# **INTRODUCTION**

## **Epidemiology of the outcome**

The NIH’s National Heart, Lung, and Blood Institute defines high cholesterol as having total blood cholesterol (TC) levels greater than or equal to 200 mg/dL (National Institutes of Health, 2001). More than one third of the United States adult population has high TC and therefore are at a heightened risk for cardiovascular disease (CVD) and stroke (Virani et al., 2021). Established risk factors of high cholesterol include obesity, lack of physical activity, diet high in saturated and trans fat, type 2 diabetes, smoking, age, gender, and familial hypercholesterolemia (CDC, 2020).

According to the American Heart Association’s *Heart Disease and Stroke Statistics—2021 Update*, adults aged 20 and older in 2015-2018 had a mean TC of 190.6 mg/dL (Virani et al., 2021). This was not within the Healthy People 2020 target goal of 177.9 mg/dL. It was also estimated that 93.9 million, or 38.1%, of U.S. adults had greater than 200 mg/dL TC. For TC greater than 240 mg/dL the estimated affected adults were 28 million, or 11.5%. Although the prevalence of high TC in adults had decreased from 18.3% in 2000 to 10.5% in 2018, the report states that the decline is likely due to greater uptake of medications rather than changes in lifestyle. The estimated economic burden of managing and preventing high cholesterol in the U.S. is between $18.5 million and $77 million every year. The estimated burden of CVD, an outcome of having high cholesterol, is $219 billion (Ferrara et al., 2021).

## **Epidemiology of the exposure**

During 2019 in the U.S., the Bureau of Labor Statistics reported full-time employees spent an average of 8.78 hours per workday on work or work-related activities. This becomes 43.9 hours throughout a 5-day workweek. Globally, 36.1% of workers exceed 48 hours each week (Rivera et al., 2020). These numbers surpass many developed countries’ standards and recommendations. The Australian government mandates employers must not work their employees over 38 hours per week without reason. The European Union states that employers ensure their workers do not exceed an average of 48 hours per week including overtime. The U.S. *Fair Labor and Standards Act* (1938) requires overtime pay after 40 hours in a week for nonexempt employees, and there is no maximum number of hours.

When defining long working hours in research, prior studies have used various cut points such as >40 per week (Rivera et al., 2020), >80 hours per week (Lee et al., 2016), and >11 hours per day (Lemke et al., 2017). According to the U.S. *Patient Protection and Affordable Care Act* (2010), employees working at least 30 hours per week on average are considered full-time. Working long hours leaves less time for reaching the CDC’s guidelines of recommended exercise, diet, and sleep (Artazcoz et al., 2009). It also can expose individuals to greater amounts of work strain and psychological stress. These experiences have been shown to increase other biomarkers such as blood pressure and heart rate instability (Kivimaki & Steptoe, 2018).

## **Literature review**

In 1999 a study examined blood cholesterol of engineers in Japan working in machinery manufacturing (Sasaki et al., 1999). No significant differences were directly shown between the weekly working hours of <57, 57-63, and >63. They did note though that a stratification by age resulted with an interaction for the age group of 30-39, but not the age group of 20-29. The group with 57-63 work hours had a higher mean TC than the other two groups.

A survey of random working adults in France described that exposure to long working hours, defined as +10-hour days in at least 50 days out of the year, was associated with adverse lipid levels in men (Virtanen et al., 2019). Their results were not significant for women.

In a meta-analysis of long working hours, coronary heart disease, and stroke resulted with a 27% increased risk of stroke in working 49-54 hours per week compared to 36-40 hours (Kivimaki et al., 2015). The risk of those working more than 55 hours was 33% greater.

Researchers examining data from the Korean NHANES data showed 1.76 times higher odds of coronary heart disease for men and 1.63 times higher odds for women working >80 hours per week compared to those working 40 hours per week (Lee et al., 2016). The risk of stroke in these two working groups for men was insignificant, but women working >80 hours had 2.32 times higher odds of stroke than women working 40 hours.

A cross-sectional study of U.S. truck drivers was performed to explore an effect of long working hours and blood cholesterol measurements (Lemke et al., 2017). The study population had a mean low-density lipoprotein cholesterol (LDL-C) of 113.66 mg/dL. When designing a linear regression model, working greater than 11 hours per day significantly increased the estimated LDL-C 14.24 mg/dL.

