on antihypertensive treatment. A family
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5 2 history of diabetes was ascertained by asking participants whether their first-degree relatives
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7 3 (parents or siblings) had ever been told they have diabetes (yes/no).
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5 **STATISTICAL ANALYSES**

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7 Statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).
8
9 The SAS survey procedure was applied to reflect the stratification and clustering of the
10
11 complex sampling design and sampling weights of the KNHANES and to ensure nationally
12
13 representative prevalence estimates. General characteristics of the study sample were
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15 described using frequency and weighted percentages. Chi-square test was used to compare
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17 participant characteristics across working hours and between normoglycemic and pre-diabetic
18
19 subjects. Multivariable logistic regression analysis was used to evaluate the association
20
21 between working hours and pre-diabetes status, and odds ratios (ORs) and 95% confidence
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23 interval (CI) were calculated after adjusting for socio-demographic and health-related
24
25 behavioural variables that showed significant association in univariate analysis and based on
26
27 clinical relevance. Additionally, we evaluated whether the association between long working
28
29 hours and pre-diabetes was dependent on age or work-related characteristics by testing
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31 interaction effects and conducting subgroup analyses. Interaction was assessed by including
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33 a cross-product interaction term (working hour×effect modifier variable) in the logistic
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35 regression model along with the main effect. All analyses were performed separately for men
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37 and women. All reported P values were based on 2-sided tests; statistical significance was set
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39 at $p < 0.05$.
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54 **RESULTS**

55 **General characteristics of the study population**

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57 Table 1 presents participants' general characteristics by HbA1c status in men and women. A
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59 total of 2,261 (34.43%) men and 1,317 (31.04%) women had pre-diabetes. Men who worked
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1 40 hours per week had the lowest pre-diabetes prevalence (30.92%), followed by those
2 working 41–52 hours (32.88%) and >52 hours (38.00%). Male workers with pre-diabetes were
3 also more likely to be older, work over 52 hours/week, have a lower level of education, to be
4 working in a manual occupations, obese, current smokers, sleep less than 6 hours and to have
5 a diagnosis of hypertension, hypercholesteremia and a family history of diabetes compared
6 with normoglycemic subjects. For women, we observed statistically significant differences in
7 prevalence of pre-diabetes for most characteristics, except for participation in aerobic activity,
8 muscle strengthening activity, family history of diabetes and work schedule.

9 Table 2 shows characteristics of study participants according to categories of working hours. A
10 total of 1,399 (22.08%) male participants reported 40 hours of work per week, 2,483 (39.03%)
11 reported 41–52 hours, and 2,442 (38.89%) reported more than 52 hours of work per week;
12 the corresponding values for women were 1,086 (27.49%), 1,574 (39.19%), and 1,341
13 (33.32%), respectively. Participants who worked more than 52 hours were more likely to be
14 older, have lower education, lower household income, higher self perceived stress, in blue-
15 collar occupation, and have shift work schedule compared to men who work 40 hours per
16 week. As regard health-related related variables, subjects who worked more than 52 hours
17 tended to be current smoker, non-drinker, have shorter sleep duration and less likely to
18 engage in muscle strengthening activity. Among women, no appreciable differences in
19 smoking status, muscle strengthening activity, and work schedule were apparent across
20 working hours per week.

Table 1. General characteristics of the study population by HbA1c status, KNHANES 2010-2017

