QATAR UNIVERSITY

COLLEGE OF HEALTH SCIENCE

CAROTID INTIMA MEDIA THICKNESS (CIMT) AND CARDIVASCULAR RISK ASSESSMENT: ANALYSIS OF QATAR BIOBANK DATA

BY

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ABSTRACT

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Title: CAROTID INTIMA MEDIA THICKNESS (CIMT) AND CARDIVASCULAR RISK ASSESSMENT: ANALYSIS OF QATAR BIOBANK DATA

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Background: Ultra-sonographic measurement of Carotid Intima Media Thickness (CIMT) has been stated as a technique to detect the early stages of atherosclerosis. CIMT is a newly established, safe, noninvasive and cost effective subclinical atherosclerosis marker that have been associated with identifying any increased cardiovascular risk even in subjects with low and intermediate risk. This study aimed to explore different socioeconomic and lifestyle factors, clinical measurements and biomedical laboratory markers as potential predictors of CIMT.

Methods: In addition to descriptive exploratory analysis to analyze the baseline characteristics of the study risk groups, further appropriate univariate regression models were performed for all lifestyle factors, clinical measurements and biomedical laboratory markers as potential predictors of CIMT. This initial univariate analysis was followed by a purposeful selection multivariate regression analysis technique and goodness of fit study of the fitted model.

Results: The study population was 1425 participants having CIMT values recorded, of which 960 (67.4%) had CIMT below 75th percentile for their gender and age and were hence termed as per evidence as low risk for CVD. The rest of the population 465 (32.6%) were having CIMT above 75th percentile and were termed as high risk for CVD. The age groups 18 – 35, >35 – 55 and >55 had 28.7 %, 39.9 5 , 48.7% of them with high risk level
of CIMT respectively. 861 of the population were females versus 564 males. 36.8% of the females were High risk while only 26.2% of the men were high risk. The main effects model was fitted with five main predictors; systolic blood pressure, C-reactive protein (CRP), gender, waist and high density lipoprotein (HDL) and interactions between HDL and systolic blood pressure and Waist.

**Conclusion:** In this study we found significant association between CIMT and various CVD risk factors such as age, gender, hypertension, diabetes, hypercholesterolemia, BMI, lipids profile. These findings are consistent with the existing literature on CIMT and provide an indirect validation of our data. This study results can permit for good comparative effort with current and future studies in Middle East. Moreover, the study can be used to develop a simple, noninvasive yet sensitive risk-prediction tool to identify the population at risk of CVD, which is a powerful public health strategy that can be more generalized to healthcare service.
DEDICATION

To my Mom, may Allah rest her soul

To my loving husband and courageous kids
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LIST OF ABBREVIATIONS

ACC: American College of Cardiology
AHA: American Heart Association
AHA-ACC-ASCVD score: the new American Heart Association and American College of Cardiology atherosclerotic cardiovascular disease risk score
ARIC (Atherosclerosis Risk In Communities
ASCVD: atherosclerotic cardiovascular disease
ASE: American Society of Echocardiography
AUC: Area under the curve
CAC: Coronary artery calcium
CHD: coronary heart disease
CIMT: carotid intima media thickness
CRP: C-reactive protein
CVD: Cardiovascular diseases
ESC: European Society of Cardiology
ESH: European Society of Hypertension
FRS: Framingham Risk Score
GCC: Gulf Cooperation Council
HDL: High density lipoprotein
HDL: high density lipoprotein
HOMA-IR: Homeostasis model assessment of insulin resistance
hsCRP: high sensitivity C-reactive protein
IGF-1: insulin like growth factor-1
IRB: Institutional Review Board
LDL: low density lipoprotein
MESA: Multi-Ethnic Study of Atherosclerosis
MET: Metabolic Equivalent of Task
MI: Myocardial Infarction
NCD: Non Communicable Diseases
OR: odds ratios
QBB: Qatar biobank
ROC curve: Receiver Operating Characteristics curve
RRS: Reynolds risk score
T2DM: type 2 diabetes mellitus
T2DM: type 2 diabetic mellitus
UKPDS: United Kingdom Prospective Diabetes study
WHO: World Health Organization
1. INTRODUCTION

The World Health Organization (WHO) predicts that Cardiovascular diseases (CVD) would be the leading cause of morbidity and mortality in the developing countries by the year 2020.\textsuperscript{1} In Qatar, CVD and other related Non Communicable Diseases (NCD) have been the leading cause of death in the last 10 years (Figure 1).\textsuperscript{7}

![Figure 1. The most common diseases leading to death (Qatar – 2010) Death rate by 100,000 population\textsuperscript{10}](image)

