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Difficulty of falling asleep and non-high-density lipoprotein cholesterol level among Canadian older adults: a cross-sectional analysis of the Canadian Longitudinal Study for Aging baseline data

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ABSTRACT

OBJECTIVE To examine whether difficulty of falling asleep (DoFA) is associated with non-high-density lipoprotein cholesterol (non-HDL-C) level among Canadian older adults.

METHODS 26,954 individuals aged 45–85 years from the baseline data of the Canadian Longitudinal Study for Aging were included in this study. DoFA was categorized into five groups by answer to the question "Over the last month, how often did it take you more than 30 min to fall asleep?" Response options are "Never, < 1 time/week, 1–2 times/week, 3–5 times/week, or 6–7 times/week". Non-HDL-C, the difference of total cholesterol and HDL-C, were categorized into five categories based on these cut-offs (< 2.6 mmol/L, 2.6–3.7 mmol/L, 3.7–4.8 mmol/L, 4.8–5.7 mmol/L, and ≥ 5.7 mmol/L). Ordinal logistic regression (logit link) continuation ratio models were used to estimate the odds of higher non-HDL-C levels for DoFA status. Adjusted means of non-HDL-C by DoFA status were estimated by general linear models. All analyses were sex separately using analytic weights to ensure generalizability.

RESULTS The proportions of DoFA in five categories were 41.6%, 25.7%, 13.6%, 9.4%, 9.7% for females and 52.9%, 24.9%, 10.5%, 6.1%, 5.6% for males, respectively. After adjustment of demographical and other covariates (such as depression, comorbidity, sleeping hour, etc.) compared to those who reported never having DoFA, the ORs (95% CIs) of higher levels of non-HDL-C for those whose DoFA status in < 1 time/week, 1–2 times/week, 3–5 times/week, and 6–7 times/week were 1.12 (1.05–1.21), 1.09 (0.99–1.18), 1.20 (1.09–1.33), 1.29 (1.17–1.43) in females and 1.05 (0.98–1.13), 0.95 (0.87–1.05), 1.21 (1.08–1.37), 0.97 (0.85–1.09) in males, respectively. The adjusted means of non-HDL-C among the five DoFA status were 3.68 mmol/L, 3.73 mmol/L, 3.74 mmol/L, 3.82 mmol/L, 3.84 mmol/L for females and 3.54 mmol/L, 3.58 mmol/L, 3.51 mmol/L, 3.69 mmol/L, 3.54 mmol/L for males, respectively.

CONCLUSIONS The results of this study have identified a risk association pattern between DoFA status and non-HDL-C levels in females but not in males. Further research is needed to confirm these findings.

The increased level of non-high-density lipoprotein cholesterol (non-HDL-C) is a reliable risk predictor for future coronary heart disease (CHD).[1–3] Evidence from studies of the relationship between non-HDL-C reduction and CHD risk has suggested that non-HDL-C is an important target of therapy for CHD prevention.[4] Non-HDL-C, the difference between total cholesterol (TC) and HDL-C, includes low-density lipoprotein cholesterol (LDL-C), intermediate-density lipoprotein cholesterol, and very-low-density lipoprotein cholesterol; they are all proatherogenic lipoproteins containing apolipoproteins B (Apo B).[5] Currently, LDL-C is the primary target of treatment of CHD since it contains the majority of Apo B and lowering its level reduces CHD risk.[6] However, LDL-C level in clinic is most likely estimated indirectly and its levels depend on fasting status and the levels of triglycerides.[7] The level of non-HDL-C is not related to triglycerides measurement and not affected

by fasting status, thus, it is considered superior to LDL-C as a treatment target for CHD risk management.

Sleep disorders are conditions that changes the way people sleep and affects the overall health and quality of life. In a study conducted among 2,000 Canadians aged 18 years or older, 40.2% of individuals reported having either trouble falling or staying asleep, or early morning awakening for at least three nights per week in a previous month.[8] Serious sleep disorders not only affects persons' life quality,[9,10] and increases risk for motor vehicle accidents,[11] but also found to be associated with an increased risk for cardiovascular diseases (CVD).[12-14] Sleep disturbance was observed to be highly associated with the increased risk of CVD, it was considered as a potential risk predictor of CVD.[13] However, whether sleep disorders are associated with dyslipidemia is uncertain since studies showed contradictory results.[15] Short sleep duration was found to be associated with an increased risk of CVD,[16,17] but there is no conclusion whether sleep duration is linked to dyslipidemia.[18] Furthermore, there is no study examined the relationship between sleep disorders and non-HDL-C levels. Therefore, the aim of this study is to examine how sleep disturbance is associated with lipid profile, particularly the levels of non-HDL-C among older adults. To explore this association, we used the baseline data collected by the Canadian Longitudinal Study on Aging (CLSA), a large population-based cohort study.