	Men (N=6,324)				Women (N=4,001)			
	Total	Pre-diabetes N (%)	Normoglycemia N (%)	p-value	Total	Pre-diabetes N (%)	Normoglycemia N (%)	p-value
Working hours per week (hours)				0.0001				<.0001
40	1,399 (22.08)	447 (30.92)	952 (69.08)		1,086 (27.49)	288 (27.15)	788 (72.85)	
41-52	2,483 (39.03)	867 (32.88)	1,616 (67.12)		1,574 (39.19)	422 (29.21)	1,082 (70.79)	
>52	2,442 (38.89)	947 (38.00)	1,495 (62.00)		1,341 (33.32)	527 (36.40)	814 (63.60)	
Age group (years)				<.0001				<.0001
30-39	1,966 (34.77)	497 (24.41)	1,469 (75.59)		994 (26.69)	333 (14.97)	851 (85.03)	
40-49	2,016 (34.82)	687 (34.75)	1,329 (65.25)		1,241 (34.82)	333 (24.39)	928 (75.61)	
50-59	1,569 (23.31)	685 (43.40)	884 (56.59)		1,220 (28.79)	524 (46.11)	656 (53.89)	
≥60	773 (7.10)	392 (52.54)	381 (47.46)		546 (9.70)	307 (54.31)	249 (45.69)	
Education				<.0001				<.0001
Elementary School	480 (5.94)	227 (49.18)	253 (50.82)		698 (14.10)	339 (51.00)	339 (49.00)	
Middle school	540 (7.75)	239 (42.72)	301 (57.28)		477 (12.07)	211 (40.56)	266 (59.44)	
High school	2,083 (33.96)	816 (37.42)	1,267 (62.58)		1,508 (40.55)	525 (31.69)	1,013 (68.31)	
University degree or above	3,221 (52.35)	979 (29.60)	2,242 (70.40)		1,318 (33.28)	322 (18.33)	1,066 (81.67)	
Total household income				0.016				<.0001
Low	265 (3.59)	113 (44.21)	152 (55.79)		319 (7.07)	140 (42.38)	179 (57.62)	
Middle-low	1,444 (22.78)	549 (35.74)	895 (64.26)		942 (22.85)	344 (33.56)	598 (66.44)	
Middle-high	2,172 (35.26)	765 (34.22)	1,407 (65.78)		1,308 (34.11)	420 (30.06)	888 (69.94)	
High	2,443 (38.37)	834 (32.94)	1,609 (67.06)		1,432 (35.97)	413 (28.12)	1,019 (71.88)	
Smoking status				<.0001				0.019
Never smoker	1,250 (20.05)	365 (28.66)	885 (71.34)		3,624 (89.27)	1,229 (31.90)	2,395 (68.10)	
Former smoker	2,373 (35.12)	830 (33.37)	1,543 (66.63)		163 (4.76)	24 (22.21)	129 (77.79)	
Current smoker	2,701 (44.83)	1,066 (37.85)	1,635 (62.15)		214 (5.97)	24 (25.21)	160 (74.79)	
Alcohol consumption				0.263				<.0001
No	201 (2.95)	79 (38.77)	122 (61.22)		464 (10.18)	212 (43.03)	252 (56.97)	
Yes	6,123 (97.05)	2,182 (34.30)	3,941 (65.70)		3,537 (89.82)	1,005 (29.68)	2,432 (70.32)	
Aerobic activity				0.223				0.254
No	4,008 (63.30)	1,451 (35.08)	2,557 (64.92)		2,643 (65.73)	838 (30.34)	1,775 (69.66)	
Yes	2,316 (36.70)	810 (33.33)	1,506 (66.67)		1,358 (34.27)	429 (32.36)	909 (67.64)	
Muscle strengthening activity				0.242				0.969
No	4,651 (73.63)	1,681 (34.92)	2,970 (65.08)		3,528 (87.71)	1,167 (31.05)	2,361 (68.95)	

