Non-HDL cholesterol level and depression among Canadian elderly—a cross-sectional analysis of the baseline data from the CLSA

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Abstract

To explore whether non-high-density-lipoprotein cholesterol (non-HDL-c) is associated with depression, a total of 26 819 Canadians aged 45–85 from the Canadian Longitudinal Study on Aging (CLSA) were included in analysis. Non-HDL-c, the difference between total-c and HDL-c, was categorized into five levels, i.e., <2.6, 2.6 to <3.7, 3.7 to <4.8, 4.8 to 5.7, and ≥5.7 mmol/L. History of clinical depression was collected by questionnaire at an in-home interview, and current potential depression status was determined by CES-D10 (Center for Epidemiological Studies Depression Scale 10 questions version) score, i.e., ≥10 vs. <10. Logistic continuation ratio model for ordinal data was used to estimate the odds of being at or above a higher non-HDL-c category for depression status. Compared with those without clinical depression history and currently undepressed, the adjusted odds ratios (95% CI) were 1.09 (1.02, 1.17) for those without clinical depression history but currently depressed, 1.05 (0.98, 1.12) for those had clinical depression history but currently undepressed, and 1.21 (1.10, 1.32) for those had clinical depression history and currently depressed. The average of non-HDL-c for four depression groups were 3.64, 3.71, 3.69, and 3.82 mmol/L, respectively, and group 4 was statistically higher than others ($p < 0.001$). In conclusion, people with both current depression and a history clinical depression are at an increased risk of having high level of non-HDL-c.

Key words: non-HDL cholesterol, CLSA, depression, senior

Introduction

Individuals with high levels of non-high-density-lipoprotein (non-HDL) cholesterol are at an increased risk for coronary heart disease (CHD) (Liu et al. 2006; Brunner et al. 2019). Non-HDL cholesterol level is the difference between total cholesterol and HDL cholesterol, which includes all proatherogenic lipoproteins containing apolipoproteins B (apo B) located in very-low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), lipoprotein (a), and low-density lipoprotein (LDL) (Emerging Risk Factors Collaboration et al. 2009). More than 90% of plasma apo B is associated with LDL particles (Barter et al. 2006) and lowering LDL cholesterol levels does indeed lower the risk for CHD; thus, LDL cholesterol levels are used as the primary target of treatment of CHD (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults 2001).

However, clinical laboratory tests do not estimate LDL cholesterol levels directly, instead approximating it by the Friedewald formula, which estimates the levels of LDL cholesterol as total cholesterol—HDL cholesterol—2.2 × triglycerides (Friedewald et al. 1972). Of concern, this approach becomes increasingly inaccurate when triglyceride levels are measured using nonfasted blood specimen (Demacker et al. 1984). For this reason, non-HDL cholesterol is considered to be superior to LDL cholesterol as the treatment target for CHD risk management because the levels of total cholesterol and HDL cholesterol are less likely to be affected by fasting status (Emerging Risk Factors Collaboration et al. 2009). Furthermore, since it contains all apo B lipoproteins, studies have found that people with normal LDL cholesterol levels but elevated levels of non-HDL cholesterol were at an increased risk for CHD (Liu et al. 2005, 2006; Brunner et al. 2019). The Canadian Cardiovascular Society 2016 guidelines recommend that all men and women of 40 years of age and older have their lipid levels measured every five years. Since LDL cholesterol levels are of greatest concern for physicians, non-HDL cholesterol is addressed as an alternative marker (Anderson et al. 2016).