METHODS

Study Population

The CLSA cohort is consist of a national, stratified, random sample of the Canadian older population. There are two sub-cohorts in the CLSA: "Tracking cohort" and "Comprehensive cohort", which together represents approximately 51,000 men and women aged 45–85 years (mean age: 60 years) at the time of recruitment (2011–2015). All participants will be followed up every three-year for at least twenty years, or until the time of death or loss to follow-up. The current study, however, used the baseline data from the "Comprehensive cohort" because the related information of both difficulty of falling asleep (DoFA) and lipid measurements was available in this cohort only. The "Comprehensive cohort" consist of 30,097 participants who are randomly selected within 25–50 km of one of eleven data collection sites (DCS). The eleven DCS are in cities of Vancouver/Surrey, Victoria, Calgary, Winnipeg, Hamilton, Ottawa, Montreal, Sherbrooke, Halifax, and St. John's across Canada. The data on demographic, social, physical/clinical, psychological, economics, and health service utilization aspects relevant to health and aging were collected through in-home interview. Data on physical examinations and biological specimen collection were collected at the DCS following standardized protocols. The detailed description of the CLSA can be found elsewhere.[19] After cleaning the missing information on non-HDL-C (n = 3,085) and DoFA within 30 min (n = 58), a total of 26,954 participants (13,511 females and 13,443 males) were included. This study was approved for a secondary data analysis by the Research Ethics Board of Brock University.

Measurements of the Key Variables

Non-HDL-C and DoFA are the two key variables in this analysis. Non-fasting venipuncture blood was collected from each participant at the DCS and shipped to Calgary Laboratory Services (CLS) with cryoshippers. Then, each person's lipid profile, composed of TC, HDL-C, and triglycerides, were measured in serum by clinical analyzer (Roche Diagnostics Cobas 8 000 series) at the CLS. Non-HDL-C was derived from the difference of TC and HDL-C, and LDL-C was estimated using the Friedewald formula (i.e., TC − HDL-C − 2.2 × triglycerides).[7] Five non-HDL categories were created based the following cut-offs related to the risk of CVD: < 2.6 mmol/L, 2.6–3.7 mmol/L, 3.7–4.8 mmol/L, 4.8–5.7 mmol/L, and ≥ 5.7 mmol/L.[2]

DoFA was assessed with a 5-point Likert scale question from the In-Home Questionnaire "Over the last month, how often did it take you more than 30 min to fall asleep?" Participants were then categorized into five groups based on their response (Never, < 1 time/week, 1–2 times/week, 3–5 times/week, or 6–7 times/week). Additionally, the information of sleep hours during night was collected with the participant's response to question

"During the past month, on average, how many hours of actual sleep did you get at night?"

Measurements of Covariates

The following covariates were considered when modeling the association between non-HDL-C levels and DoFA: age (years), education (< post-secondary, post-secondary or some college degree, and bachelor's degree or above), marital status (married or living with a partner *vs.* other), immigrant status (yes *vs.* no), ethnicity (White *vs.* non-White), alcohol use (non-drinker, less than once a month, more than once a week during the past twelve months), smoking (non-smoker, former smoker, current smoker), number of close friends, moderate physical activity > 30 min per day over the past seven days (yes *vs.* no), waist circumference (cm), systolic blood pressure (mmHg), the CES-D 10 (Center for Epidemiological Studies Depression Scale 10 questions version) scores for indicating current depressive symptomatology, and comorbidity (number of chronic diseases reported).