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Table 1 continued							
Yes	1,673 (26.37)	580 (33.08)	1,093 (66.92)		473 (12.29)	160 (30.95)	323 (69.05)
BMI				<.0001			<.0001
Underweight	113 (1.93)	23 (19.02)	90 (80.98)		166 (4.22)	10 (14.14)	137 (85.86)
Normal	1,934 (29.94)	557 (27.12)	1,377 (72.88)		1,869 (47.18)	438 (21.87)	1,431 (78.13)
Overweight	1,733 (27.61)	602 (33.77)	1,131 (66.23)		890 (22.09)	164 (35.11)	566 (64.89)
Obese	2,544 (40.52)	1,079 (41.02)	1,465 (58.98)		1,076 (26.51)	166 (46.64)	550 (53.36)
Hypertension				<.0001			<.0001
No	4,639 (74.63)	1,531 (31.96)	3,108 (68.04)		3,252 (82.90)	168 (28.05)	2,294 (71.95)
Yes	1,685 (25.37)	730 (41.70)	955 (58.30)		749 (17.10)	169 (45.53)	390 (54.47)
Hypercholesterolemia				<.0001			<.0001
No	5,469 (87.19)	1,852 (32.59)	3,617 (67.41)		3,423 (86.67)	117 (28.18)	2,406 (71.82)
Yes	855 (12.81)	409 (46.96)	446 (53.04)		578 (13.33)	160 (49.58)	278 (50.42)
Family history of diabetes				<.0001			0.579
No	5,045 (79.35)	1,739 (32.70)	3,306 (67.30)		3,086 (76.91)	103 (30.79)	2,083 (69.21)
Yes	1,279 (20.65)	522 (41.09)	757 (58.91)		915 (23.09)	114 (31.87)	601 (68.13)
Sleep duration (hours)				0.069			0.0002
< 6	738 (11.62)	282 (36.32)	456 (63.68)		562 (14.49)	123 (39.68)	339 (60.32)
6-8	5,167 (82.16)	1,850 (34.59)	3,317 (65.41)		3,083 (76.56)	106 (29.91)	2,087 (70.09)
≥9	419 (6.22)	129 (28.90)	290 (71.10)		356 (8.95)	118 (26.69)	258 (73.31)
Perceived stress				0.553			0.008
None/Low	4,513 (70.82)	1,633 (34.68)	2,880 (65.32)		2,743 (67.68)	115 (32.51)	1,798 (67.49)
Moderate/High	1,811 (29.18)	628 (33.83)	1,183 (66.17)		1,258 (32.32)	112 (27.94)	886 (72.06)
Occupation				<.0001			<.0001
White collar	2,774 (44.48)	845 (29.50)	1,929 (70.50)		1,527 (38.26)	111 (19.16)	1,216 (80.84)
Pink collar	859 (14.05)	317 (36.50)	542 (63.50)		1,263 (32.68)	103 (36.87)	770 (63.13)
Green collar	356 (4.20)	163 (44.57)	193 (55.43)		309 (5.45)	119 (52.94)	140 (47.06)
Blue collar	2,335 (37.27)	936 (38.40)	1,399 (61.60)		902 (23.61)	114 (37.15)	558 (62.85)
Work schedule				0.998			0.290
Fixed	5,801 (92.25)	2,060 (34.43)	3,741 (65.57)		3,826 (32.11)	115 (30.83)	2,571 (69.17)
Shift	523 (7.75)	201 (34.44)	322 (65.56)		175 (22.05)	112 (35.09)	113 (64.91)
Participants		2,261 (34.43)	4,063 (65.57)			1,617 (31.04)	2,684 (68.96)

*Unless otherwise stated, unweighted frequency (weighted %) are shown.
 †P value comparing prediabetes with normoglycemia

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Table 2. General characteristics of the study population according to working hours per week , KNHANES 2010-2017

	Men (N=6,324)				Women (N=4,001)				p-value
	40 hrs N (%)	41-52 hrs N (%)	>52 hrs N (%)	p-value	40 hrs N (%)	41-52 hrs N (%)	>52 hrs N (%)		
Age (years)				<.0001				<.0001	
30-39	444 (35.69)	820 (36.80)	702 (32.21)		372 (34.49)	446 (30.24)	176 (16.07)		
40-49	481 (35.91)	804 (34.68)	731 (34.33)		401 (38.94)	490 (35.01)	350 (31.18)		
50-59	351 (23.36)	592 (22.09)	626 (24.51)		242 (21.58)	344 (25.97)	544 (38.07)		
≥60	123 (5.04)	267 (6.43)	383 (8.95)		71 (4.99)	104 (8.78)	271 (14.68)		
Education				<.0001				<.0001	
Elementary School	48 (2.72)	169 (5.13)	263 (8.58)		84 (6.16)	156 (13.40)	358 (21.49)		
Middle school	64 (4.44)	201 (7.34)	275 (10.03)		62 (6.49)	166 (10.07)	249 (19.03)		
High school	396 (28.82)	780 (33.03)	907 (37.82)		413 (39.61)	715 (39.38)	520 (42.70)		
University degree or above	891 (64.02)	1,333 (54.50)	997 (43.57)		527 (47.74)	777 (37.15)	214 (16.78)		
Total household income				<.0001				<.0001	
Low	38 (2.60)	97 (3.34)	130 (4.39)		56 (5.44)	133 (6.89)	130 (8.63)		
Middle-low	234 (17.09)	539 (21.49)	671 (27.30)		201 (18.39)	459 (22.28)	382 (27.19)		
Middle-high	454 (33.59)	888 (37.15)	830 (34.31)		373 (35.53)	492 (32.91)	444 (34.67)		
High	673 (46.72)	959 (38.02)	811 (34.00)		457 (40.64)	690 (37.92)	385 (29.81)		
Smoking status				0.0003				0.207	
Never smoker	288 (21.54)	512 (21.12)	450 (18.15)		997 (90.90)	1,416 (88.95)	1,211 (88.30)		
Former smoker	578 (28.44)	908 (34.88)	887 (33.46)		41 (4.17)	44 (5.38)	48 (4.51)		
Current smoker	533 (40.02)	1,063 (44.00)	1,105 (48.39)		48 (4.93)	14 (5.67)	82 (7.19)		
Alcohol consumption				0.009				0.002	
No	24 (1.78)	76 (2.81)	101 (3.76)		95 (7.58)	178 (10.21)	191 (12.28)		
Yes	1,375 (98.22)	2,407 (97.19)	2,341 (96.24)		991 (92.42)	1,396 (89.79)	1,150 (87.72)		
Aerobic activity				0.104					
No	866 (62.56)	1,547 (61.92)	1,595 (65.10)		662 (60.13)	1,042 (66.20)	939 (69.80)	0.0001	
Yes	533 (37.44)	936 (38.08)	847 (34.90)		424 (39.87)	332 (33.80)	402 (30.20)		
Muscle strengthening activity				0.005				0.385	
No	980 (70.70)	1,809 (73.00)	1,862 (75.92)		948 (87.24)	1,375 (87.05)	1,205 (88.89)		
Yes	419 (29.30)	674 (27.00)	580 (24.08)		138 (12.76)	199 (12.95)	136 (11.11)		
BMI				0.548				<.0001	
Underweight	22 (1.72)	41 (1.84)	50 (2.13)		50 (4.32)	36 (5.03)	40 (3.18)		
Normal	405 (28.47)	760 (29.61)	769 (31.12)		578 (53.37)	448 (47.60)	543 (41.58)		
Overweight	415 (29.70)	655 (27.44)	663 (26.59)		217 (19.71)	144 (22.15)	329 (23.98)		
Obese	557 (40.11)	1,027 (41.11)	960 (40.16)		241 (22.60)	306 (25.22)	429 (31.26)		