Depression is a mood disorder that causes persistent feelings of sadness and loss of interests and at its worst can manifest with suicidal thoughts and acts and psychotic features (American Psychiatric Association 2013). It is found that depression is strongly associated with cardiovascular disease (CVD), not only with its occurrence but also with its progress (Penninx 2017). Although it is not totally understood how depression plays a role in the development of CVD, it is believed that the pathway linking depression to CVD might be through a general mediating mechanism rather than a pure organ- or disease-specific process. For example, people with depression are more likely to live with a unhealthy lifestyle (e.g., smoking, excessive alcohol use, physically inactive, etc.), which may contribute to a higher risk for CVD (Penninx 2017). Patients with depression and dyslipidemia are more likely at an increased risk for CVD (Kim et al. 2020), but the results on the relationship between depression and dyslipidemia seem contradictory. A meta-analysis found that both total cholesterol and LDL cholesterol were negatively, but HDL cholesterol was positively associated with depression (Shin et al. 2008). A study conducted among US household population found a U-shaped relationship in men between LDL cholesterol levels and severe depression but not in women (Tedders et al. 2011). When compared to those with remitted major depression disorder (MDD), those with current MDD had lower levels of HDL cholesterol, but higher levels of total and LDL cholesterol (van Reedt Dortland et al. 2010). The results from recent a study with a large sample size indicated that an elevated triglycerides level was associated with the risk of depression symptoms, the same as for HDL cholesterol, but not for total and LDL cholesterol (So et al. 2020). It is unclear why the results of the association between dyslipidemia and depression are inconsistent. This may reflect the difference in definition of depression and possible the limitation of the measurement of LDL cholesterol and (or) triglycerides. In addition, no study has examined the relationship between depression and non-HDL cholesterol. Therefore, in this analysis, we explored whether depression status is associated with the levels of non-HDL cholesterol.

Methods

Canadian Longitudinal Study on Aging (CLSA)

The CLSA has two sub-cohorts, i.e., "Tracking cohort" and "Comprehensive cohort", which together represents approximately 51 000 men and women aged 45–85 years across Canada (mean age 60 years). The detailed description of the CLSA can be found elsewhere (Raina et al. 2009). This study, however, only used data from the "Comprehensive cohort" because only in this cohort the related information of both depression and lipid measurements was available. The "Comprehensive Cohort" had 30 097 participants at the entry of the cohort baseline, after cleaning the missing data on lipid measurements ($n = 3085$) and depression measurements ($n = 193$), a total of 26 819 men

and women were included. This study was approved for a secondary data analysis by the Research Ethics Board of Brock University (REB No. 17-097-LIU).

Measurements of depression

Two types of questions related to depression were surveyed, i.e., history of clinical depression and potential current depression.

History of clinical depression

A questionnaire at an in-home interview was conducted among all participants at the cohort baseline. Under the section of chronic conditions, information was collected on long-term conditions that were diagnosed by a health professional, that are expected to last, or have already lasted, six months or more. History of clinical depression was then determined by a positive response to the question "Has a doctor ever told you that you suffer from clinical depression?"

Current potential depression

All participants were surveyed with the CES-D 10 (Center for Epidemiological Studies Depression Scale 10 questions version), a short form of the regular CES-D (Kimberlin et al. 1998), which has been tested with good reliability (Björgvinsson et al. 2013). The CES-D 10 is used to detect current depressive symptomatology that helps to identify clinically important depression. The overall CES-D 10 score ranges from 0 to 30 with a score ≥10 suggesting current depressive illness, which needs to be further assessed (Zhang et al. 2012).

Based on the response to the history of clinical depression question and CES-D10 score, all participants were then categorized into one of the four groups; i.e., Group 1: without a history of clinical depression and currently not being depressed (CES-D10 score < 10); Group 2: without a history of clinical depression but currently depressed (CES-D10 score ≥ 10); Group 3: with a history of clinical depression but currently not depressed (CES-D10 score < 10); and Group 4: with a history of clinical depression and currently depressed (CES-D10 score ≥ 10).

Measurements of lipids

Nonfasting venipuncture blood was collected from each participant at the data collection sites and then shipped to Calgary Laboratory Services by cryoshippers for all biomarker measurements. A complete lipid profile (i.e., total cholesterol, HDL cholesterol, and triglycerides), was measured in serum by clinical analyzer (Roche Diagnostics Cobas 8000 series). LDL cholesterol was estimated using the Friedewald formula. Non-HDL cholesterol was calculated as the difference between total cholesterol and HDL cholesterol. Five non-HDL categories were created based the following cut-offs related to the risk of CVD: <2.6 mmol/L, 2.6 to <3.7 mmol/L, 3.7 to <4.8 mmol/L, 4.8 to 5.7 mmol/L, and ≥5.7 mmol/L (Brunner et al. 2019).