The diseases of the circulatory system were identified by the Qatar STEPS survey report for 2012 to be one of the top causes of death during the period 2004–2010.\textsuperscript{2} Further, the Qatar Global Burden of Diseases profile concluded that the ischemic heart disease ranked one of the top causes, in terms of the number of years of life lost due to premature death in Qatar in 2010.\textsuperscript{3} Figure 2 shows the top 10 causes of death by rate in 2015 and percent change, 2005-2015 by the Institute for Health Metrics and Evaluation (IHME)
Figure 2: Top 10 causes of death by rate in 2015 and percent change, 2005-2015, by the Institute for Health Metrics and Evaluation (IHME)

It has been established that people with CVD or who are at high risk for CVD, benefits significantly from early detection and management using counselling and medicines, as appropriate. Yet, any early detection and subsequent prevention relies heavily on the ability to accurately, identify the individuals who are at high risk of developing CVD. Thus, there is a pressing need to diagnose subclinical atherosclerosis to facilitate optimum CVD risk stratification in asymptomatic individuals.

Ultra-sonographic measurement of Carotid Intima Media Thickness (CIMT) has been reported as a technique to detect the early stages of atherosclerosis. CIMT is a newly established, safe, noninvasive and cost effective subclinical atherosclerosis marker that have been associated with identifying any increased cardiovascular risk even in subjects with low and intermediate risk.
Using the data from Qatar biobank (QBB), this study aimed to explore different socio-economic and lifestyle factors, clinical measurements and biomedical laboratory markers as potential predictors of CIMT, a surrogate of CVD outcomes. This study is a first step in understanding the current situation with regards to prevalence of CVD risk factors and distribution of CIMT in the Qatari population to generate further research hypothesis. This study results shown would permit for good comparative effort with current and future studies in Middle East. Also the study can be used to develop a simple, non-invasive yet sensitive risk-prediction tool to identify the population at risk of CVD, which is a powerful public health strategy that can be more generalized to healthcare service.
2. BACKGROUND AND LITERATURE REVIEW

2.1. Regional and National Disease Burden

In 2012, Non-communicable diseases (NCD) were responsible for 68% of the 56 million deaths recorded around the world. A recent report by the Qatar supreme council of health has shown that, in the coming years, the Gulf Cooperation Council (GCC) is likely to be affected dramatically by NCD. With regards to economic burden and disability-adjusted life years, Qatar will be most affected by the 5 top NCDS; cardiovascular diseases, mental and behavioral disorders, cancer, respiratory diseases and diabetes. Despite of the different sequel of those diseases, they have common causes related to behavioral or lifestyle risk factors such as fat rich diet, insufficient exercise and tobacco use. Most of those risk factors, such as fat and sugar rich diet and physical inactivity, are related to adopting high income developed countries lifestyle and change in demographics.

2.1.1. CVD burden regionally and nationally.

Among the NCD burden, CVD is the leading cause of death worldwide. In 2012, 31% of all global deaths which is approximately 17.5 million people died from CVDs. 7.4 and 6.7 million deaths of which were due to coronary heart and stroke respectively. More than 75% of those CVD deaths take place in low- and middle-income countries. 82% of the 16 million deaths, under the age of 70, due to NCDs, are in low and middle income countries and 37% are caused by CVDs. In this context, the Gulf region of the Middle East has experienced a significant epidemiological and socioeconomic transition over the past 40 years that led to increasing prevalence of CVD risk factors. The WHO, Non-communicable Diseases Country Profiles for 2011, estimated the proportion of CVD deaths to be high in Saudi Arabia (42%), the UAE (38%), Bahrain (32%) and Qatar (23%).
Furthermore, it has been predicted that cardiovascular disease will become an enormous cost burden for the GCC.

A systematic review has revealed that those affected by CVD in GCC countries were younger than in some developing and developed countries\textsuperscript{13}. Although there was lack of nationally representative data on the prevalence of CVD in the region, high prevalence of key risk factors have been reported. This was apparent with the multiple reports on the high levels of risk factors, with patterns that were very similar amongst the Arabian Gulf population. Such higher prevalence of risk factors were attributable to similarity in lifestyle, culture, religion and shared environmental factors between these countries.\textsuperscript{13} For instance, studies have shown higher prevalence of type 2 diabetes (15-18\%) among adult populations\textsuperscript{14,15} Obesity\textsuperscript{16} and smoking\textsuperscript{17} in the Arabian Gulf populations. There were also reports on some variability in the CVD events across the GCC countries, whereas, those more affluent countries, like Qatar and Kuwait experiencing CVD events that occur 5 to 10 years younger on average than those less oil-rich GCC countries such as Yemen and Oman.\textsuperscript{18}