22-year-old Australians from the Western Australian Pregnancy Cohort Study examined the effect of long working hours on blood cholesterol measurements (Reynolds et al., 2018). There were no significant results of TC or LDL-C, but high-density lipoprotein cholesterol (HDL-C) was lower in those working >38 hours compared to those working 38 hours or less.

Note: I am planning to make major edits to this section to reduce repetitiveness and consolidate multiple studies into summaries of a single idea.

## **Gaps in the Literature**

Most prior studies of long working hours used CHD or stroke as the outcome rather than blood cholesterol measurements. Of the studies that did examine blood cholesterol they were either not done in the United States, had very high cut points for defining long hours, or did not describe comparisons in risk or odds.

## **Theoretical framework**

**Diagram

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Note: I am considering simplifying this model to make room for the other factors of working long hours that were discussed in the last paragraph of the exposure epidemiology section (lack of exercise and sleep, poor diet). These factors would connect *working hours* with *pathophysiological effects*. This would be done by removing *job demands* and *job* *decision latitude* so that there is a direct arrow to *psychological distress*, and preserving the 1 and 2 citations. I would also remove *stress response* and have a direct arrow from *psychological distress* to *pathophysiological effects*. A description of the model will be added after the changes to this model are finalized.

## **Summary**

U.S. adults spend an average of 8.78 hours per workday on work-related activities, exceeding the standardized 40-hour workweek and reducing available time for healthy behaviors such as sleep and exercise, and increasing exposure to job-related stress. During 2013-2016 U.S. adults had a mean TC of 190.6 mg/dL, which is above the Healthy People 2020 goal of 177.9 mg/dL. 93.9 million adults (38.1%) had a TC of 200 mg/dL or greater. 28 million adults (11.5%) had a TC of 240 mg/dL or greater. High cholesterol is estimated to burden the U.S. with a cost between $18.5 million and $77 million each year. CVD, a result of having high cholesterol, is estimated to cost the U.S. $219 billion dollars.

Prior research has examined long working hours and its association with blood cholesterol levels but they either studied populations outside of the U.S. or had very high cut points for working hours. This analysis is unique in that it studies a random selection of U.S. adults and lowers the cut points in order to produce results more closely related to the general U.S. adult population.

## **Research question**

Is greater self-reported number of hours worked in the prior week associated with laboratory measured…high TC among men and women aged 16-80 years who participated in NHANES 2017-2018?

## **Research hypothesis**

**HO**: There is not an association between greater working hours in the past week and high TC.

**H1**: There is a significant positive association between greater working hours in the past week and high TC.

# **METHODS**

## **Study design and setting**

The National Center for Health Statistics (NCHS) administered the National Health and Nutrition Examination Survey (NHANES) during 2017 and 2018. This survey recorded health information, status, and measurements for the purpose of estimating nationwide disease prevalence and aiding in health policy development. The sample design was a complex multi-level process that oversampled and undersampled certain demographics that later became weighted to represent the whole noninstitutionalized civilian population of the United States. Participants were interviewed about their personal demographics, health status, and behaviors, while measurements were recorded by a mobile clinic during a standardized physical examination.

## **Study population**

During 2017-2018 the National Health and Nutrition Examination Survey (NHANES) recruited 9,254 participants. Of these participants, 1,715 were selected based on their blood tests and questionnaire results. All selected observations had recorded TC measurements, at least 30 total hours worked at all jobs during the week prior to being surveyed, were not currently taking cholesterol medication, and were at least 18 years of age.

Diagram

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## **Data sources and measurement**

*Exposure:* Total working hours in the week prior to the survey administration was obtained from a series of questions. First participants were asked “In this part of the survey I will ask you questions about your work experience. Which of the following were you doing last week?” The options to answer this question were as followed: Working at a job or business; with a job or business but not at work; looking for work; not working at a job or business; refused; or don’t know. Only those who responded that they worked at a job or business were considered for this study. A follow-up question was asked to those who responded as such: “How many hours did you work last week at all jobs or businesses?” Those who answered between 1 and 5 hours were recorded as “5”. Six to 78 hours were recorded as discrete values. No respondent~~s~~ reported 79 hours, and those who reported 80 or more were recorded as “80”. Refusals to report and “Don’t know” were also recorded. The goal of this study was to examine full-time workers, so observations were dropped from the analysis if they worked less than 30 hours, refused to report, or did not know how many hours they worked last week.