Statistical Analysis

The pattern of DoFA was much different between males and females in the CLSA baseline data. Approximately 53% of males versus approximately 42% of females were in the "Never" category. While females had much higher proportion than males within the category of 6–7 times/week of having difficulty to fall asleep within 30 min in the last thirty days (9.7% *vs.* 5.6%). Therefore, all analyses were conducted sex separately. SAS 9.4 (SAS Institute Inc., Cary, NC, USA) was used for univariate analysis and ordinal logistic regression, Jamovi R was used for the calculations of effect size η^2 for lipid components and CESD-10 scores after ANOVA analyses. Statistics significancy level was set up at alpha level less than 0.05 two-sided test. In univariate analysis, one-way ANOVA were used for continuous variables and Tukey's test for pairwise comparisons afterwards, and Pearson's chi-squared tests for categorical variables. Ordinal logistic regression models (continuation ratio model) were used to estimate the impact of DoFA on non-HDL-C level that was grouped as an ordinary data. According to the method of continuation ratio model with logit link, we restructured four data sets from the original data set by sex. A dichotomous variable "beyond" was created as 1 for non-HDL-C level > 2.6 mmol/L and 0 for non-HDL-C level < 2.6 mmol/L in the first dataset (female: n = 13,249; male: n = 12,933); among those whose non-HDL-C level > 2.6 mmol/L, "beyond" = 1 for non-HDL-C level > 3.7 mmol/L and 0 for non-HDL-C level of 2.6–3.7 mmol/L in the second dataset (females: n = 11,498; males: n = 10,162); among those whose non-HDL-C level > 3.7 mmol/L, "beyond" = 1 for non-HDL-C level > 4.8 mmol/L and 0 for non-HDL-C level of 3.7–4.8 mmol/L in the third dataset (females: n = 6,439; males: n = 5,345); among those whose non-HDL-C level > 4.8 mmol/L, "beyond" = 1 for non-HDL-C level > 5.7 mmol/L and 0 for non-HDL-C level of 4.8–5.7 mmol/L in the fourth dataset (females: n = 1,999; males: n = 1,457). The four datasets were then combined by sex separately (females: n = 33,185; males: n = 29,897) and used to estimate the odds of being at or above a category of high level of non-HDL-C.[20] From the desired probability, $P(y_i > cat.j | y_i \geq cat.j)$, $j = 1,\ldots,5)$, the odds $\frac{P(y \geq j)P(y_i > cat.j | y_i \geq cat.j)}{1 - P(y_i > cat.j | y_i \geq cat.j)}$ of higher levels of non-HDL-C for DoFA status can be estimated. Four models were then created to examine the risk association of having higher levels of non-HDL-C with DoFA status and individuals from the first category were used as the reference, i.e., they never had a situation that takes them more than 30 min to fall asleep. In model 1, several key demographic characteristic variables, which included age, ethnicity as Caucasian, marital status, education, and immigrant status were adjusted. In model 2, we further adjusted for lifestyle related variables including number of friends, alcohol intake, cigarette smoking, and physical activity. In model 3, we further adjusted for waist circumference, systolic blood pressure, CES-D 10 score, and comorbidity. Finally, in model 4, the self-reported sleep hour was added into the model as well. We also examined whether there is an interaction between sleeping hour and current depression status (CES-D 10 > 10 *vs.* CES-D 10 < 10). Additionally, general linear models were used to obtain the adjusted mean levels of lipids for depression status and multiple regression was used to examine the linear relationship between lipids levels (TC, HDL-C,

LDL-C, non-HDL-C, and triglycerides) and DoFA status with adjusting for the covariates mentioned in model 4. To ensure generalizability, CLSA Sample Weights Version 1.2 was used when examining relationships between variables, i.e., the trimmed inflation weight for estimating means and proportions for the population and analytic weight.[21]

RESULTS

The characteristics of participants by sex are presented in Table 1 (females) and Table 2 (males), respectively. Among females, the proportions in the five categories of DoFA: i.e., "Never", "< 1 time/week", "1–2 times/week", "3–5 times/week",

Table 1 Characteristics of participants in CLSA Comprehensive sub-cohort baseline by difficulty of falling asleep (females).

Variable	Difficulty of falling asleep (n = 13,511)				
	Never (n = 5,510)	< 1 time/week (n = 3,472)	1–2 times/week (n = 1,857)	3–5 times/week (n = 1,290)	6–7 times/week (n = 1,382)
Average of age, yrs	59.41	60.12	60.86	60.14	60.80
White	94.38%	96.40%	94.15%	95.65%	93.80%
Education					
Less than post-secondary	38.69%	36.10%	36.02%	42.36%	47.25%
Some college degree	38.55%	37.63%	39.67%	36.42%	36.81%
Bachelor's or above	22.76%	26.27%	24.31%	21.23%	15.94%
Marital status					
Single/Separated/Divorced/Widowed	29.44%	29.78%	30.31%	33.09%	37.28%
Married	70.56%	70.22%	69.69%	66.91%	62.72%
Immigrants	17.78%	17.27%	20.55%	17.55%	16.52%
Average of body mass index, kg/m^2	28.00	27.38	27.71	28.35	28.74
Average of waist circumference	88.32	86.80	88.08	89.74	90.48
Average of systolic blood pressure, mmHg	118.76	117.81	119.27	120.36	121.20
Lipid profile					
Average of total cholesterol, mmol/L	5.33	5.42	5.47	5.43	5.39
Average of HDL-C, mmol/L	1.65	1.67	1.68	1.59	1.57
Average of non-HDL-C, mmol/L	3.68	3.75	3.79	3.84	3.82
Average of low-density lipoprotein cholesterol, mmol/L	2.94	3.01	3.03	3.02	2.97
Average of triglyceride, mmol/L	1.65	1.63	1.68	1.80	1.85
Average of glycated hemoglobin, mmol/L	5.55	5.51	5.56	5.63	5.66
Smoking					
Non-smoker	33.15%	35.85%	34.76%	32.17%	30.34%
Former smoker	56.13%	53.66%	56.18%	55.74%	50.33%
Current smoker	10.72%	10.49%	9.06%	12.09%	19.33%
Alcohol intake					
None	14.99%	13.91%	14.36%	14.17%	21.32%
Occasionally	15.58%	11.24%	16.86%	20.42%	21.86%
Regularly (at least once a month)	69.43%	74.85%	68.78%	65.42%	56.82%
Moderate physical activity > 30 min	11.80%	12.55%	11.00%	9.91%	8.80%
Average of number of close friends	5.16	5.64	5.51	5.10	4.05
Average of multimorbidity	2.82	2.93	3.19	3.32	3.87
Average of sleep hour	7.04	7.10	6.76	6.27	5.58
Average of CES-D 10 score	5.11	5.12	6.65	7.55	9.69

CLSA: the Canadian Longitudinal Study on Aging; HDL-C: high-density lipoprotein cholesterol.