2.1.2. \textit{CVD prevalence in Qatar.}

Yet, there is a paucity of published data on valid estimates of prevalence of CVD risks or events in Qatar. The Qatar biobank pilot study, is one of the few studies that evaluated the CVD risk among people in Qatar has shown that due to overweight/obesity, 76.6 \% male and 70.4\% female participants are at risk of developing CVD and that total 37\% of the participants have borderline or high levels of total cholesterol. Likewise, 52.7\% of male and 31.7\% of female participants were categorized as being hypertensive or recorded high normal/pre-hypertensive levels and despite being on medications, 21.3\% of
male and 15.6% of female participants who were categorized as hypertensive were still considered hypertensive. 19

Another study that looked into 10- year risk of coronary heart disease amongst 369 Qatar Petroleum workers based on periodic medical examination demonstrated 69.9% of the subjects were categorized as low risk as per Framingham risk scores. They classified 27.1% and 2.9% of their workers to have as intermediate and as high risk, respectively. 20 However, findings from this study were considered to be seriously flawed by the healthy worker effect as such the validity of the findings were questionable. Given that the CVD is considered to be the leading cause of mortality and morbidity, lack of validated data is a major constraint in developed evidenced public health policies related to the control and successful prevention of CVD in Qatar.

2.2. Economic impact

In addition to the disease burden associated with NCD, economic cost of managing these diseases have been enormous. Some reports that compared the cost of managing NCD among the GCC countries demonstrated that in Qatar NCD’s cost $416 per capita of total healthcare spending, which is 22% of the total health care cost in Qatar in 2013. It is interesting to note that neighboring GCC countries like Bahrain, Kuwait, Saudi Arabia, and the UAE spent only around 7% - 11% of their healthcare spending on managing NCDs, 10 which is expected to double by 2025. Meaning that the expenditure for CVD will grow at a double rate of that for health care as a whole. 12
2.3. CVD Risk Scores

With such spread of the CVD pandemic, there is a global, regional and local mandate to detect the individuals at risk and focus on the primary prevention of CVD through the modification and management of prevalent risk factors. A well-established primary prevention strategy uses prediction rules or risk scores to identify those at higher risk. Individuals identified to be at higher risk can then be targeted for specific behavioral or drug interventions. In this context, researchers have suggested the use of various risk stratification tools and scores in asymptomatic individuals to estimates individual 10-year risk of death from CVD. These risk scores were developed using a range of observational studies that identified the major CVD risk factors. These were subsequently incorporated into the development of a number of risk assessment systems/scores now in use.\textsuperscript{21}

The most commonly used score is that originally developed in the Framingham study in the early 1970s, using 5,573 American men and women. The Framingham Risk Score (FRS) was shown to be performing well in America, but not so well in other populations.\textsuperscript{22} Nonetheless, Framingham study has provided profound knowledge base on atherosclerosis and CVD disease risk factors that all subsequent risk assessment studies relied on.\textsuperscript{23,24}

Since Framingham study, there were a number of cohort studies that aimed at refining the risk scores based on well-established CVD risk factors. However, this approach of using traditional risk factors alone in the model, had demonstrated limited performance in the Multi-Ethnic Study of Atherosclerosis (MESA).\textsuperscript{25} DeFilippis et al. evaluated the performance of five major risk factor based scores. They used scores developed by the new American Heart Association (AHA) and American College of Cardiology (ACC) atherosclerotic cardiovascular disease (ASCVD) risk score (AHA-
Acc-ASCVD score) as well as three older Framingham-based risk and the Reynolds Risk Score. They could demonstrate that these risk factor based assessment tools overestimated the risk by a range of 25% to 115%. Overestimation of CVD risk may have substantial implications for individual patients and the health care system.

Another study including 68 randomly selected patients with Type 2 Diabetes Mellitus T2DM with no history or symptoms of CVD studied different risk assessment scores and tools used to estimate the CVD risk such as the United Kingdom Prospective Diabetes study (UKPDS) risk score, FRS and WHO risk score. The study aimed to test the ability of CVD risk scores to predict underlying atherosclerotic in most developing countries.26 and the association between such scores and CIMT, a surrogate marker of atherosclerosis. It is proven that both UKPDS risk engine and FRS have nearly similar ability in identifying subclinical atherosclerotic vascular disease in patients with type 2 diabetes mellitus (T2DM) and they had positive but weak associations with CIMT and moderate agreement between them, which shows the need of developing countries for developing a more reliable and sensitive CVD risk assessment tool.

An average of eight predictors were used by most of the prediction models to predict 10-year risk. Most commonly used of which were age, gender, systolic blood pressure, diabetes, smoking, and cholesterol levels (Appendix B)

Figure 3 shows the Main categories of predictors included in several developed models.67
Figure 3 shows the Main categories of predictors included in several developed models.

2.4. Limitations of CVD Risk Scores and the Emergence of Imaging Surrogates

Several studies also highlighted concerns about possible limitations of the FRS including lack of race and ethnic diversity in the derivation sample and the absence of certain newly identified risk factors. This led to the development of competing risk scores including the Reynolds risk score (RRS). The 2008, RRS added family history and high sensitivity C-reactive protein (hsCRP) to the risk algorithm along with the traditional Framingham risk factors.

