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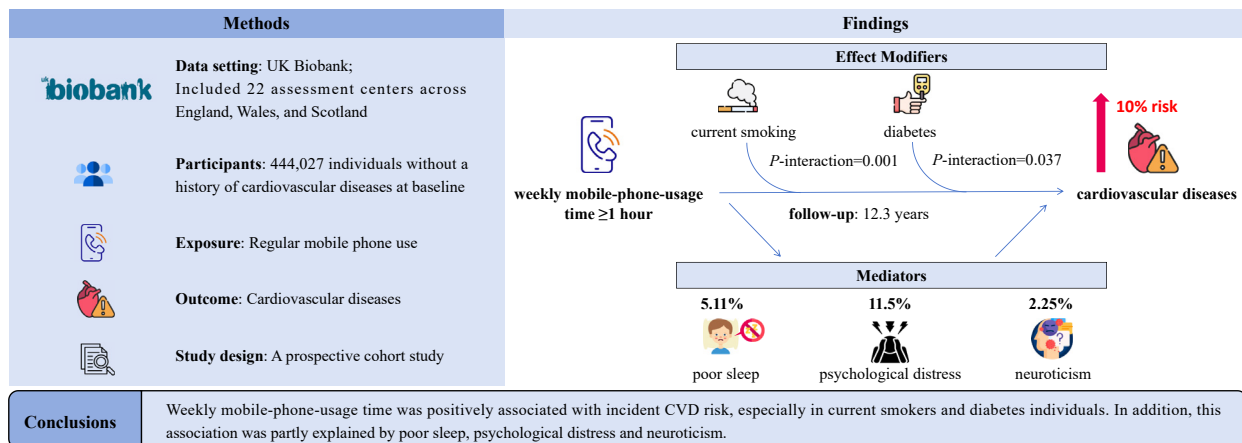
Clinical Research

Regular Mobile Phone Use and Incident Cardiovascular Diseases: Mediating Effects of Sleep Patterns, Psychological Distress, and Neuroticism

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The association between mobile phone use and incident cardiovascular diseases



ABSTRACT

Background: The relationship between mobile phone use and incident cardiovascular disease (CVD) is uncertain. We aimed to examine the association of regular mobile phone use with incident CVD and explore the mediating effects of sleep and mental health.

Methods: A total of 444,027 individuals from the UK Biobank without a history of CVD were included. Regular mobile phone use was defined as at least 1 call per week. Weekly mobile phone usage time was self-reported as the average time of calls per week over the previous 3 months. The primary outcome was incident CVD. The secondary outcomes included each component of CVD and increased carotid intima-media thickness (CIMT). We applied Cox proportional hazard models to assess the association between mobile phone use and incident CVD, and mediation analyses to investigate the role of sleep patterns, psychological distress, and neuroticism.

RÉSUMÉ

Contexte : La relation entre l'utilisation du téléphone mobile et l'incidence des maladies cardiovasculaires (MCV) est incertaine. Nous avons voulu examiner l'association entre l'utilisation régulière du téléphone cellulaire et les maladies cardiovasculaires incidentes et explorer les effets médiateurs du sommeil et de la santé mentale.

Méthodes : Au total, 444 027 personnes de la biobanque britannique (UK Biobank) sans antécédents de MCV ont été incluses. L'utilisation régulière d'un téléphone mobile était définie par un appel par semaine au minimum. La durée d'utilisation hebdomadaire du téléphone cellulaire était rapportée par les utilisateurs eux-mêmes comme étant la durée moyenne des appels par semaine au cours des trois derniers mois. Le critère de jugement principal était l'incidence des MCV. Les critères secondaires comprenaient chaque composante des MCV et l'augmentation de l'épaisseur de l'intima-média carotidienne (EIMc).

Results: In a median follow-up period of 12.3 years, 56,181 individuals developed incident CVD. Compared with nonregular mobile phone users, regular mobile phone users had a significantly higher risk of incident CVD (hazard ratio 1.04, 95% confidence interval 1.02-1.06) and increased CIMT (odds ratio 1.11, 95% CI 1.04-1.18). Among regular mobile phone users, weekly mobile phone usage time was positively associated with the risk of incident CVD, especially in current smokers (P for interaction = 0.001) and diabetic individuals (P for interaction = 0.037). Of the relationship between weekly mobile phone usage time and incident CVD, 5.11% was mediated by sleep patterns, 11.5% by psychological distress, and 2.25% by neuroticism. **Conclusions:** Weekly mobile phone usage time was positively associated with incident CVD risk, which was partly explained by poor sleep, psychologic distress, and neuroticism.

Nous avons appliqué des modèles de risques proportionnels de Cox pour évaluer l'association entre l'utilisation du téléphone portable et l'incidence des MCV, ainsi que des analyses de médiation pour étudier le rôle des habitudes de sommeil, de la détresse psychologique et du neuroticisme.

Résultats : Au cours d'une période de suivi médiane de 12,3 ans, 56 181 individus ont développé une MCV incidente. Par rapport aux utilisateurs non réguliers de téléphone mobile, les utilisateurs réguliers de téléphone portable présentaient un risque significativement plus élevé de MCV (rapport de risque [RR] 1,04, intervalle de confiance [IC] à 95 % 1,02-1,06) et d'augmentation de l'EIMc (RR 1,11, IC à 95 % 1,04-1,18). Parmi les utilisateurs réguliers de téléphones cellulaires, le temps d'utilisation hebdomadaire du téléphone portable était positivement associé au risque de MCV, en particulier chez les fumeurs actuels (p pour l'interaction = 0,001) et les diabétiques (p pour l'interaction = 0,037). La relation entre le temps d'utilisation hebdomadaire du téléphone cellulaire et les MCV incidentes a été influencée à hauteur de 5,11 % par les habitudes de sommeil, de 11,5 % par la détresse psychologique et de 2,25 % par le neuroticisme.