*Outcome:* TC was recorded by a combined effort of collecting blood samples by the mobile examination clinic and enzymatic assay methods performed by contracted laboratories. Collection of the samples occurred immediately prior to questionnaire data was obtained. After the completion of the laboratory analyses, TC was recorded as discrete values with units of milligrams per deciliter (mg/dL) of blood. No parameters were placed to make exclusions based on these results.

*Covariates:* Variables included in the study were chosen based on modern knowledge of risk factors related to high TC, along with common covariates of past research with similar topics. Two variables were modified from the NHANES 2017-2018 dataset to consolidate similar categories. Those who self-reported being Mexican American or Other Hispanic were collapsed into a single Hispanic category. Also, having not attended high school was combined with not finishing high school or obtaining a GED. This group was considered as No High School Diploma.

## **Efforts to address bias**

Those who worked less than full-time in the prior week, defined as less than 30 hours, were removed from the study to prevent a potential bias that could come from observations who had not worked at all or worked very little. Children and adolescents were removed as they may not have lived long enough to observe direct effects of working hours on TC. The final model controlled for the effects of the selected covariates to measure the association more accurately between prior week working hours and TC.

## **Statistical methods**

Descriptive and analytic statistics were calculated with R 4.1.1 “Kick Things” and utilized the weights included with the NHANES 2017-2018 dataset. No unweighted statistics are listed in Tables 1-3. TC was normally distributed amongst the weighted population; therefore, the mean and standard deviation were included in Table 1. All other continuous variables were nonnormal and the medians with minimum and maximum values were reported.

Simple linear regression was used to determine the effects of the continuous variables on TC for the bivariate analysis. Pearson’s correlation was used to describe the strength of these effects. Bartlett’s test for homogeneity was used to determine the inclusion of a categorical variable in the bivariate analysis. Independent t-tests and ANOVA were performed to calculate differences in means for the included categorical variables. Multiple linear regression was used to build the adjusted model of determining the effect of prior week working hours on TC.

# **RESULTS**

## **Key findings**

* 37.0% of the weighted population had clinically high TC.
* 47.0% reported working more than 40 hours in the prior week.
* Each hour worked was associated with a decrease of TC by 0.28 mg/dL after adjusting for covariates.
* Race and vigorous recreational activity had the largest effect on TC in the adjusted model.

## **Study Population**

The NHANES 2017-2018 dataset consisted of 9,254 observations that was reduced to 1,715 observations due to the exclusion criteria of this study. The final study population was weighted to represent 95,960,477 non-institutionalized adults of the United States.

## **Demographics**

The weighted interquartile range for age was 29 – 51 years old. A BMI of 25 or greater was recorded for 72.9% of the weighted population (SE = 1.6%). The prevalence of either college attendance or completion of an advanced degree was 66.2% (SE = 1.7%). Household income at or below poverty lines was calculated in 9.0% of the weighted population (SE = 0.7%).

## **Total Blood Cholesterol**

TC was normally distributed within the weighted population and had a mean of 190.0 mg/dL (SE = 1.4). Approximately 37.0% had a clinically high TC of over 200 mg/dL (SE = 1.8%) and 9.9% had a very high TC of 240 mg/dL or higher (SE = 1.1%).

## **Working Hours**

Approximately 33.6% of the weighted population worked exactly 40 hours (SE = 1.7%) and 46.9% worked more than 40 hours (SE = 1.8%). The proportion of those who worked between 30-39 hours was 19.4% (SE = 1.4%). Male mean working hours was 46.7 hours (SE = 0.6) whereas the female mean was 42.8 hours (SE = 0.5).

Table 1. Frequencies, means, and medians of select characteristics of U.S adults from NHANES 2017-2018 (n = 1,715)