Table 2 Continued

Hypertension				0.163			<.0001
No	1,024 (74.57)	1,844 (76.00)	1,771 (73.29)		947 (82.52)	290 (83.96)	1,015 (77.83)
Yes	375 (25.43)	639 (24.00)	671 (26.71)		139 (12.48)	84 (16.04)	326 (22.17)
Hypercholesterolemia				0.027			0.005
No	1,187 (84.96)	2,149 (87.411)	2,133 (88.24)		967 (89.16)	353 (86.99)	1,103 (84.23)
Yes	212 (15.04)	334 (12.59)	309 (11.76)		119 (10.84)	71 (13.01)	238 (15.77)
Family history of diabetes				0.549			0.033
No	1,103 (78.15)	1,991 (79.65)	1,951 (79.74)		799 (74.23)	211 (76.63)	1,076 (79.47)
Yes	296 (21.85)	492 (20.35)	491 (20.26)		287 (25.77)	63 (23.37)	265 (20.53)
Sleep duration (hours)				<.0001			0.004
< 6	120 (8.63)	256 (10.72)	362 (14.22)		128 (12.06)	99 (14.35)	225 (16.65)
6-8	1,182 (84.61)	2,070 (83.19)	1,915 (79.74)		836 (76.99)	223 (76.30)	1024 (76.50)
≥9	97 (6.76)	157 (6.09)	165 (6.04)		122 (10.95)	42 (9.35)	92 (6.85)
Perceived stress				<.0001			0.005
None/Low	1,083 (76.16)	1,785 (71.21)	1,645 (67.39)		788 (71.80)	276 (67.40)	879 (64.41)
Moderate/High	316 (23.84)	698 (28.79)	797 (32.61)		298 (28.20)	98 (32.60)	462 (35.39)
Occupation				<.0001			<.0001
White collar	873 (61.51)	1,200 (49.05)	701 (30.23)		665 (60.23)	272 (42.70)	190 (14.90)
Pink collar	130 (10.25)	252 (10.26)	477 (20.01)		168 (15.96)	19 (27.97)	676 (52.01)
Green collar	25 (1.20)	132 (3.72)	199 (6.39)		17 (0.83)	24 (5.78)	168 (8.87)
Blue collar	371 (27.04)	899 (36.97)	1,065 (43.37)		236 (22.98)	59 (23.55)	307 (24.22)
Work schedule				<.0001			0.283
Fixed	1,334 (95.41)	2,297 (92.38)	2,170 (90.33)		1,034 (94.20)	507 (95.77)	1,285 (95.41)
Shift	65 (4.59)	186 (7.62)	272 (9.67)		52 (5.80)	27 (4.23)	56 (4.59)
Participants	1,399 (22.08)	2,483 (39.03)	2,442 (38.89)		1,086 (27.49)	1,574 (39.19)	1,341 (33.32)

*Unless otherwise stated, unweighted frequency (weighted %) are shown.