Such limitations in the use of risk factor based risk scores have led to the emergence of an increasing interest in searching for new markers of atherosclerosis. Several risk markers have been proposed to improve CHD risk prediction when added to the evidenced Framingham risk factors. In MESA, these most prominently have included measures of subclinical CVD (Coronary artery calcium (CAC), CIMT, carotid plaque, and ankle brachial index), vascular function (flow-mediated dilation), inflammation (especially hsCRP), and family history of CHD.
In this context, researchers have suggested the use of atherosclerosis imaging surrogates to refine the conventional heart scores. Such an approach was thought to improve the adherence and better matching of preventive interventions based on more realistic magnitude of risk, in particular among the low-medium risk patients and in young populations.²⁰

2.5. **Carotid Artery Intima-Media Thickness (CIMT), as a surrogate of subclinical atherosclerosis and CVD risk predictor**

Among the genetic and radiological markers which were proposed to be valid and reliable proxies for CVD events, was the CIMT. The B-mode ultrasound imaging of carotid arteries is a safe and available, noninvasive diagnostic tool for the detection of subclinical atherosclerosis, as well as cardiovascular and stroke event risk stratifications, by measuring the CIMT, a technique that is safe and carries no risk of radiation exposure.³⁴ There is a need to encourage randomized, controlled clinical trials on the efficacy of image-guided risk assessment yet most of the observational cohort and prospective longitudinal studies support the use of noninvasive imaging assessment, especially in intermediate risk groups. It is noted that although the value of image-guided management using carotid calcium score and CIMT, in particular, has not yet been proven using randomized, controlled prospective studies, yet the Framingham score-based management has also not been proven by similar randomized, controlled clinical trials. In that context image guided assessment is accepted as a reasonable strategy for risk detection, although, researchers have debated judging imaging-based risk assessment by a different standard although its prognostic value has been established to be a significant value add to FRS, especially in low and intermediate-risk categories.³¹
Findings from a cohort study supported the significant impact that subclinical atherosclerosis detection adds to FRS risk assessment, thus supporting it’s use to refine cardiovascular risk assessment. In the same prospective cohort, the presence of coronary calcification was associated with an independent 3-fold greater likelihood of statin and aspirin usage. 32

Gepner et al. compared the predictive use of CAC, carotid plaque, and CIMT for incident CVD, CHD, and stroke/transient ischemic attack. CAC presence was the strongest predictor of CVD events after adjustment for traditional risk factors (HR: 3.12; 95% CI: 2.44 to 3.99). Presence of carotid plaque was also significantly associated with incident CVD (HR: 1.61; 95% CI: 1.17 to 2.21). Carotid plaque/CIMT 75th percentile was a better predictor of CVD than carotid plaque alone (HR: 2.06; 95% CI: 1.46 to 2.91). CAC presence was a stronger predictor of CHD events (HR: 4.48; 95% CI: 3.24 to 6.17) than CVD. CAC presence, carotid plaque presence, and carotid plaque/CIMT 75th percentile independently predicted stroke/transient ischemic attack (HR: 1.54; 95% CI 1.09 to 2.18, HR: 1.40; 95% CI: 1.35 to 1.45, and HR: 1.86; 95% CI: 1.10 to 3.13) respectively. 33

In a meta-analysis on eight relevant general population-based cohort studies, involving a total of 37,197 subjects followed for a mean of 5.5 years, it has been concluded that CIMT was able to predict future CV events. Every 0.1 mm increase in the CIMT was associated with an increase in the future risk of Myocardial Infarction (MI) and stroke by 10–15%, and 13–18% respectively. 35 For each SD greater level of log transformed carotid calcium score there was a 2.1-fold increase in the traditional risk factor-adjusted hazard versus 1.3-fold increase for each SD greater maximum CIMT.
In several studies, CIMT was established as a marker of subclinical atherosclerosis which is associated with evidenced risk factors for CVD and with both prevalent and incident CVD. There is widespread use of CIMT in outcome trials as a surrogate of CVD outcomes. Over 20 cohort studies on subjects with or without history of previous vascular disease or CVD risk factors, showed reliably that increased CIMT relates to increased cardiovascular risk, independent of evidenced CVD risk factors.

The Multi-Ethnic Study of Atherosclerosis (MESA), of asymptomatic subjects, compared the ASCVD risk score (ACC/AHA; 2013), Framingham-based risk scores, and the RRS for the prediction of atherosclerotic CVD events. The study established that independent of established vascular risk factors and above 75th percentile for a person’s age and sex, the CIMT was associated with future risk of myocardial infarction, stroke, and death from coronary heart disease.