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **Unweighted n** | **Weighted n** | **Value** |
| Total blood cholesterol (mg/dL) a | 1,715 | 95,960,477 | 190.0 (1.4) |
| Prior week working hours b | 1,715 | 95,960,477 | 40.0 (30.0 – 80.0) |
| Age b | 1,715 | 95,960,477 | 39.0 (18.0 – 80.0) |
| BMI b | 1,715 | 95,960,477 | 28.4 (15.5 – 68.2) |
| Gender c  Male  Female | 917  798 | 53,762,535  42,197,943 | 56.0 (1.8)  44.0 (1.8) |
| Doctor says cholesterol is high c  Yes  No | 306  1,404 | 17,815,106  77,993,989 | 18.6 (1.5)  81.4 (1.5) |
| Sitting minutes daily b | 1,712 | 95,871,954 | 300.0 (2.0 – 1,140.0) |
| Vigorous work activity c  Yes  No | 551  1,163 | 33,618,508  62,313,737 | 35.0 (1.7)  65.0 (1.7) |
| Vigorous recreational activity c  Yes  No | 553  1,162 | 33,773,462  62,187,015 | 35.2 (1.8)  64.8 (1.8) |
| Race/Ethnicity c  Hispanic  Non-Hispanic White  Non-Hispanic Black  Non-Hispanic Asian  Other race or Multi-Racial | 414  553  380  282  86 | 15,809,379  60,436,789  9,793,855  5,381,098  4,539,357 | 16.5 (1.0)  63.0 (1.5)  10.2 (0.6)  5.6 (0.4)  4.7 (0.8) |
| Education c  No H.S. diploma  High school or GED  Some college or AA degree  College graduate or above | 232  388  561  490 | 7,288,350  24,621,029  33,284,597  30,055,543 | 7.7 (0.7)  26.1 (1.6)  31.8 (1.6)  34.4 (1.8) |
| Income-to-poverty ratio b | 1,715 | 95,960,477 | 3.5 (0.0 – 5.0) |

a Value is weighted mean (SE)

b Value is weighted median (min – max)

c Value is weighted percentage (SE)

## **Bivariate Analysis**

Prior week working hours had a weak negative unadjusted correlation with TC (R = -0.08) and accounted for a decrease in TC by 0.31 mg/dL for every hour worked (95% CI = -0.53 – -0.09). The strongest positive unadjusted correlation with TC were age (R = 0.31) and BMI (R = 0.12). An increase of 1 year in age was associated with an increase of 0.93 mg/dL (95% CI = 0.72 – 1.1) in TC. For BMI, an increase of 1 unit was associated with an increase of TC by 0.65 mg/dL (95% CI = 0.32 – 0.97). Taking part in vigorous recreational physical activity reduced TC by 11.1 mg/dL (95% CI = 5.8 – 16.3). Non-Hispanic Blacks had the lowest mean TC (mean = 182.5 mg/dL, SE = 2.2) while the Other and Multi-racial category had the highest (mean = 200.0 mg/dL, SE = 5.3). Higher levels of education generally decreased mean TC, but these differences were not significant.

Table 2. Unadjusted associations with total blood cholesterol

|  |  |  |
| --- | --- | --- |
| **Bivariate correlations with total blood cholesterol** | | |
| Variable | Weighted n | Correlation |
| Prior week working hours | 95,960,477 | -0.08\*\* |
| Age | 95,960,477 | 0.31\*\*\* |
| BMI | 95,960,477 | 0.12\*\*\* |
| Sitting minutes daily | 95,871,954 | 0.03 |
| Income-to-poverty ratio | 95,960,477 | 0.10\*\* |
|  |  |  |
| **Mean total blood cholesterol by categorized features** | | |
| Variable | Weighted n | Mean (SE) |
| Gender  Male  Female | 53,762,535  42,197,943 | 190.3 (1.8)  189.7 (2.0) |
| Doctor says cholesterol is high  Yes  No | 17,815,106  77,993,989 | \*\*\*  213.9 (3.2)  184.5 (1.4) |
| Vigorous work activity  Yes  No | 33,618,508  62,313,737 | 189.5 (2.5)  190.3 (1.6) |
| Vigorous recreational activity  Yes  No | 33,773,462  62,187,015 | \*\*\*  182.8 (2.0)  193.9 (1.8) |
| Race/Ethnicity  Hispanic  Non-Hispanic White  Non-Hispanic Black  Non-Hispanic Asian  Other race or Multi-Racial | 15,809,379  60,436,789  9,793,855  5,381,098  4,539,357 | \*\*  191.0 (2.3)  189.6 (2.0)  182.5 (2.2)  196.3 (2.4)  200.0 (5.3) |
| Education  No H.S. diploma  High school or GED  Some college or AA degree  College graduate or above | 7,288,350  24,621,029  33,284,597  30,055,543 | 198.0 (3.9)  189.9 (3.2)  190.0 (2.3)  190.0 (2.2) |

~ p<0.10

\* p<0.05

\*\* p<0.01

\*\*\* p<0.001

## **Multivariable Analysis**

The adjusted model more accurately predicted the variance in TC (Adjusted R2 = 0.12) compared to the unadjusted model of prior week working hours (Adjusted R2 = -0.0004), though both were not strong predictors. Each hour worked was associated with an average reduction in TC by 0.28 mg/dl (95% CI = -0.44 – -0.11) after adjusting for age, BMI, rigorous recreational activity, income-to-poverty ratio, and race/ethnicity. Race and self-reporting vigorous recreational physical activity had the largest effects on TC in the adjusted model.