Row percentages are shown.

Association between long working hours and pre-diabetes

Results from the logistic regression analysis are shown in Table 3. In univariate logistic regression analyses, long working hours was significantly associated with increased odds of having pre-diabetes in both men and women. Compared with the individuals who worked 40 hours, the ORs of pre-diabetes for the those who belong to the >52 hours category were 1.37 (95% CI 1.17-1.61; p for trend <0.0001) and 1.54 (95% CI 1.25-1.88; p for trend <0.0001) for men and women, respectively. For women, the positive association between the working hours and pre-diabetes was no longer significant after controlling for age, with OR of 1.06 (95% CI 0.84-1.32). In the case of men, those who worked >52 hours were 1.22 times more likely to have pre-diabetes after adjusting for covariates (multivariable-adjusted Odds Ratio (OR): 1.40; 95% Confidence Interval (CI): 1.03-1.46; P for trend 0.017). Age, smoking status, hypercholesteremia, family history of diabetes and sleep duration were also found to associated with increased odds of pre-diabetes in men, but there were no statistically significant differences based on educational level, monthly household income, alcohol consumption, muscle strengthening activity, hypertension, perceived stress, occupation and work schedule.

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2
3 Table 4 presents the ORs for subgroup analyses by age and work-related characteristics. We
4 did not observe a significant interaction between the number of hours worked per week and
5 age (Men:P for interaction =0.309) nor between work schedule and working hours (Men: P for
6 interaction 0.864). The relationship between long working hours and pre-diabetes was more
7 pronounced among male shift workers, albeit not statistically significantly, (41-52 hrs: aOR=
8 1.64, 95% CI: 0.77-3.47; >52 hrs: aOR= 1.64, 95% CI: 0.78-3.44; p for interaction=0.864). In
9 the subgroup analysis by occupational categories, male workers who worked in blue-collar
10 occupation were likely to have pre-diabetes as their average weekly working hours increased,
11 after adjustment for all covariates. The adjusted ORs were 1.13 (95% CI 0.84-1.53) and 1.54
12 (95% CI 1.15-2.06) for the 41-52 hrs and >52 hrs categories, respectively (p for trend= 0.041).
13 However, the interaction effect by occupational categories was not statistically significant (p
14 for interaction=0.146).
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Table 3. Results of the logistic regression analysis for the association between long working hours and pre-diabetes (HbA1c 5.7-6.4%)

	Case	Participants	Crude			Model 1			Model 2		
			OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Men (N=6,324)											
Working hours per week (hours)											
40	447	1,399	1.00			1.00			1.00		
41-52	867	2,483	1.09	0.93-1.29	0.278	1.10	0.93-1.29	0.279	1.07	0.90-1.27	0.477
>52	947	2,442	1.37	1.17-1.61	0.0001	1.31	1.11-1.55	0.001	1.22	1.03-1.46	0.026
P for trend				<0.0001			0.001			0.017	
Women (N=4,001)											
Working hours per week (hours)											
40	298	1,086	1.00			1.00			1.00		
41-52	492	1,574	1.11	0.91-1.35	0.307	0.98	0.80-1.20	0.84	0.89	0.72-1.12	0.338
>52	527	1,341	1.54	1.25-1.88	<0.0001	1.06	0.84-1.32	0.64	0.90	0.70-1.15	0.405
P for trend				<0.0001			0.601			0.436	

Note: OR, Odds ratio; CI, confidence interval;

Model 1 adjusted for age

Model 2 adjusted for age, educational attainment, total household income, obesity, smoking status, alcohol consumption, participation in aerobic activity, muscle strengthening activity, hypertension, hypercholesterolemia, family history of diabetes, sleep duration, perceived stress, occupation, work schedule

Table 4. Results of subgroup analysis of association between pre-diabetes and working hours by age and work characteristics