Conclusions : Le temps d'utilisation hebdomadaire du téléphone mobile est positivement associé au risque de MCV, ce qui s'explique en partie par un sommeil insuffisant, un détresse psychologique et le neuroticisme.

Cardiovascular diseases (CVDs) are major causes and contributors to mortality and disability worldwide. The global cases of total prevalent CVD nearly doubled from 271 million to 523 million from 1990 to 2019.¹ Therefore, exploring modifiable risk factors and preventable strategies for CVD has important clinical and public health value.

The number of mobile phone subscriptions has increased dramatically worldwide in recent decades and surpassed 8.2 billion in 2020.² Mobile phones emit radiofrequency electromagnetic fields (RF-EMFs), which could induce hypothalamic-pituitary-adrenal axis deregulation, inflammatory reaction, and oxidative stress,³ and therefore are expected to affect various organs, such as heart and blood vessels.^{4,5} Two previous studies have linked mobile phone use with the increased risk of several CVD outcomes, such as internal carotid artery dissection⁶ and ischemic heart disease,⁷ but not for stroke.⁷ However, these studies were not well designed for estimating the association between mobile phone use and the risk of CVD: One was a case report,⁶ and the primary end points of the other⁷ were cancers and vascular diseases were included largely for comparison with the analyses for cancer. Therefore, to date, the association of mobile phone use with the risk of CVD remains unclear.

Moreover, sleep and mental health have been implicated in the pathogenesis of CVD.^{8,9} Although a high frequency of

mobile phone use has been associated with sleep disturbances and poor mental health,¹⁰⁻¹² it is unknown whether these factors mediate the relationship between mobile phone use and the incidence of CVD.

To fill such gaps in knowledge, we aimed to estimate the relationship between regular mobile phone use and incident CVD, using data from the UK Biobank. If this association was observed, we further assessed the effects of characteristics of mobile phone use, including the duration of use, weekly usage time, and hands-free device/speakerphone use, on the incidence of CVD. Moreover, we also examined the extent to which sleep patterns, neuroticism, and psychologic distress could mediate the relationship between mobile phone use and incident CVD.

Methods

Study participants

The UK Biobank is a large-scale cohort study, that recruited more than a half-million individuals aged 37-73 years at 22 assessment centres across England, Wales, and Scotland from 2006 to 2010. At enrollment, participants were asked to complete touchscreen questionnaires, face-to-face interviews, and physical measurements, as well as provide biological samples for laboratory and genetic analyses. The study design and data collection have been detailed previously.^{13,14} Through linkage to national health records, participants were followed for health conditions.¹⁵

The present study was performed among participants who had complete answers on mobile phone use and its characteristics and did not have a history of CVD at baseline. Thus, there were 444,027 individuals included in the current analyses (Supplemental Fig. S1).

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See page 9 for disclosure information.

Measurements of mobile phone use characteristics

Mobile phone use characteristics were collected by means of self-reported touchscreen questionnaires designed by the UK Biobank at baseline (2006-2010). Participants were first asked about their duration of mobile phone use as follows, "For approximately how many years have you been using a mobile phone at least once per week to make or receive calls?" and selected one of the following answers: "Never used mobile phone at least once per week," "One year or less," "Two to four years," "Five to eight years," and "More than eight years." Regular mobile phone users were defined as those who have used a mobile phone at least once per week to make or receive calls.^{10,16,17}

Then, regular mobile phone users were asked about their weekly mobile phone usage time as follows, "Over the last 3 months, on average how much time per week did you spend making or receiving calls on a mobile phone?" and selected one of the following answers: "Less than 5 minutes," "5-29 minutes," "30-59 minutes," "1-3 hours," "4-6 hours," and "More than 6 hours." In addition, hands-free device/speakerphone use during calls was estimated by asking the question, "Over the last 3 months, how often have you used a hands-free device/speakerphone when making or receiving calls on your mobile?" and answered "Never or almost never," "Less than half the time," "About half the time," "More than half the time," or "Always or almost always." These represent habitual behaviours of weekly mobile phone usage time and hands-free device/speakerphone use and minimise within-person variation.

Measurements of mediators

A healthy sleep score was estimated by considering chronotype, sleep duration, insomnia, snoring, and excessive daytime sleepiness, based on a previous study⁸ (Supplemental Table S1).

The 4-item version of the Patient Health Questionnaire (PHQ-4)¹⁸ was used to define psychologic distress. The PHQ-4 has a total score ranging from 0 to 12. A higher score of the PHQ-4 denotes greater distress. The PHQ-4 has acceptable agreement with longer scales, and has been validated as a measure of depression and anxiety in the general population¹⁹ (Supplemental Table S1).

Neuroticism was evaluated with the 12-item Eysenck Personality Questionnaire-Revised Short Form.²⁰ A total score was calculated as the number of answering "Yes" on the 12 items, and higher scores indicate higher neuroticism (Supplemental Table S1).

Measurements of covariates

The collection and processing of baseline blood samples was conducted under validating standard procedures.²¹ Biochemistry measures, including creatinine, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), blood glucose, glycated hemoglobin A_{1c} (HbA_{1c}), and C-reactive protein (CRP), were carried out at a dedicated central laboratory. The creatinine-based Chronic Kidney Disease Epidemiology Collaboration equation²² was used to calculate the estimated glomerular filtration rate (eGFR).