Measurements of covariates

The following covariates were considered when modeling the association between non-HDL cholesterol levels and depression: age (years), sex (male vs. female), 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 (Caucasian vs. other), alcohol use (nondrinker, less than once a month, more than once a week during the past 12 months), smoking (nonsmoker, former smoker, current smoker), number of close friends, moderate physical activity 30+ min per day over the past 7 d (yes vs. no), waist circumference (cm), systolic blood pressure (mm Hg), and comorbidity (number of chronic diseases reported).

Analytic strategies

All analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, North Carolina, USA). Statistical significance was set at two-sided α <0.05. For the univariate analysis, one-way ANOVA were used for continuous variables, and χ^2 tests for categorical variables. According to the method of continuation ratio model with logit link, we restructured four data sets from the original data set ($n = 26\ 819$). A dichotomous variable "beyond" was created as 1 for non-HDL cholesterol level ≥ 2.6 mmol/L and 0 for non-HDL cholesterol level < 2.6 mmol/L in the first data set ($n = 26\ 819$); among those whose non-HDL cholesterol level ≥ 2.6 mmol/L, "beyond" = 1 for non-HDL cholesterol level ≥ 3.7 mmol/L and 0 for non-HDL cholesterol level 2.6–3.7 mmol/L in the second data set ($n = 22\ 277$); among those whose non-HDL cholesterol level ≥ 3.7 mmol/L, "beyond" = 1 for non-HDL cholesterol level ≥ 4.8 mmol/L and 0 for 3.7–4.8 mmol/L in the third data set ($n = 12\ 295$); among those whose non-HDL cholesterol level ≥ 4.8 mmol/L, "beyond" = 1 for non-HDL cholesterol level ≥ 5.7 mmol/L and 0 for 4.8–5.7 mmol/L in the fourth data set ($n = 3768$). The four data sets were then combined ($n = 65\ 159$) and used to estimate the odds of being at or above a category of high level of non-HDL cholesterol (O'Connell 2006). From the desired probability, $p(y_i > \text{cat.}j | y_i \geq \text{cat.}j), j = 1, \ldots, 5)$, the odds $\dfrac{p(y \geq j) p(y_i > \text{cat.}j | y_i \geq \text{cat.}j)}{1 - p(y_i > \text{cat.}j | y_i \geq \text{cat.})}$ of higher levels of non-HDL cholesterol for depression status can be estimated. Three models were then created to examine the risk association of having higher levels of non-HDL cholesterol with depression status and people in Group 1 (i.e., without a history of clinical depression and currently not being depressed were used as the reference. In model 1, we adjusted for several key demographic characteristic variables, which included age, sex, ethnicity as Caucasian, marital status, education, and immigrant status. In model 2, we further adjusted for four variables that might reflect lifestyle, i.e., friends, alcohol, smoking, and physical activity. In model 3, three variables, i.e., waist circumference, systolic blood pressure, and co-morbidity, related to cardio-vascular health status were further adjusted. We also examined whether there is an interaction between sex and depression status since females usually have a higher prevalence of depression. Additionally, general linear models (GLMs) were used to obtain the adjusted mean levels of lipids for depression status, and multiple regression was used to examine the linear relationship between non-HDL cholesterol levels and CESD-10 scores with adjusting for the covariates mentioned in model 3. To ensure generalizability, the trimmed inflation weight was used for estimating means and proportions for the population and analytic weight was used when examining relationships between variables (CLSA 2017).