# **DISCUSSION**

The…

# **CONCLUSION**

The…

**Table 3.** Multiple Linear Regression Analysis of Total Blood Cholesterol using NHANES 2017-2018 data of men and women aged 18 years and older

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Adjusted Parameter Estimates | | | | |
| **Characteristic** | **Estimate** | **95% Confidence Interval** | **p-value** |
| Intercept | 149.6 | 137.0 – 162.1 | \*\*\* |
| Working hours | -0.3 | -0.4 – -0.1 | \*\* |
| Age | 0.8 | 0.7 – 1.0 | \*\*\* |
| BMI | 0.5 | 0.2 – 0.7 | \*\*\* |
| Rigorous recreational activity | -4.9 | -8.7 – -1.1 | \* |
| Income-to-poverty ratio | 1.7 | 0.5 – 2.8 | \*\* |
| Race / Ethnicity |  |  |  |
| White | Reference |  |  |
| Hispanic | 5.3 | 0.4 – 10.2 | \* |
| Black | -4.5 | -10.4 – 1.4 | 0.14 |
| Asian | 9.2 | 1.6 – 16.8 | \* |
| Other / Multiple | 10.1 | 1.9 – 18.3 | \* |

~ p<0.10

\* p<0.05

\*\* p<0.01

\*\*\* p<0.001

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**CODEBOOK**

|  |  |  |
| --- | --- | --- |
| **Variable Description** | **Response Options** | **Final Categorization** |
| **Outcome:** | | |
| Total cholesterol (mg/dL), laboratory measurement | Continuous | Continuous |
| **Key Exposure:** | | |
| Working Hours  “How many hours did you work last week at all jobs or businesses?” | Continuous;  Refused;  Don’t Know | Continuous |
| **Covariates:** | | |
| Age  Age in years of the participant at the time of screening. Individuals 80 and over are topcoded at 80 years of age. | Continuous;  80 years of age and over | Continuous |
| BMI  Body Mass Index (kg/m2), laboratory measurement | Continuous | Continuous |
| Gender  Gender of the participant. | Male;  Female | Male;  Female |
| Doctor Says High Cholesterol  “Have you ever been told by a doctor or other health professional that your blood cholesterol level was high?” | Yes;  No;  Refused;  Don’t Know | Yes;  No |
| Daily Sitting Time  “How much time do you usually spend sitting on a typical day?” | Continuous;  Refused;  Don’t Know | Continuous |
| Work Activity  “Does your work involve vigorous-intensity activity that causes large increases in breathing or heart rate like carrying or lifting heavy loads, digging or construction work for at least 10 minutes continuously?” | Yes;  No;  Refused;  Don’t Know | Yes;  No |
| Recreational Activity  “In a typical week do you do any vigorous-intensity sports, fitness, or recreational activities that cause large increases in breathing or heart rate like running or basketball for at least 10 minutes continuously?” | Yes;  No;  Refused;  Don’t Know | Yes;  No |
| Race  Recode of reported race and Hispanic origin information, with Non-Hispanic Asian Category. | Mexican American;  Other Hispanic;  Non-Hispanic White;  Non-Hispanic Black;  Non-Hispanic Asian;  Other Race – Including Multi-Racial | Hispanic;  Non-Hispanic White;  Non-Hispanic Black;  Non-Hispanic Asian;  Other Race – Including Multi-Racial |
| Education  “What is the highest grade or level of school you have completed or the highest degree you have received?” | Less than 9th grade;  9-11th grade (Includes 12th grade with no diploma);  High school graduate/GED or equivalent;  Some college or AA degree;  College graduate or above;  Refused;  Don’t know | No high school diploma or equivalent;  High school graduate/GED or equivalent;  Some college or AA degree;  College graduate or above; |
| Poverty Ratio  A ratio of family income to poverty guidelines. | Continuous up to 5 | Continuous up to 5 |