In another meta-analysis, they concluded that the use of CIMT measurements over time is a valid, suitable, and evidence-based choice to evaluate the effect of a pharmaceutical intervention. Such interventions are expected to beneficially affect atherosclerosis progression and to reduce CVD event risk since a graded relation existed between raising LDL cholesterol and increased CIMT which predicted future vascular. Also, lipid-lowering therapy was also shown to affect CIMT progression within 12–18 months.

The ARIC (Atherosclerosis Risk In Communities) study concluded that including CIMT and the presence or absence of plaque improved coronary heart disease (CHD) risk prediction when added to traditional risk factors. The Rotterdam study followed a large group of non-diabetic people, with no history of CVD for a median of 12.2 years. They
looked into whether using CIMT measurement we could classify individuals into low (<10%), intermediate (10-20%) and high (>20%) 10-year risk groups of stroke and CHD, compared to FRS based models. They proved that only for women of old age, but not of men, CIMT added value to traditional risk factors in the CVD risk stratification.\textsuperscript{41} Appendix A is a summary of the large studies focusing on the prognostic value of CIMT.\textsuperscript{42}

2.5.1. **Guidelines recommendations with regards to CIMT**

The European guidelines on cardiovascular disease prevention in clinical practice recommends that individuals with a moderate CVD risk (1% - 5% 10-year risk of fatal CVD), should be considered for carotid artery ultrasound for CIMT measurement and/or screening for atherosclerotic plaques. The fact is that a huge percentage of middle-aged adults who are asymptomatic belong to this category. Also, the European Society of Cardiology (ESC) / European Society of Hypertension (ESH) guidelines (2013) recommend hypertensive individuals at moderate risk for carotid arteries ultrasound scanning in search for vascular hypertrophy or asymptomatic atherosclerosis. They advised to measure CIMT to detect asymptomatic vascular damage and target organ damage as an independent predictor of cardiovascular death. Damage was defined as the presence of CIMT >0.9 mm or plaque.\textsuperscript{43}

The American Society of Echocardiography (ASE) (2012); recommend Carotid ultrasound scanning to refine FRS cardiovascular disease risk assessment in patients at intermediate risk: 6-20% 10-year risk of myocardial infarction or coronary heart disease death, without established coronary artery disease or its equivalents, those with a family history of premature cardiovascular disease in a first-degree relative, individuals younger than 60 years old with severe abnormalities in a single risk factor who otherwise would not
be candidates for pharmacotherapy and women younger than 60 years old with at least two risk factors. On the other hand, the ACC/AHA guidelines on the assessment of cardiovascular risk (2013) did not recommend ultrasound CIMT routine measurement for risk assessment in a first atherosclerotic CVD event neither is serial studies of CIMT to assess progression or regression in individual patients.

In the absence of larger cohort with long term follow up, that can identify the risk factors related to long term health events in countries like Qatar, one option is to look for sensitive markers of long term health events. The objective of this study examines the association of the CIMT with established CVD risk factors to develop a noninvasive cardiac score in low, intermediate risk Qatari population. The study also explores the prevalence of CVD risk factors and the distribution of carotid intima-media thickness (CIMT) in Qatari population represented by Qatar Biobank (QBB) sample.
3. RESEARCH METHODES

3.1. Study Design:

This is an analytic cross-sectional study, exploring the association between socioeconomic and lifestyle factors, clinical measurements and biomedical laboratory tests as predictors and risk factors of cardiovascular diseases and the CIMT as a surrogate of CVD outcomes, as per the Qatar biobank data collected from a total of 3018 Qatari subjects till February 2016.

3.2. Study population

Qatari nationals aged 18 or more years (3018 subjects), who comprise the eligible population and presented as volunteer subjects to the QBB.

As the focus of the study being on association between outcome and potential predictors, rather than estimating the prevalence per se, the QBB study sample being not random is considered less critical.

3.2.1. Inclusion and Exclusion Criteria:

Only 1425 participants with CIMT measurement (left and/or right CIMT measurement) were included without any exclusion. The remaining 1593 subjects were missing their CIMT measurement. All the available data were used to maximize the power of the study, given the association were tested using multiple regression methods.
3.3. Description of variables:

3.3.1. Risk factors:

The data used was obtained by comprehensive questionnaire information, clinical examination and biological samples. The data used were the literature evident predictors of CVD and related risk factors such as socio-demographic factors, current and past health, family history of health conditions, smoking habits (cigarettes and water pipe or shisha), physical activity levels, sleeping patterns, diet, lifestyle.

Most of literature studying CVD risk factors were targeting the study of age group with a lower cut off from 35 to 50 years of age. However, as in middle eastern population the incidence of CVD is higher in younger population age, our population will be stratified to three groups; young 18-35, middle >35-55, old > 55.