Characteristics	Case	Participants	Odds ratio (95% CI)			p for trend	p for interaction
			40 hrs	41-52 hrs	>52 hrs		
Men (N=6,324)							
Occupational categories							
White collar	845	2,774	1.00	1.04 (0.83-1.30)	1.06 (0.82-1.38)	0.664	0.146
Pink collar	317	859	1.00	1.22 (0.72-2.06)	0.99 (0.60-1.65)	0.714	
Green collar	163	356	1.00	0.52 (0.16-1.65)	0.90 (0.32-2.55)	0.247	
Blue collar	936	2,335	1.00	1.13 (0.84-1.53)	1.54 (1.15-2.06)	0.001	
Work schedule							
Fixed	2,060	5,801	1.00	1.04 (0.87-1.25)	1.21 (1.01-1.45)	0.031	0.864
Shift	201	523	1.00	1.64 (0.77-3.47)	1.64 (0.78-3.44)	0.317	
Age (years)							
30-39	497	1,966	1.00	1.31 (0.94 to 1.83)	1.44 (1.01 to 2.06)	0.047	0.309
40-49	687	2,016	1.00	0.89 (0.67 to 1.19)	1.20 (0.89 to 1.61)	0.124	
50-59	685	1,569	1.00	1.05 (0.76 to 1.47)	1.11 (0.80 to 1.55)	0.529	
≥60	392	773	1.00	1.29 (0.77 to 2.17)	1.12 (0.68 to 1.87)	0.079	
Women (N=4,001)							
Occupational categories							
White collar	311	1,527	1.00	1.14 (0.82-1.60)	0.78 (0.48-1.27)	0.619	0.442
Pink collar	493	1,263	1.00	0.62 (0.39-0.98)	0.77 (0.50-1.19)	0.706	
Green collar	169	309	1.00	1.42 (0.45-4.45)	0.94 (0.30-2.93)	0.309	
Blue collar	344	902	1.00	0.89 (0.58-1.35)	0.93 (0.59-1.45)	0.769	
Work schedule							
Fixed	1,255	3,826	1.00	0.85 (0.68-1.06)	0.87 (0.68-1.11)	0.302	0.202
Shift	62	175	1.00	2.71 (0.88-8.30)	2.57 (0.80-8.25)	0.121	
Age (years)							
30-39	143	994	1.00	0.79 (0.48 to 1.29)	0.79 (0.39-1.58)	0.451	0.978
40-49	313	1,241	1.00	0.89 (0.62-1.31)	0.81 (0.54-1.23)	0.327	
50-59	564	1,220	1.00	0.95 (0.64-1.39)	1.02 (0.69-1.52)	0.828	
≥60	297	546	1.00	0.94 (0.46-1.92)	0.82 (0.42-1.62)	0.485	

1 DISCUSSION

2 In this population-based study of Korean working adults without diabetes, we found that
3 men who worked over 52 hours per week exhibited 22% increased odds for pre-diabetes than
4 did those who worked 40 hours per week. This association was robust to adjustments for
5 socio-demographic variables and lifestyle factors, such as obesity, participation in aerobic and
6 muscle strengthening activity, smoking, and alcohol consumption and other covariates.
7 Importantly, we found that the increased odds of pre-diabetes associated with long working
8 hours was – albeit not statistically significant – more pronounced among workers of blue collar
9 occupations and shift workers. These findings are in line with the evidence from a prospective
10 study conducted in Japan which found that long working hours are related to the risk of incident
11 diabetes among shift workers.²² Further studies with larger sample sizes are warranted to
12 explore whether the lack of statistical significance observed is a result of sample size, or
13 reflects a true lack of association. Additionally, assessment of additive interaction between
14 long working hours and lifestyle factors would be a fruitful venue for further research for more
15 in depth understanding of the impacts of such interaction.

16 In the present study, the prevalence of pre-diabetes in the Korean working population was
17 34.4% and 31.0% for men and women, respectively. These prevalence estimates are
18 comparable to general population estimates reported in the U.S²³, U.K²⁴ and those of other
19 Asian countries.²⁵ Several previous studies have yielded prevalence estimates for pre-
20 diabetes in Korea. Using the HbA1c cutoff, pre-diabetes prevalence in 2011 was reported to
21 be 38.3% (Men: 41%; women: 35.7%) in a community-based cross-sectional study of Korean
22 adults aged 30 years or over.²⁶ Another Korean study reported a pre-diabetes prevalence of
23 26.1% in men and 20.5% according to American diabetes association criteria.²⁷ However, this
24 study was based on a sample from rural areas. Pre-diabetes is a well-recognized risk factors
25 for future diabetes, that gives rise to micro- and macrovascular complications and have
26 enormous social and economic burden^{28, 29}; increased attention needs to be paid to the high
27 prevalence of pre-diabetes in Korea.