Information on covariates was collected by means of touchscreen questionnaires or face-to-face interviews, including sex, age, ethnicity, urban residence, household income, education, alcohol consumption, smoking, physical activity, and use of antihypertensive drugs and hypoglycemic drugs. Area-based socioeconomic status was evaluated by means of the Townsend deprivation index (TDI). Body mass index (BMI) was computed as weight in kilograms divided by height in meters squared. Blood pressure was measured twice with a manual sphygmomanometer or Omron HEM-7015IT digital blood pressure monitor. The average of the 2 blood pressure measurements was used. The UK Biobank online protocol (www.ukbiobank.ac.uk) shows the details of these measures. History of diabetes was defined as random blood glucose ≥ 11.1 mmol/L, HbA_{1c} $\geq 6.5\%$, use of hypoglycemic drugs, self-reported diabetes,²³ or medical record of diabetes. History of hypertension was defined as a systolic blood pressure or diastolic blood pressure $\geq 140/90$ mm Hg, use of antihypertensive drugs, self-reported hypertension, or medical record of hypertension.

Outcomes

The primary outcome was incident CVD, a composite of incident stroke, coronary heart disease (CHD), atrial fibrillation (AF), and heart failure (HF). The secondary outcomes included incident stroke, CHD, AF, and HF individually.

Through linkage with hospital admission data and death register, the first occurrence of outcomes was recognised and defined based on the codes of the Office of Population Censuses and Surveys Classification of Interventions and Procedures, version 4, and the International Classification of Diseases editions 9 and 10 (Supplemental Table S2). The follow-up time for each participant was calculated from the date of baseline to the date of the first outcome diagnosis, death, loss to follow-up, or end of follow-up (February 28, 2018, for Wales, September 30, 2021, for England, and July 31, 2021, for Scotland), whichever occurred first.

In the present study, a subset of participants ($n = 43,885$) underwent carotid ultrasound imaging in the years 2014-2020. Individuals whose measurements of carotid intima-media thickness (CMT) did not pass the quality control or were invalid (equal to zero), were excluded from the analyses. Thus, there were 43,839 subjects in the analyses for the association between mobile phone use and increased CMT. CMT measures were performed with the use of a CardioHealth Station (Panasonic Biomedical Sales Europe, Leicestershire, UK).²⁴ After the 2-dimensional scan, measuring each carotid at 2 predefined angles, 4 CMT measurements were conducted, including left 210°, left 240°, right 150°, and right 120°, and the minimum, maximum, and mean of each CMT measurement were recorded. Scans were performed according to standard operating procedures and were deemed to be of sufficient quality by both the UK Biobank senior radiographer and by external validation at the Oxford Cardiovascular Clinical Research Facility.²⁴ In the primary analyses, the average of 4 mean measurements was used. Increased CMT, another secondary outcome, was defined as CMT being at or above the sex-specific 75th percentile.^{25,26}

Genetic risk scores for CVD

Information on genotyping, imputation, and quality control in the UK Biobank study has been detailed previously.¹⁵ The genetic risk scores (GRS) were computed based on previous studies for CHD,²⁷ stroke,²⁷ HF,²⁸ and AF²⁹ with the use of a weighted method.³⁰ A higher GRS denotes a higher genetic susceptibility to the corresponding CVD.

Statistical analyses

Baseline characteristics were described as mean $\pm$ SD and n (%) for continuous and categorical data, respectively. Comparisons of characteristics among different categories of weekly mobile phone usage time (< 5 minutes, 5-29 minutes, 30-59 minutes, 1-3 hours, 4-6 hours, and > 6 hours) were conducted by means of 1-way analysis of variance for continuous data or chi-square test for categorical data in regular mobile phone users.

Cox proportional hazards regression analyses were applied to estimate the association of regular mobile phone use (regular users vs nonregular users) with the risk of incident CVD in the whole sample, as well as the association of duration of mobile phone use, weekly mobile phone usage time, and hands-free device/speakerphone use during calls with the risk of incident CVD in regular mobile phone users. Potential confounding factors that were chosen *a priori* according to evidence of associations with mobile phone use or CVD,^{7,10,31-34} or variables that showed significant differences between regular mobile phone users and nonregular users, were selected as covariates. Model 1, the minimally adjusted model, adjusted for age and sex. Model 2 adjusted for age, sex, ethnicity, urban residents, education, TDI, income, BMI, moderate and vigorous physical activity, alcohol consumption, smoking status, HDL-C, LDL-C, TG, CRP, eGFR, and history of hypertension and diabetes at baseline. Model 2 further considered other potential confounding factors to estimate the independent association between mobile phone use and CVD. Model 3 adjusted for all covariates in model 2 and mutually adjusted for different characteristics of mobile phone use to evaluate the independent effects of each characteristic of mobile phone use. Model 3 was the primary analytical model in the present analyses. In examining the significance of the product term of follow-up time and exposure, no significant deviation from the proportional hazards assumption was found. Logistic regression models including the same covariates above, plus duration from baseline to CIMT measurement, were used for increased CIMT as an outcome. The linear trend was analysed across weekly mobile phone usage time categories by treating the grouping as numeric variables. For covariates with selections of “prefer not to answer” or “do not know,” or with missing data, continuous variables were imputed with mean values, and categorical variables were created as an additional category. The numbers and percentages of participants for missing covariates are presented in [Supplemental Table S3](#).