Table 2 Characteristics of participants in CLSA Comprehensive sub-cohort baseline by difficulty of falling asleep (males).

Variable	Difficulty of falling asleep (n = 13,443)				
	Never (n = 7,233)	< 1 time/week (n = 3,322)	1–2 times/week (n = 1,342)	3–5 times/week (n = 789)	6–7 times/week (n = 757)
Average of age, yrs	59.82	59.63	57.77	57.62	58.14
White	93.89%	95.55%	95.57%	91.09%	93.02%
Education					
Less than post-secondary	36.16%	32.36%	30.73%	42.19%	48.39%
Some college degree	33.86%	36.91%	41.58%	39.17%	36.25%
Bachelor's or above	29.98%	30.72%	27.69%	18.64%	15.36%
Marital status					
Single/Separated/Divorced/Widowed	16.03%	17.28%	19.74%	27.69%	31.24%
Married	83.97%	82.72%	80.26%	72.31%	68.76%
Immigrants	20.50%	20.77%	17.53%	16.05%	19.77%
Average of body mass index, kg/m^2	28.60	28.19	28.77	28.32	28.91
Average of waist circumference	101.02	99.72	101.59	100.70	102.26
Average of systolic blood pressure, mmHg	122.32	121.52	122.44	121.49	122.15
Lipid profile					
Average of total cholesterol, mmol/L	4.93	5.01	4.97	5.08	4.89
Average of HDL-C, mmol/L	1.29	1.31	1.24	1.28	1.24
Average of non-HDL-C, mmol/L	3.64	3.71	3.72	3.80	3.65
Average of low-density lipoprotein cholesterol, mmol/L	2.79	2.81	2.80	2.84	2.74
Average of triglyceride, mmol/L	1.91	2.03	2.12	2.13	2.05
Average of glycated hemoglobin, mmol/L	5.70	5.69	5.74	5.70	5.77
Smoking					
Non-smoker	27.63%	29.33%	26.93%	25.51%	18.70%
Former smoker	62.85%	60.38%	59.92%	63.29%	56.84%
Current smoker	9.53%	10.29%	13.14%	11.20%	24.46%
Alcohol intake					
None	12.17%	11.40%	12.21%	11.19%	15.75%
Occasionally	9.44%	6.26%	9.41%	12.18%	17.74%
Regularly (at least once a month)	78.39%	82.34%	78.38%	76.63%	66.51%
Moderate physical activity > 30 min	13.96%	12.64%	12.53%	11.02%	9.48%
Average of number of close friends	5.19	5.17	4.43	4.79	5.16
Average of multimorbidity	2.26	2.24	2.31	2.53	3.12
Average of sleep hour	6.92	6.94	6.58	6.23	5.58
Average of CES-D 10 score	4.29	4.81	6.13	7.91	8.43

CLSA: the Canadian Longitudinal Study on Aging; HDL-C: high-density lipoprotein cholesterol.

and "6–7 times/week" for having difficulty to fall asleep within 30 min during the past month were 41.6%, 25.7%, 13.6%, 9.4%, and 9.7%, respectively (Table 1). All continuous variables were statistically significant ($P < 0.05$) in the ANOVA analysis. The values of η^2 were between 0.001 and 0.006 for lipid components and 0.068 for CESD-10 scores. Based on the recommendation by Serdar, *et al.*,[22] the effect size was small for the lipid components, but medium for CESD-10 scores. All categorical variables were statistically significant in Pearson's chi-squared tests ($P < 0.05$). The mean age was approximately sixty years though females who were in "Never" having difficulty to fall asleep were

slightly younger. Over 93% of females were White and 16% of them were immigrants. Females with "< 1 time/week" or more often in DoFA categories were similar in many ways. Compared to those in "Never" category, they were more likely to be with lower proportions of education achieved as "bachelor's or above", being married or living with a partner, and moderate physical activity; their cardiovascular profiles showed getting worser, i.e., higher mean levels of lipids (except of HDL-C), body mass index, waist circumference, glycated hemoglobin, smoking, comorbidity, and CESD-10 score; but lower number of close friends and sleep hours.

For males, the proportions in the five categories of DoFA were 52.9%, 24.9%, 10.5%, 6.1%, and 5.6%, respectively (Table 2). Like females, all continuous variables were statistically significant ($P < 0.05$) in ANOVA analysis except for the levels of LDL-C, systolic blood pressure, and glycated hemoglobin. The values of η^2 were less than 0.004 for lipid components but 0.071 for CESD-10 scores. All categorical variables were statistically significant as well ($P < 0.05$). Majority were White (≥ 90%). The mean age was approximately fifty-nine years, but unlike females, males were slightly younger for those more often in DoFA categories. Like females, those males who were more often in DoFA had higher proportions of education achieved in "less than post-secondary", lived as single, and current smoker; but lower proportion of moderate physical activity, lower number of close friends, and sleep hours. Like females, males in more often DoFA had higher comorbidity and CESD-10 scores. However, the cardiovascular profiles did not show dramatically differences among males in the categories of DoFA as the smaller values of values of η^2 indicated.