1 We are not aware of other studies that has reported a relationship between long working
2 hours and pre-diabetes, although our findings are comparable with a meta-analysis showing
3 that long working hours is associated with the incidence of type 2 diabetes among individuals
4 from low socioeconomic status groups.¹² Another study have also reported a similar finding,
5 indicating that extended working hours is positively correlated with non-insulin dependent
6 diabetes mellitus in men.³⁰ However, our results conflict with a previous study that found
7 relative risks of T2DM significantly decreased with an increase in hours of work per day.¹⁴

8 The mechanisms underlying the association between long working hours and pre-diabetes
9 are yet unknown. It is likely that a similar mechanism to that of diabetes could be responsible
10 for the observed findings. Plausible explanations are that longer working hours impacts pre-
11 diabetes risk via their association with behavioural risk factors. As shown in this study, prior
12 research has indicated that working longer than recommended hours is linked to many
13 behavioural risk factors, such as binge drinking ^{31, 32} and low physical activity ³³, possibly
14 because individuals feel that they lack the time to engage in leisure-time physical activity due
15 to demands and responsibilities at work. In the present study, working hour–pre-diabetes
16 association attenuated but remained statistically significant in men after adjustment for
17 behavioural risk factors. As such, conventional risk factors for pre-diabetes are likely to explain
18 only part of the association between long working hours and pre-diabetes.

19 Meanwhile, there has been a proposition that extended working hours are related to
20 cortisol secretion ³⁴, a known risk factor for impaired glucose metabolism.³⁵ Cortisol induces
21 the formation of glucose in the liver and have insulin-antagonistic effects in the peripheral
22 tissues; both processes have the potential to contribute to risk of hyperglycemia. Furthermore,
23 individuals work longer hours are more often exposed to harmful psychological factors in the
24 work environment, such as job strain ^{36, 37} and effort-reward imbalance ³⁸, which are known to
25 be associated with subsequent elevation of Hba1c.³⁹ As such, stress-related mechanisms that
26 trigger dysregulation of neuroendocrine pathways, might be a potentially promising areas for
27 future research studying the differences in risk of pre-diabetes according to work hours.

28 The present study has several strengths. First, this study is based on a nationally

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3 1 representative survey, and to the best of our knowledge, this is the first report of an association
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5 2 between long working hours and pre-diabetes among individuals without diabetes. Second,
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7 3 blood samples were collected using standardized laboratory procedures, ensuring an accurate
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9 4 estimate of HbA1c. Finally, we were able to control for several important confounding variables,
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11 5 such as sleep duration and perceived control. However, this study is not without limitations.
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13 6 Our analyses are based on data from observational studies and, as such, preclude direct
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15 7 causal inference. Information on working hours and other covariates were self-reported and
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17 8 thus subject to recall bias. Moreover, we cannot exclude the possibility that the results were
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19 9 affected by residual confounding caused by imprecisely measured covariates or some other
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21 10 unmeasured occupational factors, such as job strain and job satisfaction. Working hours was
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23 11 measured at a single point in time that might not represent long-term exposure. In future
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25 12 studies, use of repeated measurements is needed to characterize longitudinal relation
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27 13 between long working hours and pre-diabetes.
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33 **CONCLUSIONS**

34 16 In conclusion, extended working hours in men was significantly correlated with the odds of
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36 17 pre-diabetes, independent of conventional risk factors. No statistically significant relationship
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38 18 was found for women. In the subgroup analysis, the association between long working hours
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40 19 and pre-diabetes was apparent only in male workers of blue collar occupations and shift
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42 20 workers. Additional large-scale longitudinal studies are needed to verify these findings.
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49 23 **Ethical statement:** The survey protocols for the KNHANES were approved by the Institutional Review
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51 24 Board of the Korea Centers for Disease Control and Prevention (IRB No. 2013-07CON-03-4C, 2013-
52
53 25 12EXP-03-5C, and 2015-01-02-6C), and informed consent was obtained from all participants.
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57 27 **Conflict of interest:** The authors have no conflict of interest to declare.
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4 commercial, or not-for-profit sectors.
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9 **Data sharing statement:** Data used in this study are available from the KNHANES official website
10 (<http://knhanes.cdc.go.kr/>).
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15 **Author contributions:** BYS, MK, GRK contributed to the conception and design of the study. BYS,
16 MK, GRK, ECP contributed to analyses and interpretation of the data, BYS, MK, GRK drafted the
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22 18 **Figure legends**