Results

Overall, the mean level of non-HDL cholesterol was 3.72 mmol/L among participants from the CLSA Comprehensive cohort at baseline; approximately 28% exhibited non-HDL cholesterol levels of 4.3 mmol/L or higher, a level needed to initiate primary prevention measures according to the 2016 Canadian Cardiovascular Society guidelines (Anderson et al. 2016); 17.3% of participants had a history of clinical depression; and 15.1% of participants might be currently depressed (CES-D10 score ≥ 10). Summary statistics for demographics and other covariates across the five categories of non-HDL cholesterol levels can be found in Table 1. All univariate analyses results were statistically significant ($p < 0.05$). The mean age of the participants was 60 years. Compared with those within the lowest levels of non-HDL cholesterol (<2.6 mmol/L), those within the highest (≥ 5.7 mmol/L) were approximately five years younger (58.1 vs. 62. 7 years). In addition, they were more likely to be female (52.4% vs. 42.4%), an immigrant (19.5% vs. 16.9%), current smoker (14.7% vs. 8.3%), and have fewer close friends (4.8 vs. 5.2). They also tended to have the highest mean levels of CES-D10 scores, systolic blood pressure, and waist circumference, and the worst lipid profile (e.g., the levels of total cholesterol were 3.8, 4.7, 5.6, 6.5, and 7.5 mmol/L, respectively for the five non-HDL cholesterol level categories).

Table 1. Selected characteristics for 26 819 participants from the baseline data of the CLSA by non-HDL cholesterol level.

	Non-HDL cholesterol (mmol/L)				
	<2.6	~3.7	~4.8	~5.7	≥5.7
	$n = 4542$	$n = 9982$	$n = 8527$	$n = 2796$	$n = 972$
Age, years (mean (SE))	62.7 (0.2)	59.5 (0.1)	58.6 (0.1)	58.2 (0.2)	58.1 (0.3)
Female (%)	42.4	51.6	49.7	50.7	52.4
Married or living with partner (%)	74.7	76.5	77.1	77.2	74.5
Caucasian (%)	96.8	95.8	96.0	96.1	96.7
Education (%)					
Less than post-secondary	22.0	19.7	20.1	21.5	22.5
Some college degree	31.3	32.4	33.3	34.3	35.7
Bachelor's degree or above	46.7	47.9	46.6	44.2	41.8
Immigrated (%)	16.9	17.6	17.6	18.0	19.5
Alcohol intake during past 12 months (%)					
Nondrinker	11.7	10.9	9.9	11.1	12.6
Less than once in a month	11.9	10.8	11.1	10.1	14.0
More than once in a week	76.4	78.3	78.9	78.8	73.5
Smoking (%)					
Nonsmoker	30.4	34.9	34.1	33.0	26.6
Former smoker	61.3	56.9	56.9	56.9	58.8
Current smoker	8.3	8.2	9.0	10.1	14.7
CESD-10 score (mean (SE))	5.0 (0.07)	5.1 (0.05)	5.2 (0.06)	5.4 (0.09)	6.0 (0.02)
Moderate physical activity 30+ min (%)	11.6	13.5	13.8	13.6	13.4
Lipid profile, mmol/L (mean (SE))					
Total cholesterol	3.8 (0.01)	4.7 (0.006)	5.6 (0.005)	6.5 (0.009)	7.5 (0.02)
HDL cholesterol	1.6 (0.008)	1.6 (0.005)	1.5 (0.005)	1.4 (0.007)	1.3 (0.01)
Non-HDL cholesterol	2.2 (0.005)	3.2 (0.003)	4.2 (0.003)	5.2 (0.005)	6.3 (0.02)
LDL cholesterol	1.6 (0.006)	2.5 (0.004)	3.3 (0.005)	4.1 (0.009)	5.0 (0.02)
Triglyeride	1.2 (0.009)	1.5 (0.008)	1.9 (0.01)	2.5 (0.02)	3.2 [0.05]
Systolic blood pressure, mm Hg (mean (SE))	117.5 (0.2)	117.7 (0.2)	119.6 (0.2)	121.9 (0.3)	122.7 (0.6)
WC, cm (mean (SE))	93.4 ((0.2)	91.4 ((0.2)	93.4 (0.2)	94.5 (0.2)	95.7 (0.4)
No. of close friends (mean (SE))	5.2 (0.09)	5.4 (0.06)	5.4 (0.06)	5.3 (0.1)	4.8 (0.1)
No. of comorbid diseases (mean (SE))	3.4 (0.04)	2.6 (0.02)	2.3 (0.02)	2.3 (0.04)	2.4 (0.07)

Note: CLSA, Canadian Longitudinal Study on Aging; CESD-10, 10-item Center for Epidemiologic Studies Depression Scale; HDL, high-density lipoprotein; LDL, low-density lipoprotein; WC, waist circumference.