Table 3 summarizes the adjusted odds ratio (OR) and its confidence interval (CI) from the continuation ratio models for the status of DoFA by gender. In females, compared to "Never" category, after adjusting for age, ethnicity, education, marital status, and immigrant status (model 1), the ORs (95% CIs) of high levels of non-HDL-C in model 1 were 1.14 (1.07–1.21), 1.08 (1.00–1.17), 1.19 (1.09–1.30), and 1.21 (1.11–1.31), for those who were in DoFA categories of "< 1 time/week", "1–2 times/week", "3–5 times/week", and "6–7 times/week", respectively. Further adjustment for other covariates (models

Table 3 Adjusted ORs of high levels of non-high-density lipoprotein cholesterol from continuation ratio models for status of difficulty of falling sleep by sex.

	OR (95% CI)			
	Model 1	**Model 2**	**Model 3**	**Model 4**
Female (n = 13,511)				
Never (n = 5,510)	Reference	Reference	Reference	Reference
< 1 time/week (n = 3,472)	1.14 (1.07–1.21)***	1.13 (1.06–1.21)**	1.13 (1.05–1.21)**	1.12 (1.05–1.21)**
1–2 times/week (n = 1,857)	1.08 (1.00–1.17)*	1.05 (0.97–1.14)	1.08 (0.99–1.18)	1.09 (0.99–1.18)
3–5 times/week (n = 1,290)	1.19 (1.09–1.30)***	1.17 (1.07–1.28)**	1.18 (1.07–1.30)**	1.20 (1.09–1.33)**
6–7 times/week (n = 1,382)	1.21 (1.11–1.31)***	1.21 (1.11–1.32)***	1.23 (1.12–1.36)***	1.29 (1.17–1.43)***
R^2_L	0.21	0.21	0.23	0.23
Male (n = 13,443)				
Never (n = 7,233)	Reference	Reference	Reference	Reference
< 1 time/week (n = 3,322)	1.07 (1.00–1.14)*	1.07 (1.00–1.14)	1.05 (0.98–1.13)	1.05 (0.98–1.13)
1–2 times/week (n = 1,342)	0.91 (0.83–0.99)*	0.93 (0.85–1.01)	0.953 (0.87–1.05)	0.95 (0.87–1.05)
3–5 times/week (n = 789)	1.14 (1.03–1.26)*	1.18 (1.06–1.31)**	1.217 (1.08–1.37)**	1.21 (1.08–1.37)**
6–7 times/week (n = 757)	0.99 (0.90–1.10)	0.93 (0.84–1.04)	0.973 (0.86–1.10)	0.97 (0.85–1.09)
R^2_L	0.20	0.21	0.22	0.22

Model 1: adjusted for age, ethnicity, education, marital status, and immigrant status. Model 2: adjusted for variables in Model 1 plus the number of close friends, alcohol intake, smoking, and physical activity. Model 3: adjusted for variables in Model 2 plus the CES-D 10 score, waist circumference, systolic blood pressure, and comorbidity. Model 4: adjusted for variables in Model 3 plus the sleep hour. *Refers to the P-value was less than 0.05. **Refers to the P-value was less than 0.01. ***Refers to the P-value was less than 0.0001. CI: confidence interval; OR: odds ratio.

2–4) did not change the observed risk association. For instance, after further adjusting for number of close friends, alcohol intake, smoking, physical activity, waist circumference, systolic blood pressure, comorbidity, CESD-10 score, and sleep hours (model 4), the ORs (95% CIs) for the four DoFA categories were 1.12 (1.05–1.21), 1.09 (0.99–1.18), 1.20 (1.09–1.33), and 1.29 (1.17–1.43), respectively. In males, compared to "Never" category, however, those who were in other categories of DoFA did not show an increased odds pattern. The ORs (95% CIs) of high levels of non-HDL-C in model 1 were 1.07 (1.00–1.14), 0.91 (0.83–0.99), 1.14 (1.03–1.26), and 0.99 (0.90–1.10), respectively. Further adjustment of other covariates made a lower odds observed in "1–2 times/week" category no more statistically significant, but the increased odds in the category of "3–5 times/week" persisted. In model 4, compared to "Never" category, the odds of having higher levels of non-HDL-C increased 21% (OR = 1.21, 95% CI: 1.08–1.37) for those in the category of "3–5 times/week". There was no interaction between sleep hours and DoFA in both genders ($P > 0.05$). The R^2_L in model 4 reflected that the model significantly reduced the deviance of null model ($D_0 = -2LL_0$) by approximately 23% in females and 22% in males.