To examine the robustness of the results, several sensitivity analyses were conducted. First, GRS for each CVD component was further adjusted for the association between weekly mobile phone usage time and incident CVD. Second, to minimise reverse causality, CVD cases identified during the first 2 years of follow-up were excluded. Third, considering

non-CVD death as a competing risk event, we performed a sensitivity analysis using the Fine-Gray subdistribution hazards regression model. Fourth, the missing data were imputed with the use of multiple imputations by chained equations, using the “mice” R package. Five imputed data sets were generated, and the results were combined using Rubin’s rules.

To evaluate the potential effect modifications on the association between weekly mobile phone usage time and incident CVD, stratified analyses were performed according to sex, age, urban residence, BMI, current smoking, CRP, eGFR, history of diabetes, history of hypertension, duration of mobile phone use, and hands-free device/speakerphone use during calls. Stratum-specific estimates were derived by including an interaction term into a multivariable survival model. The Wald test was used to examine the significance of the interactions between potential modifiers and weekly mobile phone usage time categories (< 1 hour or $\geq$ 1 hour).

The model-based causal mediation analysis framework was performed to estimate the potential mediators, including sleep patterns, psychological distress, and neuroticism, between weekly mobile phone usage time and incident CVD, using the “mediation” R package.³⁵ First, potential mediators were regressed by weekly mobile phone usage time and covariates adjusted in model 3 in linear regression models. Second, incident CVD was regressed by weekly mobile phone usage time, potential mediators, and covariates adjusted in model 3 in Weibull regression models. Finally, combining the results of the outcome and mediator models, we estimated the proportion of mediation. *P* values of the mediating effect were examined by means of quasibayesian estimation with 1000 iterations. We adjusted for major confounders in mediation analysis, to consider reasonably the confounding assumptions for mediation analyses, that is, that there is no unmeasured exposure-mediator confounding, mediator-outcome confounding, and exposure-outcome confounding, and no mediator-outcome confounding affected by the exposure. A directed acyclic graph displayed the hypothetical causal pathways between mobile phone use and the risk of incident CVD ([Supplemental Fig. S2](#)).

Statistical significance was defined as 2-tailed *P* < 0.05 in all analyses. R software (version 4.1.1; www.R-project.org) was used to perform statistical analyses.

Results

Baseline characteristics of study population

The flow chart is illustrated in [Supplemental Figure S1](#). The present study included 444,027 individuals, with 378,161 individuals being regular mobile phone users. The study population had a mean age of 56.1 ± 8.1 years and included 195,623 men (44.1%).

Compared with nonregular mobile phone users, regular mobile phone users were younger, had higher proportions of current smokers and urban residents, and had lower proportions of history of hypertension and diabetes. They also had higher income, TDI, and BMI, and lower education levels ([Supplemental Table S4](#)). In addition, compared with regular mobile phone users with a shorter weekly mobile phone usage time, those with a longer weekly mobile phone usage time were younger, had higher proportions of men,

current smokers, and using hands-free device/speakerphone during calls, had a lower proportion of history of hypertension, had higher TDI, income, BMI, eGFR, and duration of mobile phone use, and had lower HDL-C (Supplemental Table S5). In nonregular mobile phone users or regular mobile phone users in different categories of weekly mobile phone usage time, older participants had higher BMI and a higher proportion of history of hypertension (Supplemental Tables S6 and S7).

Regular mobile phone use and incident CVD

During a median 12.3 years follow-up, a total of 56,181 individuals (12.7%) developed incident CVD. Compared with nonregular mobile phone users, regular mobile phone users had a significantly higher risk of incident CVD (hazard ratio [HR] 1.04, 95% confidence interval [CI] 1.02-1.06) (Table 1). Further excluding cases identified during the first 2 years of follow-up, using the Fine-Gray subdistribution hazard models, or imputing missing values for covariates by multiple imputation methods did not materially change the results (Supplemental Tables S8-S10).

Characteristics of mobile phone use and incident CVD in regular mobile phone users

Overall, in regular mobile phone users, the duration of mobile phone use and hands-free device/speakerphone use during calls were not significantly associated with incident CVD (Table 1). However, there was a significant and positive dose-response relationship between weekly mobile phone usage time and the risk of CVD (Supplemental Fig. S3; Table 1). Compared with participants who used a mobile phone < 5 minutes per week, the risk of incident CVD was significantly higher in those who used a mobile phone 5-29 minutes (HR 1.03, 95% CI 1.01-1.06), 30-59 minutes (HR 1.07, 95% CI 1.04-1.10), 1-3 hours (HR 1.13, 95% CI 1.09-1.16), 4-6 hours (HR 1.15, 95% CI 1.09-1.21) and > 6 hours per week (HR 1.21, 95% CI 1.14-1.28; P for trend < 0.001; Table 1). Accordingly, compared with participants who used a mobile phone < 1 hour per week, those who used a mobile phone $\geq$ 1 hour had a significantly increased risk of incident CVD (HR 1.10, 95% CI 1.08-1.13) (Table 1). Further excluding cases identified during the first 2 years of follow-up, using Fine-Gray subdistribution hazard models, or imputing missing values for covariates by multiple imputation method showed similar results (Supplemental Tables S8-S10). Similar trends were also observed for each CVD component, including incident CHD, stroke, HF, and AF (Table 2).

Further adjustments for the GRS of each CVD component did not materially change the relationship of weekly mobile phone usage time with each CVD component (Supplemental Table S11).