The estimated parameters from the continuation ratio model are shown in Table 2. After adjusting for age, sex, ethnicity, education, marital status, and immigrant status (model 1), compared with those without a history of clinical depression and currently not being depressed (Group 1), the

Table 2. Parameter estimates for continuation ratio models with logit-link on restructured data set ($n = 65\ 159$) and on original dataset ($n = 26\ 819$).

	Model 1				Model 2				Model 3			
	b	SE (*b*)	OR	95% CI	*b*	SE (*b*)	OR	95% CI	*b*	SE (*b*)	OR	95% CI
Inter1	0.004	0.087	—	—	−0.134	0.094	—	—	−2.1835***	0.132	—	—
Inter2	2.842***	0.040	—	—	2.876***	0.042	—	—	3.0319***	0.045	—	—
Inter3	1.329***	0.039	—	—	1.353***	0.040	—	—	1.453***	0.043	—	—
Inter4	0.269***	0.041	—	—	0.285***	0.043	—	—	0.3279***	0.045	—	—
Depression 1 vs. 0	0.025	0.031	1.03	(0.97, 1.09)	0.032	0.033	1.03	(0.97, 1.10)	0.0896*	0.035	1.09	(1.02, 1.17)
Depression 2 vs. 0	0.006	0.029	1.01	(0.95, 1.07)	0.018	0.030	1.02	(0.96, 1.08)	0.0462	0.033	1.05	(0.98, 1.12)
Depression 3 vs. 0	0.144**	0.040	1.16	(1.07, 1.25)	0.133**	0.042	1.14	(1.05, 1.24)	0.187***	0.046	1.21	(1.10, 1.32)
Age, years	−0.018***	0.001	0.98	(0.98, 0.98)	−0.018***	0.001	0.98	(0.98, 0.98)	−0.015***	0.001	0.99	(0.98, 0.99)
Sex	−0.095***	0.018	0.91	(0.88, 0.94)	−0.094***	0.019	0.91	(0.88, 0.95)	−0.293***	0.023	0.75	(0.71, 0.78)
Ethnicity	0.104*	0.045	1.11	(1.02, 1.21)	0.135**	0.048	1.15	(1.04, 1.26)	0.1239*	0.051	1.13	(1.02, 1.25)
Education	−0.066***	0.012	0.94	(0.92, 0.96)	−0.063***	0.013	0.94	(0.92, 0.96)	−0.0408**	0.013	0.96	(0.94, 0.99)
Marital status	−0.002	0.015	1.00	(0.97, 1.21)	0.005	0.016	1.01	(0.97, 1.04)	0.01	0.017	1.01	(0.98, 1.04)
Immigrant status	0.099***	0.025	1.10	(1.05, 1.16)	0.097**	0.026	1.10	(1.05, 1.16)	0.1017**	0.028	1.11	(1.05, 1.17)
Friend	—	—	—	—	0.0005	0.002	1.00	(1.00, 1.01)	0.002	0.001	1.00	(1.00, 1.01)
Alcohol	—	—	—	—	0.016	0.015	1.02	(0.99, 1.05)	0.0019	0.016	1.00	(0.97, 1.03)
Smoker	—	—	—	—	0.041*	0.016	1.04	(1.01, 1.07)	0.0402*	0.017	1.04	(1.01, 1.08)
Physical activity	—	—	—	—	0.047	0.028	1.05	(0.99, 1.11)	0.066*	0.029	1.07	(1.01, 1.13)
WC	—	—	—	—	—	—	—	—	0.008***	0.001	1.01	(1.01, 1.01)
SBP	—	—	—	—	—	—	—	—	0.0107***	0.007	1.01	(1.01, 1.01)
Multimorbidity	—	—	—	—	—	—	—	—	−0.0967***	0.006	0.91	(0.90, 0.92)
Model χ^2 (df)	14 842.6 (12)***				14 028.1 (16)***				13 626.4 (19)***			
R_L^2	0.204				0.207				0.223			