Figure 1 and Figure 2 present the adjusted mean levels of lipids by sex. General linear models were used to obtain the adjusted means for each category of DoFA. After adjusting for the same covariates as did in the model 4 of logistical regression,

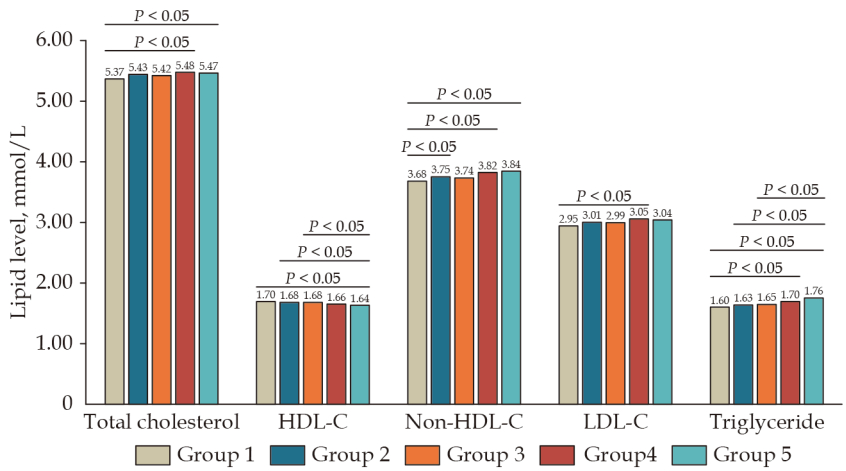

Figure 1 Adjusted mean levels of lipids (females). Covariates adjusted including age, ethnicity, education, marital status, immigrant status, number of close friends, alcohol intake, smoking, physical activity, CES-D 10 score, waist circumference, systolic blood pressure, comorbidity, and sleep hour. HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.

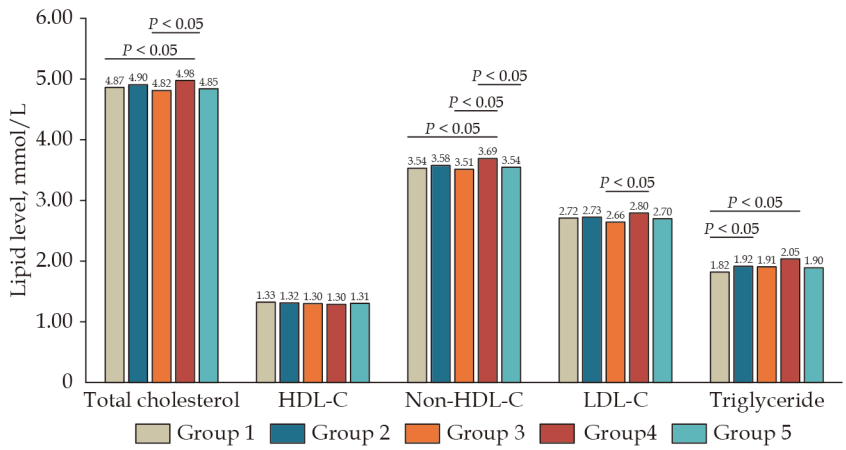

Figure 2 Adjusted mean levels of lipids (males). Covariates adjusted including age, ethnicity, education, marital status, immigrant status, number of close friends, alcohol intake, smoking, physical activity, CES-D 10 score, waist circumference, systolic blood pressure, comorbidity, and sleep hour. HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.

the mean levels of lipids in females, except the changes in LDL-C mean levels, showed a clear pattern that the mean levels of lipid components increase (HDL-C showed opposite) with more often DoFA. For instance, the mean levels for the five categories of DoFA were 3.68 mmol/L, 3.73 mmol/L, 3.71 mmol/L, 3.78 mmol/L, and 3.86 mmol/L for non-HDL-C, 5.37 mmol/L, 5.43 mmol/L, 5.42 mmol/L, 5.48 mmol/L, and 5.47 mmol/L for TC, 1.70 mmol/L, 1.68 mmol/L, 1.68 mmol/L, 1.66 mmol/L, and 1.64 mmol/L for HDL-C, and 1.60 mmol/L, 1.63 mmol/L, 1.65 mmol/L, 1.70 mmol/L, and 1.76 mmol/L for triglycerides, respectively. For LDL-C, the change between different categories was trivial (the mean levels in the five categories of DoFA were 2.95 mmol/L, 3.01 mmol/L, 2.99 mmol/L, 3.05 mmol/L, and 3.04 mmol/L). In males, the mean levels of lipids did not show a clear increasing pattern as did in females. There was no statistical difference in mean levels of HDL-C among people in different categories of DoFA. People in different categories of DoFA had similar mean levels of lipids except for those who were in the category of "3–5 times/week", which had higher mean levels than other categories.