23
24 19 Figure 1 Flowchart of participant selection
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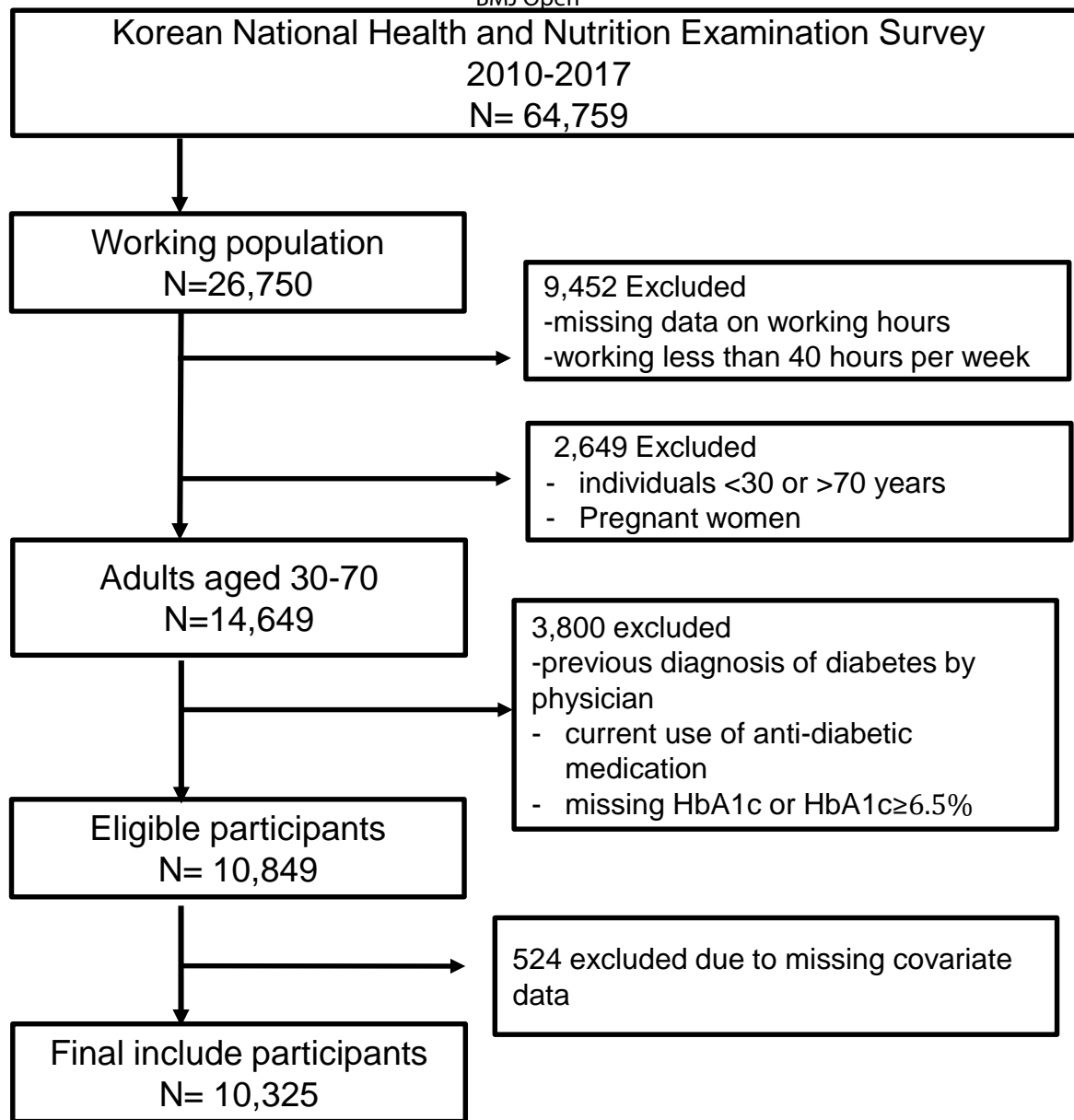


Figure 1 Flow chart of participant selection

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STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up and data collection	4,5,6
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	4,5,6
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Data sources/measurement	8*	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4,5,6
Bias	9	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4,5,6
Study size	10	Describe any efforts to address potential sources of bias	6,7
Quantitative variables	11	Explain how the study size was arrived at	4
Statistical methods	12	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5,6,7
		(a) Describe all statistical methods, including those used to control for confounding	6,7
		(b) Describe any methods used to examine subgroups and interactions	6,7
		(c) Explain how missing data were addressed	4
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8,9,10,11,12
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	7,14
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13,14
		(b) Report category boundaries when continuous variables were categorized	5,6
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13,15
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17,18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16, 17
Generalisability	21	Discuss the generalisability (external validity) of the study results	16,17
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.