Note: *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$. Depression 0 (reference): 10-item Center for Epidemiologic Studies Depression Scale (CES-D10) <10 and no clinical depression history; Depression 1: CES-D10 ≥10 and no clinical depression history; Depression 3: CES-D10 <10 and having clinical depression history; Depression 4: CES-D10 ≥10 and having clinical depression history.
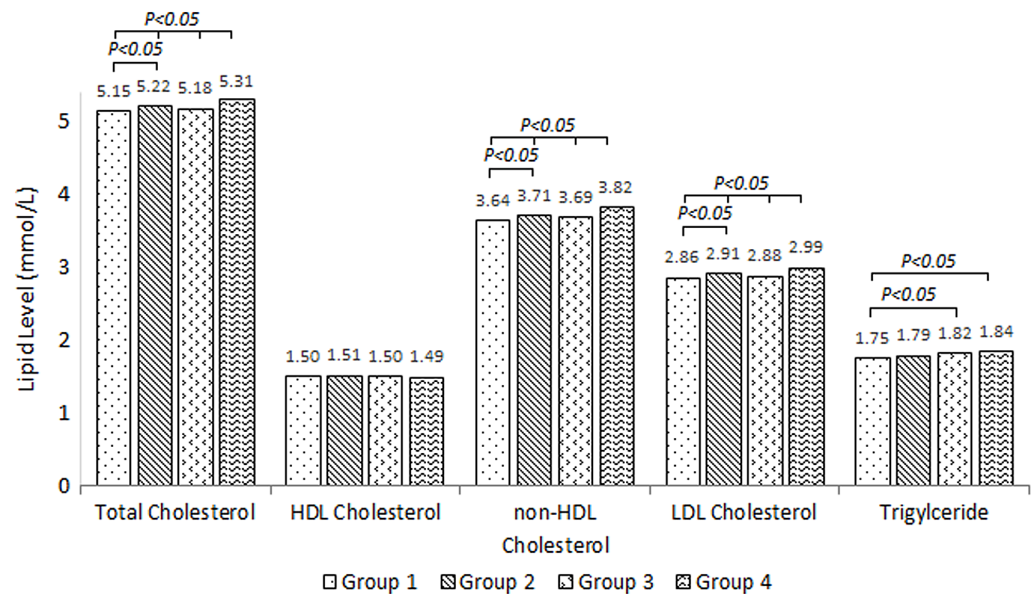
Fig. 1. Adjusted mean levels of lipids by depression status. Depression status: Group 1: no history of clinical depression and Center for Epidemiological Studies Depression Scale 10 questions version (CES-D10) score < 10; Group 2: no history of clinical depression but CES-D10 score ≥ 10; Group 3: having history of clinical depression but CES-D10 score < 10; and Group 4: having history of clinical depression and CES-D10 score ≥ 10.

ORs (95% CIs) of being in a higher non-HDL cholesterol category for those in Group 2 to Group 4 were 1.025 (0.965, 1.090), 1.006 (0.950, 1.066), and 1.155 (1.068, 1.248), respectively. A further adjustment for the number of close friends, alcohol intake, smoking, and physical activity (model 2) had a little effect on these estimates. However, when further adjusting for waist circumference, systolic blood pressure, and number of comorbidities (model 3), the ORs (95% CIs) for depression status were slightly increased: the ORs (95% CIs) of being in higher non-HDL cholesterol category for those in Group 2 to Group 4 were 1.094 (1.021, 1.172), 1.047 (0.983, 1.116), and 1.206 (1.101, 1.321), respectively. The significant covariates in model 3 included age (OR (95% CI): 0.985 (0.982, 0.987)), sex as male (0.746 (0.713, 0.781)), Caucasian (1.132 (1.024, 1.251)), education (0.96 (0.935, 0.986)), immigrant (1.107 (1.048, 1.169)), smoking (1.041 (1.007, 1.076)), moderate physical activity (1.068 (1.009, 1.076)), waist circumference (1.008 (1.007, 1.010)), systolic blood pressure (1.011 (1.009, 1.012)), and comorbidity (0.908 (0.897, 0.919)). All models were statistically significant ($p < 0.001$). The interaction term of sex with depression status was not statistically significant ($p = 0.111$) when being added into model 3. The R^2_L in model 3 reflected that the model significantly reduced the deviance of null model ($D_0 = -2LL_0$) by 22.3%.