Association of regular mobile phone use and weekly mobile phone usage time with risk of increased CIMT

In the 2014-2020 CIMT measurements (median duration from baseline to CIMT measurement 9.2 years; interquartile range 7.7-10.3 years), there were 10,978 participants with increased CIMTs. Compared with nonregular mobile phone users, regular mobile phone users had a significantly higher risk of increased CIMT (odds ratio [OR] 1.11, 95% CI 1.04-1.18) (Table 3).

In regular mobile phone users, longer weekly mobile phone usage time was significantly associated with a higher risk of increased CIMT (P for trend < 0.001). Compared with

participants who used a mobile phone < 1 hour per week, a higher risk of increased CIMT was observed among those who used a mobile phone $\geq$ 1 hour per week (OR 1.09, 95% CI 1.02-1.16) (Table 3).

Mediation analyses on the association between mobile phone use and incident CVD

Compared with nonregular mobile phone users, regular mobile phone users were associated with a poorer sleep pattern and higher levels of neuroticism and psychologic distress (Supplemental Table S12). In regular mobile phone users, compared with those who used a mobile phone < 1 hour per week, those who used a mobile phone $\geq$ 1 hour per week had a poorer sleep pattern, higher levels of neuroticism, and psychologic distress (Table 4). Furthermore, a poorer sleep pattern and higher levels of psychologic distress and neuroticism were significantly associated with the increased risk of incident CVD (Table 4; Supplemental Table S12).

The mediation analyses showed that a poor sleep pattern, psychologic distress, and neuroticism significantly mediated the positive association between weekly mobile phone usage time and the risk of incident CVD, with a mediating proportion of 5.11% (95% CI 3.80%-7.00%), 11.50% (95% CI 8.79%-16.00%), and 2.25% (95% CI 1.40%-3.00%), respectively (Table 4). A poor sleep pattern, psychologic distress, and neuroticism also significantly mediated the association between regular mobile phone use and a higher risk of CVD (Supplemental Table S12).

Stratified analyses

Stratified analyses for the relationship of weekly mobile phone usage time (< 1 vs $\geq$ 1 hour) with incident CVD were conducted in different subgroups (Supplemental Fig. S4).

The positive association of weekly mobile phone usage time with incident CVD was stronger in current smokers (vs noncurrent smokers; P for interaction = 0.001) and diabetes individuals (vs nondiabetic individuals; P for interaction = 0.037) (Supplemental Fig. S4). However, the positive association of weekly mobile phone usage time with incident CVD did not significantly vary by sex, age, urban residence, BMI, CRP, eGFR, history of hypertension, duration of mobile phone use, and hands-free device/speakerphone use during calls (all P for interaction > 0.05) (Supplemental Fig. S4).

Discussion

In this population-based cohort study, we first demonstrated that regular mobile phone use was associated with a significantly increased risk of incident CVD. In regular mobile phone users, a longer weekly mobile phone usage time was related to a significantly increased risk of incident CVD and each component of it, including incident CHD, stroke, HF, and AF. Sleep patterns, psychologic distress, and neuroticism significantly mediated 2.25%-11.50% of the association between weekly mobile phone usage time and incident CVD. In addition, regular mobile phone use and a longer weekly mobile phone usage time were associated with a higher risk of increased CIMT, which is a clinical measure of carotid atherosclerosis. This suggests a the role of mobile phone use in vascular damage, which may be one of the mechanisms by which mobile phone use affects the risk of CVD. However, no

Table 1. Associations of mobile phone use and different mobile phone use characteristics with incident cardiovascular disease

			Model 1*		Model 2 [†]		Model 3 [‡]	
Mobile phone use	n	Cases	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
All participants (n = 444,027)								
Regular mobile phone use (at least once per week)								
No	65,866	10,515	Ref		Ref		—	—
Yes	378,161	45,666	1.04 (1.02-1.06)	< 0.001	1.04 (1.02-1.06)	< 0.001	—	—
Regular mobile phone users (n = 378,161)								
Duration of mobile phone use								
≤ 1 y	11,573	1720	Ref		Ref		Ref	
2-4 y	77,037	9961	0.96 (0.91-1.01)	0.098	1.00 (0.95-1.05)	0.957	0.99 (0.94-1.04)	0.587
5-8 y	137,678	16,092	0.91 (0.86-0.95)	< 0.001	0.98 (0.93-1.03)	0.385	0.96 (0.91-1.01)	0.088
> 8 y	151,873	17,893	0.92 (0.88-0.97)	0.001	1.00 (0.95-1.05)	0.904	0.96 (0.91-1.01)	0.128
Weekly mobile phone usage time								
<5 min	77,603	10,751	Ref		Ref		Ref	
5-29 min	147,430	18,108	1.03 (1.01-1.06)	0.011	1.03 (1.00-1.05)	0.035	1.03 (1.01-1.06)	0.014
30-59 min	65,643	7511	1.08 (1.05-1.12)	< 0.001	1.06 (1.03-1.09)	< 0.001	1.07 (1.04-1.10)	< 0.001
1-3 h	54,771	5969	1.16 (1.12-1.19)	< 0.001	1.11 (1.08-1.15)	< 0.001	1.13 (1.09-1.16)	< 0.001
4-6 h	16,066	1646	1.20 (1.14-1.26)	< 0.001	1.13 (1.08-1.20)	< 0.001	1.15 (1.09-1.21)	< 0.001
> 6 h	16,648	1681	1.30 (1.24-1.37)	< 0.001	1.19 (1.13-1.26)	< 0.001	1.21 (1.14-1.28)	< 0.001
P for trend			< 0.001		< 0.001		< 0.001	
Categories								
<1 h	290,676	36,370	Ref		Ref		Ref	
≥ 1 h	87,485	9296	1.15 (1.12-1.17)	< 0.001	1.10 (1.07-1.13)	< 0.001	1.10 (1.08-1.13)	< 0.001
Hands-free device/speakerphone uses during calls								
Never or almost never	310,111	38,189	Ref		Ref		Ref	
Less than half the time	36,120	3821	0.97 (0.94-1.00)	0.063	1.00 (0.97-1.04)	0.970	0.97 (0.94-1.01)	0.147
About half the time	13,957	1500	1.00 (0.95-1.05)	0.948	1.02 (0.96-1.07)	0.564	0.98 (0.93-1.04)	0.525
More than half the time	7884	870	1.03 (0.96-1.10)	0.378	1.03 (0.96-1.10)	0.444	0.99 (0.92-1.06)	0.683
Always or almost always	10,089	1286	1.14 (1.08-1.20)	< 0.001	1.07 (1.01-1.13)	0.027	1.02 (0.97-1.09)	0.399