The data also included anthropometry and body composition (Height, weight, waist circumference and Bioimpedance analysis (Tanita)), blood pressure (used average of two, or three times measurements if first and second measurements differed by ≥5 mm Hg) and respiratory function using Pneumotrac Vitalograph Spirometry test. Hematology and blood biochemistry were analyzed by the laboratories of the Hamad Medical Centre Laboratory, Doha. Clinical biomarkers used were CRP, Cholesterol, Fibrinogen, Fasting Glucose, HBA1C, HDL, LDL and Triglycerides.
3.3.2. **Outcome variable:**

The approach of using CIMT as a surrogate of CVD outcomes was taken in this study, since it is evidenced and widespread. The cut-off of 75th percentile was chosen based on results from previous studies pointing to highly increased risk of future cardiovascular events when progression rates exceed the 75th percentile. In literature, the CIMT cutoff points are based on some large population studies, where normal CIMT values were defined. CIMT above the 75th percentile of average for the age, gender were considered an abnormal result, and people with CIMT in less than the 50th percentile were classified in the low risk group. Also, in the report of the Screening for Heart Attack Prevention and Education Task Force, individuals were categorized into high, average and low risk according to CIMT values. High category was indicative of increased cardiovascular risk where CIMT was ≥ 75th percentile. Measurement values from the 25th to the 75th percentile are categorized as average risk and indicative of unchanged cardiovascular risk. Lower than the expected cardiovascular risk had values ≤ 25th percentile.

The QBB studied intima media thickness was studied using 3D carotid ultrasound imaging of both left and right carotid arteries using a Philips ultrasound system and mechano-transducer probe. (Figure 4) It is better noted that all IMT studies included in this study were done and analyzed by same single radiographer.

Average CIMT (Outcome surrogate/dependent variable): Mean CIMT values were used, as it is more reproducible than maximal values. It is calculated as the average value of CIMT in mm between right and left CIMT.
Figure 4: Longitudinal image of carotid bifurcation showing distal part of common carotid artery, carotid bifurcation and the proximal segment of external and internal carotid arteries. CIMT is defined as a double-line pattern visualized by echo 2D on both walls of the common carotid artery (CCA) in a longitudinal view. Two parallel lines (leading edges of two anatomical boundaries) from it: lumen intima and media-adventitia interfaces

3.4. Analysis plan and Statistical Analysis Methods

Standard descriptive analysis was performed to analyze the baseline characteristics of the study risk groups. Continuous values were expressed as mean, standard deviation and median with minimum and maximum values. The categorical values are displayed as actual numbers with percentages. Variables like BMI, CRP, cholesterol, fibrinogen, fasting glucose, HBA1C, HDL, LDL, Triglycerides were analyzed as continues & categorical data. A comorbidities index and family comorbidities index were calculated based on the presence of one to five comorbidities

The Average CIMT variable was coded as a binary variable using evident CIMT 75th
percentile cutoffs as follows: CIMT below 75th percentile for age and gender; low risk CVD group and CIMT above 75th percentile for age and gender; High risk CVD group. (Appendix E)

Pearson's chi-squared test were used to explore statistically significant association between the literature evident predictors of CVD and related risk factors and the CIMT risk groups. Also, Fisher exact test was employed when sample sizes are small. Cochran–Armitage test for trend was used to compute P value in case of ordinal predictor/independent variables. This approach was used to modify the Pearson chi-squared test to incorporate a suspected ordering in the effects of the k categories of the predictor/independent variable.

In addition to descriptive exploratory analysis, further appropriate univariate regression models were performed for all lifestyle factors, clinical measurements and biomedical laboratory markers as potential predictors of CIMT.

This initial univariate analysis was followed by a purposeful selection multivariate regression analysis technique that included all the clinically meaningful predictors that were statistically confirmed as significant at P value less than 0.25. This constituted the initial full multivariable model. The P-value of each covariate Wald-statistics was used to drop all covariates with P-value >0.05. Later on, Likelihood ratio test was used to compare the initial full multivariable model and the smaller model and to prove that the smaller model was a better fit. Variables were considered confounders if >20% change in the β coefficient of variables in the smaller model. The clinically significant individual covariates excluded in univariate analysis were then added one by one to the model and judged to their P values.
The main effects model was then considered for all possible interactions between pairs of included covariates. This was followed by goodness of fit study using Hosmer-Lemeshow test, Classification study, Receiver operating characteristics (ROC) Area and specification errors analysis to prove that the model has all the relevant predictors and the linear combination of these predictors was sufficient. Stata 14 software was used for data analysis.