DISCUSSION

With the baseline data collected in the CLSA "Comprehensive cohort", we examined the relationship between the levels of non-HDL-C and DoFA. We found that in females compared to those who were in the "Never" category of having DoFA within 30 min during the past month, those who were in more often DoFA had significant elevated average levels of non-HDL-C when it was treated as a continuous variable. These females had the increased odds of having higher levels of non-HDL-C when it was treated as a category variable. The observed associations were independent of the impact of sleep hour. However, we did not observe such pattern in males.

Sleep disorders become common health problems in Canadian adults.[8] Our results indicated that among older people, approximately 60% of women and 48% of men had DoFA at least once per week in the last month. Extensive evidence suggests a risk association between sleep disorders and CVD. Sleep disorders such as sleep apnea and sleep disturbance are recognized as independent risk factors for CVD development.[12–14] Canadian adults who reported being diagnosed with sleep apnea were 2.5 times more likely to report having diabetes mellitus, 1.8 times more likely to have hypertension, and 2.2 times more likely to have heart disease.[23] The comorbid sleep disorders and dyslipidemia will significantly put people at an increased risk for CVD.[24] Our results indicate that those who reported having more sleep disturbance were more likely to have elevated levels of non-HDL-C, which is a strong risk factor for CVD.[1]

Sleep duration, particularly the short sleep duration, is also found to be associated with an increased risk for CVD.[16,17] However, it is unknown whether sleep disorders or sleep duration is a risk factor of dyslipidemia. The evidence from animal studies and/or laboratory experiments indicate that intermittent hypoxia is independently associated with dyslipidemia, but the role of obstructive sleep apnea in the causality of dyslipidemia remains to be established.[15] A systematic review of thirteen studies examining the association of sleep disturbances with dyslipidemia found insufficient evidence to conclude the significant relationship between sleep duration and the development of dyslipidemia.[25] The authors further noted the small number of included studies and heterogeneity in the sleep quality aspects and lipid profile, which might have limited the interpretation.[25] However, the association of dyslipidemia with sleep disorders is somewhat consistent in previous studies despite the variations in sleep quality measurement and lipid profile.[26–29] An elevated levels of TC, LDL-C and/or triglycerides were associated with sleep duration,[26,27] while only LDL-C was associated with sleep fragmentation.[28] Another study observed the association between objective sleep duration and lipid profile, but not for objective sleep fragmentation and self-reported sleep quality.[29] Since TC levels contains both "good" and "bad" cholesterol and the measurements of triglycerides and LDL-C are very sensitive to fasting status, it is difficult to conclude that those observed variations in association between sleep disorder and dyslipidemia are the true picture or due to the aforementioned limitations. While non-HDL-C contains all proatherogenic lipoproteins Apo B, and its measurement overcomes the limitation when measuring triglycerides or LDL-C.[30,5] In addition,

studies demonstrate that people with normal LDL-C levels, but elevated levels of non-HDL-C were at an increased risk for CHD.[12,31] Thus, exploring the association between sleep disorders and the levels of non-HDL-C may provide us a reliable approach to examine whether sleep disorders increase the risk of CVD by increasing proatherogenic lipoproteins Apo B. Non-HDL-C includes all lipoproteins Apo B, but no studies have examined its association with sleep disorders. While from our analyses, it indeed showed that the elevated levels of non-HDL-C were associated with sleep disturbance even after adjusting the well-known risk factors of CVD, but this was observed among women only. It is not clear why sleep disturbance associated with the elevated levels of non-HDL-C was observed only among women. Certainly, this needs more research to explore.

Since the CLSA was a large population-based study, we were able to examine impact of many covariates on the observed association (Figures 3 & 4). Although the significant ORs for covariates varied by sex, they go alone the similar direction from other studies. For example, smoking, ethnicity as White, waist circumference, systolic blood pressure, and depression were found to be positively associated an elevated level of cholesterol, and immigrant status was associated with a higher odds of elevated non-HDL-C level as well.[32–36] While sleep hour as a continuous variable was associated with a slightly higher odds in females but adjusting its impact did not change the observed relationship between sleep disturbance and abnormal lipids levels. This suggests that sleep disturbance and sleep duration may have different effect on the development of arthrosclerosis, and, it needs more research to examine their role. We are not sure why comorbidity was negatively associated with the odds of higher levels of non-HDL-C. Our previous analysis found that over 30% of CLSA participants had at least one of common cardiovascular system related diseases,[37] those who were with comorbidity might be more likely to be treated with cardiovascular risk factors. However, since the information of the history of medication use in the CLSA was not released yet when conducting the analysis, we could not verify whether this is the case.