* Model 1: adjusted for age and sex.

† Model 2: adjusted for covariates in model 1 plus ethnicity, urban residence, education, Townsend deprivation index, income, body mass index, moderate and vigorous physical activity, alcohol consumption, smoking status, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride, C-reactive protein, estimated glomerular filtration rate, and history of hypertension and diabetes.

‡ Model 3: adjusted for covariates in model 2 plus mutually adjustments for different characteristics of mobile phone use.

significant relationships of the duration of mobile phone use or hands-free device/speakerphone use during calls with incident CVD were observed. These results indicated that it is the frequency of mobile phone use, rather than the total duration of mobile phone use, that determined the effect of mobile phone use on CVD risk.

Only a few previous studies have evaluated the relationship of mobile phone use and CVD risk. A case report indicated a possible relationship between a long-lasting phone conversation with hyperflexion of the head and internal carotid artery dissection.⁶ However, another study with incident cancers as the primary outcome reported that ever using a mobile phone was not consistently related to the incidence of admission for ischemic heart disease and stroke, observing a higher risk of admission for ischemic heart disease but a lower risk of admission for stroke.⁷ Notably, those authors reported that the study included the analyses of vascular disease largely for comparison with those for cancers, and they could not suggest the direct association between mobile phone use and vascular diseases. In addition, the study did not consider other CVDs, such as HF and AF. More importantly, it did not collect and report some important mobile phone use characteristics, such as weekly mobile phone usage time and hands-free device/speakerphone use during calls. Our study, taking into account mobile phone use and a series of important characteristics of mobile phone use simultaneously, and focusing on CVD outcomes, observed a significantly increased risk of incident CVD related to regular mobile phone users compared with

nonregular users, and a significant positive relationship of weekly mobile phone usage time with incident CVD among regular mobile phone users. A previous study found that mobile phone use and a longer weekly mobile phone usage time were associated with an increased risk of hypertension.³⁶ However, our study demonstrated that mobile phone use was significantly associated with CVD risk even after adjustment for cardiovascular risk factors, including hypertension, diabetes, dyslipidemia, obesity, and inactivity, indicating that this association was independent from those cardiovascular risk factors.

The underlying mechanisms linking mobile phone use with an increased risk of CVD remain unclear. The present study indicated that sleep patterns, psychologic distress, and neuroticism may be potential mechanisms of the association between mobile phone use and CVD. Consistently with previous studies,¹⁰⁻¹² our findings showed that a longer weekly mobile phone usage time was associated with a poorer sleep pattern and higher levels of psychologic distress and neuroticism. A poor sleep pattern may adversely affect the development of CVD through disrupted circadian rhythm, endocrine and metabolic disruption, increased sympathetic nervous activity and inflammation, and increased CIMT, plaque, and atherosclerosis.⁸ Poor mental health may lead to disturbance of cardiometabolic metrics (eg, blood pressure, lipid profile, and blood glucose level), autonomic dysfunction, and increased immune and inflammatory processes, and therefore result in the increased risk of CVD.⁹ Supporting this

Table 2. Associations between weekly mobile phone usage time and incident coronary heart disease, stroke, heart failure, atrial fibrillation in mobile phone users