The adjusted mean levels of lipids by depression status are shown in **Fig. 1**. After adjusting for covariates similar to those in model 3, the mean levels of total cholesterol for people in depression status Group 1 to 4 were 5.15, 5.22, 5.18, and 5.31 mmol/L; for HDL cholesterol were 1.50, 1.51, 1.50, and 1.49; for non-HDL cholesterol were 3.64, 3.71, 3.69, and 3.82 mmol/L; for LDL cholesterol were 2.86, 2.91, 2.88, and 2.99 mmol/L; for triglycerides were 1.75, 1.79, 1.82, and 1.84 mmol/L, respectively. The differences in mean levels between Group 4 and other groups, between Group 2 and Group 1 were statistically significant ($p < 0.01$) for total, non-HDL, and LDL cholesterol. For triglycerides, the statistical significance in mean differences were only observed between Group 4 and Group 1 and between Group 3 and Group 1 ($p < 0.01$). The results from the multiple regression model showed that with 1 standard deviation increase in CESD-10 scores, the level of non-HDL
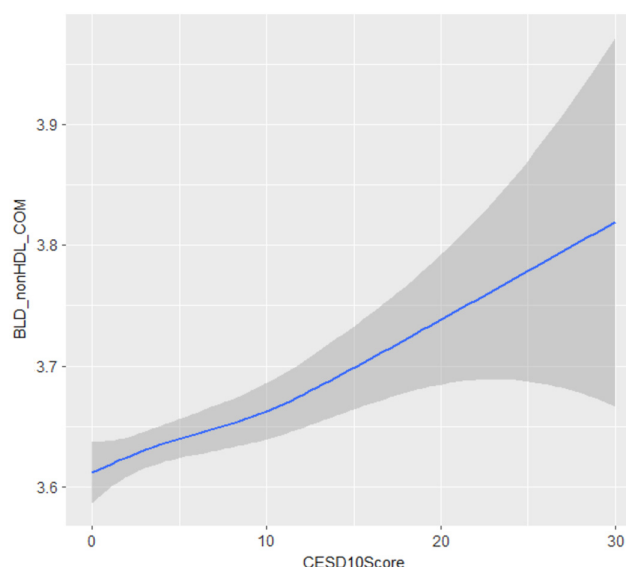
Fig. 2. A smooth, fitted line of the data of Center for Epidemiological Studies Depression Scale 10 questions version scores and levels of non-high-density lipoprotein cholesterol.

cholesterol would increase, on average, approximately 0.03 (95% CI: 0.02, 0.05) mmol/L ($p < 0.05$). A smooth line fitted to data of the association between the levels of non-HDL cholesterol and CESD-10 scores is shown in **Fig. 2**.

Discussion

In this study, we explored the relationship between non-HDL cholesterol and depression status among the CLSA participants. We found that compared with those who had no history of clinical depression and were also not currently depressed, those who were currently depressed regardless of their history of clinical depression had significantly higher average level of non-HDL cholesterol when treated as a continuous variable. They also had higher odds of having higher levels of non-HDL cholesterol when treated as a categorical variable.

Extensive evidence indicates that there is an association between depression and CVD. Depression may not only increase the risk of CVD, but it also affect its pathogenesis and prognosis; yet, the link between depression and CVD is mutual and bidirectional (Dhar and Barton 2016; Penninx 2017). The complicated link between depression and CVD makes it difficult to explore the association between depression and lipids. Previously, a lot of efforts have been made to explore whether lipids are one of the potential etiological factors of depression or suicide. Most studies have focused on the association of LDL cholesterol level with depression and the results have been inconsistent with either a negative, positive, or no association. Overall, several meta-analysis studies have reported negative associations, but the small sample size and high heterogeneity among those existing studies were a notable limitation (Persons and Fiedorowicz 2016; Wu et al. 2016). Further examination of those studies indicated a wide range of age (e.g., aged <30 years in one but >70 years in another), and differences in measurement of lipids (e.g., LDL cholesterol levels measured by directly, Friedewald, or no report), which may contribute to the high heterogeneity. Many studies also examined the relationship between other lipids (i.e., total, HDL cholesterol, triglycerides) and depression, but the results were inconsistent as well. Recently, the results from a large Mendelian randomization analysis suggested that the levels of triglycerides, not LDL cholesterol, were causally related to depression