3.5. Ethical approval:

The QBB data and specimens collection was performed in accordance with the ethical guidelines of the Declaration of Helsinki and all participants gave informed consent. QBB Institutional Review Board (IRB) approval was obtained from the Hamad Medical Corporation Ethics Committee. The QBB-IRB approval was obtained to use unidentified data for this research. (IRB number: QF-QBB-RES-ACC-0051, approved on 26/12/2016)
4. RESULTS

The study population were 3018 participants with 1425 participants having CIMT values recorded, of which 960 (67.4%) had CIMT below 75th percentile for their gender and age and were hence termed as per evidence as low risk for CVD. The rest of the population 465 (32.6%) were having CIMT above 75th percentile for their gender and age and were termed as high risk for CVD.

Table 1 shows the CIMT distribution, mean, median and 75th percentile values of mean CIMT were derived for each age-group, for men and women separately, while Figure 5 shows the histogram distribution of the average CIMT values.

<table>
<thead>
<tr>
<th>Age</th>
<th>Men (N=564)</th>
<th>Females (N=861)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>18 – 35</td>
<td>219</td>
<td>0.48 (0.06)</td>
</tr>
<tr>
<td>&gt;35 – 55</td>
<td>280</td>
<td>0.54 (0.09)</td>
</tr>
<tr>
<td>&gt;55</td>
<td>65</td>
<td>0.66 (0.13)</td>
</tr>
</tbody>
</table>
Table 2 summarizes the demographics of the study population among the two risk levels of CIMT. The age groups 18 – 35, >35 – 55 and >55 had 28.7 %, 39.9 %, 48.3% of them with high risk level of CIMT respectively. 861 of the population were females versus 564 males. 36.8% of the females were High risk while only 26.2 % of the men were high risk. The association between age or gender and CIMT was statistically significant ( P <0.001) for both variables.
### Table 2: Association between demographics & risk levels of CIMT (N=1425)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Average CIMT$^1$</th>
<th>Low Risk N (%)</th>
<th>High risk$^2$ N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>960 (67.4)</td>
<td>465 (32.6)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 – 35</td>
<td></td>
<td>429 (71.3)</td>
<td>173 (28.7)</td>
</tr>
<tr>
<td>&gt;35 – 55</td>
<td></td>
<td>440 (68.1)</td>
<td>207 (39.9)</td>
</tr>
<tr>
<td>&gt;55</td>
<td></td>
<td>91 (51.7)</td>
<td>85 (48.3)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>416 (73.8)</td>
<td>148 (26.2)</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>544 (63.2)</td>
<td>317 (36.8)</td>
</tr>
</tbody>
</table>

1. Average CIMT is the average value in mm., between right and left Carotid intima media thickness.
2. CIMT risk stratification is around 75th percentile, as per age and gender.

Table 3 shows the association between socio-economic status and the risk levels of CIMT. Monthly Income, house ownership status, level of education and current employment status were all statistically significantly related to the level of CIMT risk. The risk seemed to increase as the income and level of education decrease. On the contrary the subgroup with house outright had higher risk CIMT levels than the mortgage, rented and employer provided groups. Stratification analysis showed that age confounded the house ownership, where older participants owned their houses while younger participants rented or had employer provided residential. The same case was seen with the employment status, where the retired had higher risk due to age confounding the association.
Table 4 showed the association between the different physical activity factors and the CIMT risk levels. Hours spent sitting was the most significantly associated with risk, yet in a direction opposite to the expected plausible hypothesis that more sitting would lead to higher risk of atherosclerosis and CVD. In our analysis, the subgroup long sitting more than 12 hours per days were having the less risk than the rest of the subgroups (Short, sitting <5 hour/day and Moderate, sitting 5-12 hours) with percentage with high risk CIMT of (29.8%), (37.2%) and (30.8%) respectively. Again confounding by age explained this finding. Almost two third the of subgroup long sitting more than 12 hours per days (60.3%) were of young age (18 -35 years) while two third the subgroup Short, sitting <5 hour/day were >35 years old. Also the subgroup sitting longer seemed to do more vigorous exercise (17.4%) than the group sitting shorter (11.84) with significant P value 0.001.
Table 3: Association between socio-economic status & risk level of CIMT (N=1425)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Average CIMT¹</th>
<th></th>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Risk N (%)</td>
<td>High risk N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>960 (67.4)</td>
<td>465 (32.6)</td>
<td>0.011 ⁷</td>
<td></td>
</tr>
<tr>
<td>Monthly Income in QR per month ³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 10,000</td>
<td>682 (65.4)</td>
<td>360 (34.6)</td>
<td>0.011 ⁷</td>
<td></td>
</tr>
<tr>
<td>Between 10,000 and 49,999</td>
<td>185 (74.3)</td>
<td>64 (25.7)</td>
<td>0.011 ⁷</td>
<td></td>
</tr>
<tr>
<td>More than 50,000</td>
<td>32 (72.7)</td>
<td>12 (27.2)</td>
<td>0.011 ⁷</td>
<td></td>
</tr>
<tr>
<td>House ownership ⁴</td>
<td></td>
<td></td>
<td>0.045</td>
<td></td>
</tr>
<tr>
<td>Rented</td>
<td>89 (76.1)</td>
<td>28 (23.9)</td>
<td>0.045</td>
<td></td>
</tr>
<tr>
<td>Employer provided</td>
<td>32 (72.7)</td>
<td>12 (27.3)</td>
<td>0.045</td>
<td></td>
</tr>
<tr>
<td>Mortgage</td>
<td>96 (72.7)</td>
<td>36 (27.3)</td>
<td>0.045</td>
<td></td>
</tr>
<tr>
<td>Outright</td>
<td>682 (65.4)</td>
<td>360 (34.6)</td>
<td>0.045</td>
<td></td>
</tr>
<tr>
<td>Level of education ⁵</td>
<td></td>
<td></td>
<td>0.002 ⁷</td>
<td></td>
</tr>
<tr>
<td>Primary or less</td>
<td>43 (50.0)</td>
<td>43 (50.0)</td>
<td>0.002 ⁷</td>
<td></td>
</tr>
<tr>
<td>Secondary or technical</td>
<td>301 (66.7)</td>
<td>150 (33.3)</td>
<td>0.002 ⁷</td>
<td></td>
</tr>
<tr>
<td>University or more</td>
<td>615 (69.4)</td>
<td>271 (30.6)</td>
<td>0.002 ⁷</td>
<td></td>
</tr>
<tr>
<td>Current Employment Status ⁶</td>
<td></td>
<td></td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Employed or business owner</td>
<td>599 (69.9)</td>
<td>257 (30.1)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Housewife or Unemployed</td>
<td>147 (62.8)</td>
<td>87 (37.2)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>84 (55.6)</td>
<td>67 (44.4)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Student or trainee</td>
<td>88 (72.1)</td>
<td>34 (27.9)</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