Weekly mobile-phone-usage time	n	Cases	Model 1 [*]		Model 2 [†]		Model 3 [‡]	
			HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Coronary heart disease								
< 5 min	77,603	5759	Ref		Ref		Ref	
5-29 m	147,430	9973	1.05 (1.02-1.08)	0.003	1.05 (1.02-1.08)	0.004	1.05 (1.02-1.09)	0.003
30-59 m	65,643	4257	1.11 (1.07-1.16)	< 0.001	1.09 (1.04-1.13)	< 0.001	1.09 (1.05-1.14)	< 0.001
1-3 h	54,771	3512	1.20 (1.15-1.25)	< 0.001	1.16 (1.11-1.21)	< 0.001	1.16 (1.11-1.22)	< 0.001
4-6 h	16,066	1008	1.27 (1.19-1.36)	< 0.001	1.20 (1.12-1.29)	< 0.001	1.21 (1.12-1.29)	< 0.001
> 6 h	16,648	1051	1.38 (1.29-1.48)	< 0.001	1.25 (1.17-1.34)	< 0.001	1.26 (1.17-1.35)	< 0.001
<i>P</i> for trend			< 0.001		< 0.001		< 0.001	
Stroke								
< 5 min	77,603	2124	Ref		Ref		Ref	
5-29 m	147,430	3424	1.01 (0.95-1.06)	0.836	1.01 (0.96-1.07)	0.728	1.02 (0.96-1.07)	0.594
30-59 m	65,643	1389	1.07 (1.00-1.14)	0.055	1.06 (0.99-1.14)	0.091	1.07 (1.00-1.15)	0.055
1-3 h	54,771	1038	1.11 (1.03-1.20)	0.007	1.09 (1.01-1.18)	0.028	1.10 (1.02-1.19)	0.015
4-6 h	16,066	304	1.26 (1.12-1.42)	< 0.001	1.22 (1.08-1.38)	0.001	1.24 (1.09-1.40)	0.001
> 6 h	16,648	275	1.25 (1.10-1.42)	0.001	1.18 (1.04-1.34)	0.012	1.20 (1.05-1.37)	0.008
<i>P</i> for trend			< 0.001		< 0.001		< 0.001	
Heart failure								
< 5 min	77,603	1864	Ref		Ref		Ref	
5-29 m	147,430	3062	1.04 (0.99-1.11)	0.145	1.04 (0.98-1.10)	0.232	1.05 (0.99-1.11)	0.107
30-59 m	65,643	1256	1.13 (1.05-1.21)	0.001	1.08 (1.01-1.17)	0.028	1.11 (1.03-1.19)	0.007
1-3 h	54,771	940	1.18 (1.09-1.27)	< 0.001	1.11 (1.02-1.20)	0.015	1.13 (1.04-1.23)	0.003
4-6 h	16,066	227	1.11 (0.96-1.27)	0.160	1.01 (0.88-1.17)	0.837	1.04 (0.90-1.20)	0.586
> 6 h	16,648	247	1.33 (1.16-1.52)	< 0.001	1.16 (1.02-1.33)	0.030	1.19 (1.03-1.37)	0.016
<i>P</i> for trend			< 0.001		0.006		0.001	
Atrial fibrillation								
< 5 min	77,603	4629	Ref		Ref		Ref	
5-29 m	147,430	7411	1.02 (0.98-1.06)	0.347	1.00 (0.96-1.04)	0.962	1.00 (0.97-1.04)	0.830
30-59 m	65,643	2960	1.07 (1.02-1.12)	0.004	1.03 (0.99-1.08)	0.160	1.04 (0.99-1.09)	0.103
1-3 h	54,771	2202	1.11 (1.05-1.17)	< 0.001	1.06 (1.01-1.12)	0.025	1.07 (1.01-1.13)	0.013
4-6 h	16,066	547	1.07 (0.98-1.17)	0.129	1.00 (0.92-1.10)	0.917	1.02 (0.93-1.11)	0.737
> 6 h	16,648	547	1.19 (1.09-1.30)	< 0.001	1.10 (1.00-1.20)	0.040	1.11 (1.01-1.22)	0.028
<i>P</i> for trend			< 0.001		0.008		0.004	

* Model 1: adjusted for age and sex.

† Model 2: adjusted for covariates in model 1 plus ethnicity, urban residents, education, Townsend deprivation index, income, body mass index, moderate and vigorous physical activity, alcohol consumption, smoking status, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride, C-reactive protein, estimated glomerular filtration rate, and history of hypertension and diabetes.

‡ Model 3: adjusted for covariates in model 2 plus duration of mobile phone use and hands-free device/speakerphone use during calls.

Table 3. Association of regular mobile phone use and weekly mobile phone usage time with the risk of increased carotid intima-media thickness

		Model 1 [*]			Model 2 [†]		Model 3 [‡]	
	n	Cases	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value
All participants (n = 43,839)								
Regular mobile phone use (at least once per week)								
No	5805	1682	Ref		Ref		—	—
Yes	38,034	9296	1.14 (1.07-1.22)	< 0.001	1.11 (1.04-1.18)	0.003	—	—
Regular mobile phone users (n = 38,034)								
Weekly mobile-phone-usage time								
< 5 min	7640	2086	Ref		Ref		Ref	
5-29 m	15,002	3813	1.05 (0.98-1.12)	0.135	1.04 (0.97-1.11)	0.284	1.04 (0.97-1.11)	0.235
30-59 m	6639	1547	1.08 (1.00-1.17)	0.049	1.06 (0.98-1.16)	0.134	1.07 (0.98-1.16)	0.109
1-3 h	5603	1221	1.13 (1.04-1.24)	0.004	1.11 (1.01-1.21)	0.026	1.11 (1.01-1.22)	0.023
4-6 h	1591	309	1.14 (0.99-1.31)	0.071	1.08 (0.94-1.25)	0.270	1.09 (0.94-1.27)	0.233
> 6 h	1559	320	1.36 (1.18-1.57)	< 0.001	1.27 (1.10-1.47)	0.001	1.29 (1.11-1.49)	0.001
<i>P</i> for trend			< 0.001		< 0.001		< 0.001	
Categories								
<1 h	29,281	7446	Ref		Ref		Ref	
≥ 1 h	8753	1850	1.12 (1.05-1.19)	< 0.001	1.09 (1.02-1.16)	0.008	1.09 (1.02-1.16)	0.013

* Model 1: adjusted for age and sex.

† Model 2: adjusted for covariates in model 1 plus duration from baseline to carotid intima-media thickness measurement, ethnicity, urban residents, education, Townsend deprivation index, income, body mass index, moderate and vigorous physical activity, alcohol consumption, smoking status, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride, C-reactive protein, estimated glomerular filtration rate, and history of hypertension and diabetes.