phenotypes (So et al. 2020). We did observe that people who were currently depressed had higher mean levels of total cholesterol, LDL cholesterol, and triglycerides, but not HDL cholesterol (Fig. 1). Since lipid measurements in the CLSA were nonfasting blood samples, it is hard to compare the association for LDL cholesterol and triglycerides in this analysis with other studies. However, we are not aware of any studies that have examined the relationship between non-HDL cholesterol and depression. We observed that those who are currently depressed had higher levels of non-HDL cholesterol and total cholesterol, particularly those who had a history of clinical depression, after adjustment of well-known covariates. Interestingly, among those people the levels of LDL cholesterol and triglycerides measured with a nonfasting blood specimen were also higher as well as the ORs for being in higher levels of non-HDL cholesterol. When depression status alone was in the model, the proportionate reduction in deviation expressed as R_L^2 was 0.199 (results of the model are not shown), and the R_L^2 in the full model (model 3) was 0.223. This suggests that non-HDL cholesterol levels are highly associated with people's depression status. Our multiple regression results also confirmed there is a linear association between CESD-10 scores and the levels of non-HDL cholesterol. In our previous analysis, we found that people who had a history of clinical depression and were currently depressed had a higher odd of both heart-related disorders and peripheral/vascular related disorders (Liu et al. 2019). The significantly higher levels of non-HDL cholesterol among people in that group may support the observed risk association. This is similar to a previous cohort study, in which they found that when the depressed individuals whose symptoms progressed were at much higher risk for CVD if they were physically inactive (Meyer et al. 2019). Among the statistically significant covariates in model 3, we observed a significant lower odd for age, sex as male, education, and co-morbidity, but a significant higher odd for ethnicity as Caucasian, immigration, smoking, moderate physical activity, waist circumference, and systolic blood pressure. Although we did not find literature that exactly describes the relationship between non-HDL cholesterol and these covariates, the results of for some covariates in our study seem follow other studies. For example, total cholesterol was found to be negatively associated with age in seniors (Volpato et al. 2001). People with a higher education seemed more likely to choose healthy food, thus showing a lower level of cholesterol (Paalanen et al. 2012). Smoking, ethnicity as Caucasian, waist circumference, and systolic blood pressure were found to be positively associated with an elevated level of cholesterol (Eliasson et al. 2006; Sliwa et al. 2012; Nepal et al. 2018; Zhao et al. 2018). We did not find any literature with lower odds for males and comorbidity and higher odds for immigrants; these odds may simply reflect observations of univariate analysis that people with higher levels of non-HDL cholesterol were more likely to be females, immigrants, and with a higher number of co-morbidities.

Several limitations may need to be considered when interpreting the results. First, we used cross-sectional data for our analyses and therefore cannot rule out bidirectional relationships in the associations we observed. Second, the self-reported history of clinical depression might have a misclassification among participants. However, this should be a nondifferential 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.

Conclusion

In conclusion, people who are currently depressed regardless of their history of clinical depression are at an increased risk of having high level of non-HDL cholesterol. Whether the impact of depression on CVD mediates through high level of non-HDL cholesterol, however, needs to be examined through future longitudinal studies.

Acknowledgements

Author contributions

JL conceived and designed the study. JL, SS, and MG analyzed and interpreted the data. JL, CPV, and MN drafted or revised the manuscript.

Competing interests

The authors have declared that no competing interests exist.

Data availability statement

All relevant data are within the paper.

Disclaimer

The opinions expressed in this manuscript are the author's own and do not reflect the views of the Canadian Longitudinal Study on Aging.

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