LIMITATIONS

When interpreting the results, we may need to bear the following two limitations. On the one hand, the observed associations between sleep dis-

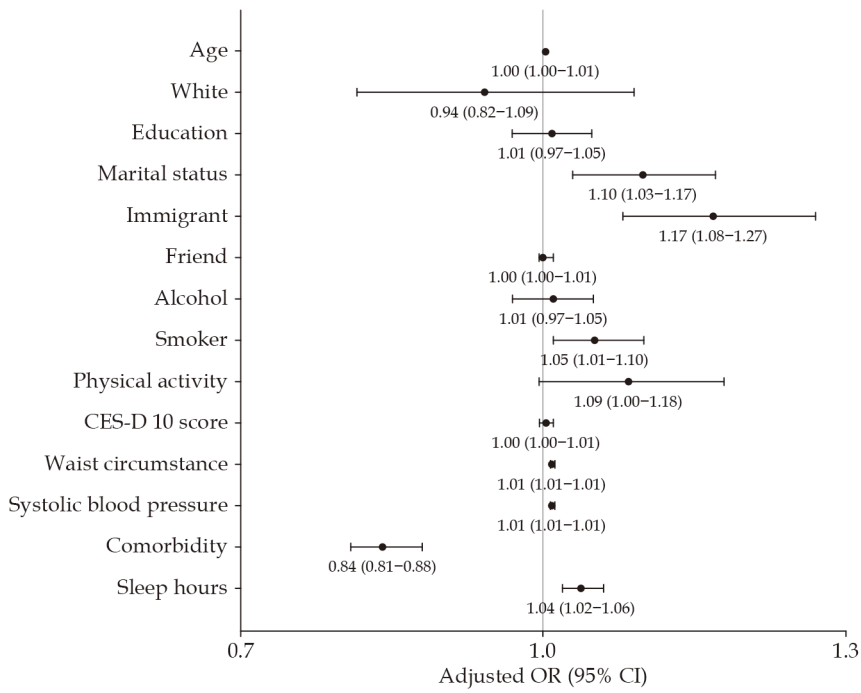

Figure 3 Adjusted ORs from model 4 for covariates (females). Model 4: adjusted for covariates including age, ethnicity, education, marital status, immigrant status, number of close friends, alcohol intake, smoking, physical activity, CES-D 10 score, waist circumference, systolic blood pressure, comorbidity, and sleep hour. CI: confidence interval; OR: odds ratio.

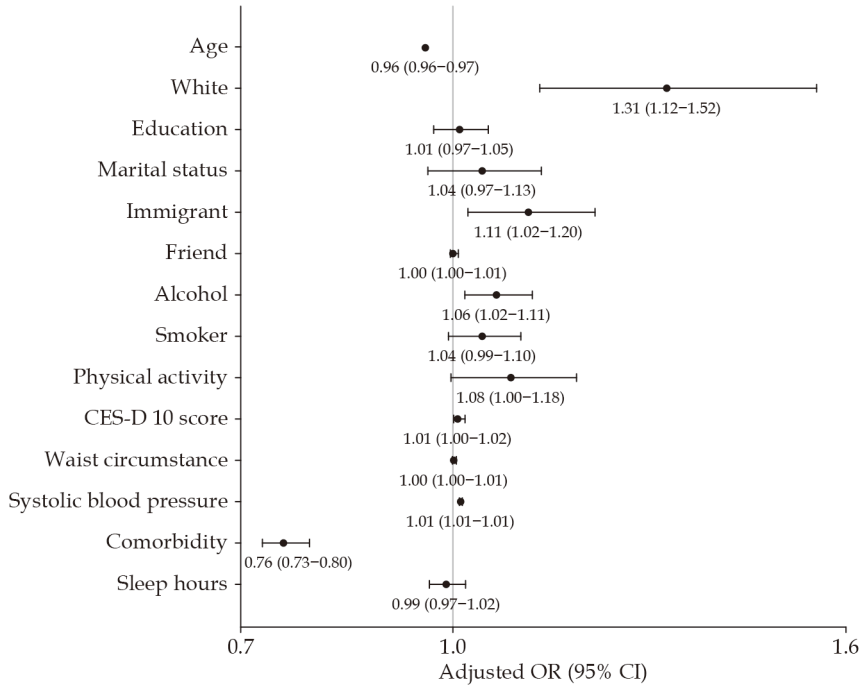

Figure 4 Adjusted ORs from model 4 for covariates (males). Model 4: adjusted for covariates including age, ethnicity, education, marital status, immigrant status, number of close friends, alcohol intake, smoking, physical activity, CES-D 10 score, waist circumference, systolic blood pressure, comorbidity, and sleep hour. CI: confidence interval; OR: odds ratio.

turbance and high levels of non-HDL-C in this study were from a cross-sectional analysis and may need longitudinal cohort to examine whether this can be a causality relationship. On the other hand, the 5-point Likert scale question for sleep disturbance might have a misclassification among participants. However, this should be a non-differential misclassification that will generally bias towards the null. Nevertheless, the large sample size, population-based sampling design and weighting, and adjustment of many well-known covariates would enhance the generalization of this study.

CONCLUSIONS

In conclusion, females who are more often in DoFA currently are at an increased risk of having high level of non-HDL-C. This observed relationship is independently from the impact of sleep duration. However, whether the impact of sleep disturbance on CVD mediates through high level of non-HDL-C may need to be examined through future longitudinal studies.

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