‡ Model 3: adjusted for covariates in model 2 plus duration of mobile phone use and hands-free device/speakerphone use during calls.

Table 4. Mediation analyses of sleep pattern, psychologic distress, and neuroticism in the association of weekly mobile phone usage time (≥ 1 h vs < 1 h) with incident cardiovascular disease

	Outcome model*		Mediator model†		Percent mediated (95% CI)	P value
	HR (95% CI)	P value	β (95% CI)	P value		
Healthy sleep score	0.93 (0.92-0.94)	< 0.001	-0.07 (-0.08 to -0.07)	< 0.001	5.11 (3.80-7.00)	< 0.001
Neuroticism	1.02 (1.02-1.03)	< 0.001	0.09 (0.07-0.12)	< 0.001	2.25 (1.40-3.00)	< 0.001
PHQ-4	1.06 (1.05-1.06)	< 0.001	0.19 (0.17-0.21)	< 0.001	11.5 (8.79-16.00)	< 0.001

All analyses were adjusted for age, sex, ethnicity, urban residents, education, Townsend deprivation index, income, body mass index, moderate and vigorous physical activity, alcohol consumption, smoking status, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride, C-reactive protein, estimated glomerular filtration rate, history of hypertension and diabetes, duration of mobile phone use, and hands-free device/speakerphone use during calls. Outcome models were further adjusted for weekly mobile phone usage time.

* Outcome model: Weibull regression models with potential mediators as independent variables and incident cardiovascular disease as a dependent variable.

† Mediator model: linear models with potential mediators as dependent variables, weekly mobile-phone-usage time as an independent variable.

evidence, the present study found that sleep patterns, psychologic distress, and neuroticism significantly mediated the association of mobile phone use with incident CVD.

The interactions between weekly mobile phone usage time and various factors on CVD risk were explored. We observed a stronger positive relationship between weekly mobile phone usage time and CVD among current smokers and diabetic individuals. Smoking and diabetes both increase oxidative stress,^{37,38} which is one of the crucial mechanisms of endothelial dysfunction and the development of CVD.⁴ In addition, chronic exposure to RF-EMFs emitted from mobile phones could lead to oxidative stress and inflammatory response.³ Therefore, RF-EMF exposure from mobile phones in combination with smoking and diabetes may have a stronger effect in increasing CVD risk. However, the positive relationship between weekly mobile phone usage time and incident CVD did not significantly vary among different CRP levels. In addition, despite the sex differences in CVD risk,³⁹ we did not find a statistically significant sex difference in the association between weekly mobile phone usage time and incident CVD.

There are several limitations to this study. First, owing to the availability of data, the questionnaires on mobile phone use were restricted to the characteristics of phone calls, and other use patterns of mobile phones were not taken into account, such as use of messaging apps, watching videos, and browsing the web. Nevertheless, phone calls have traditionally been regarded as a crucial mobile phone function and have been widely used as a leading characteristic of mobile phone use in some large population-based studies, including COSMOS (Cohort Study of Mobile Phone Use and Health)¹⁰ and the UK Million Women Study.⁴⁰ Future studies collecting more information on mobile phone use are needed to validate our findings and evaluate the applicability of our findings in current society. Second, this study was observational and cannot prove causality. Third, although many potential confounders were adjusted, unmeasured confounding bias cannot be eliminated, for example, the type of mobile phone technology used and other sources of RF-EMFs. In mediation analyses, residual confounding is also possible in the exposure-outcome, exposure-mediator, and mediator-outcome relationships; therefore, these results should be interpreted with caution. Fourth, information on mobile phone use and its characteristics was self-reported. Therefore, despite using a prospective design and robust

results after further excluding CVD cases identified during the first 2 years of follow-up, the impact of exposure misclassification due to recall bias may still exist. Our findings need to be validated by future studies using other methods to collect information on mobile phone use, such as linking with phone providers. Fifth, mobile phone use was assessed only once at baseline, limiting the ability to assess the influence of change in mobile phone use on our results. With the spread of mobile phones, mobile phone users are likely to spend more time using mobile phones, and thus our study may underestimate the relationship of weekly mobile phone usage time with incident CVD. In the UK Biobank study, based on the answers to the question, "Is there any difference between your mobile phone use now compared to two years ago?," only 12.6% and 14.6% of the individuals at baseline and at the 2012-2013 follow-up reported using the mobile phone less frequently. Finally, the study population was mainly of European ancestry and healthier than the general population in the UK.⁴¹ Therefore, our results may not be generalisable to other populations. Considering these limitations, our findings should be confirmed in future studies.

Conclusion

Regular mobile phone use was significantly related to an increased risk of incident CVD and increased CIMT, particularly in those with a longer weekly mobile phone usage time. The relationship between weekly mobile phone usage time and incident CVD was partly mediated by sleep patterns, psychologic distress, and neuroticism. If further confirmed, this study encourages measures to decrease the time spent on mobile phones for promoting the primary prevention of CVD events, such as facilitating the mobile phones' function of displaying and reminding mobile phone users of mobile phone usage time. On the other hand, improving sleep and mental health status may help reduce the higher risk of CVD associated with mobile phone use.

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Ethics Statement

Ethical approval for the UK Biobank was from the North West Research Ethics Committee (11/NW/0382).

Patient Consent

All participants gave an informed consent before enrollment.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at <https://doi.org/10.1016/j.cjca.2024.06.006>.