3. Average CIMT is the average value in mm., between right and left Carotid intima media thickness.
4. CIMT risk stratification is around 75th percentile, as per age and gender.
5. Monthly income: 90 observations “Do Not Know” or “Prefer Not to Answer”
6. House ownership: 88 observations “None of the above” or “Prefer Not to Answer”
7. Level of education: 2 observations “None of the above” or “Prefer Not to Answer”
8. Current Employment status: 62 observations “None of the above” or “Prefer Not to Answer”
9. P value computed using chi-square test for trend

Neither the hours of sleep nor the level of physical activity as per the Metabolic Equivalent of Task (MET) intensities seems to be significantly associated with the CIMT level of risk. (Table 4)
Table 4: Association between Physical Activity & risk level of CIMT (N=1425)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Average CIMT</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Risk</td>
<td>High risk</td>
<td>P value</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>960 (67.4)</td>
<td>465 (32.6)</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td><strong>MET intensities</strong> ³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Activity</td>
<td>340 (65.5)</td>
<td>179 (34.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low MET (&lt;3)</td>
<td>357 (68.4)</td>
<td>165 (31.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate MET (3-6)</td>
<td>79 (63.7)</td>
<td>45 (36.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vigorous MET (&gt;6)</td>
<td>184 (70.8)</td>
<td>76 (29.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Time spent sitting in the past week</strong> ⁴</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short, sitting &lt;5 hour/day</td>
<td>191 (62.8)</td>
<td>113 (37.2)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Moderate, sitting 5-12</td>
<td>643 (69.2)</td>
<td>286 (30.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long, &gt;12 hours/day</td>
<td>85 (70.2)</td>
<td>36 (29.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hours of sleep in 24 hours</strong> ⁵</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 5</td>
<td>95 (69.9)</td>
<td>41 (30.2)</td>
<td>0.49</td>
<td></td>
</tr>
<tr>
<td>5 - 8</td>
<td>707 (67.7)</td>
<td>337 (32.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;8</td>
<td>144 (64.3)</td>
<td>80 (35.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Average CIMT is the average value in mm., between right and left Carotid intima media thickness.
2. CIMT risk stratification is around 75th percentile, as per age and gender.
3. Metabolic Equivalent of Task (MET)
4. Time spent sitting: 71 missing data
5. Hours of sleep: 2 missing data and 18 "Prefer Not to Answer"
6. P value computed using chi-square test for trend

The results of studying the relation between smoking habits (smoking cigarettes, water-pipe, and passive smoking) with the different CIMT levels of risk is shown in Table 5. There was a significantly protective effect for water-pipe smoking!. This was again explained by studying the age distribution of water-pipe smoker. 48.6% of the water-pipe smoker were of the 18-35 years old subgroup while 5.3% only were >55 years old. It is worth mentioning that more than 30% of the study population opted out the smoking questionnaire. Such deficiency in smoking data (whether cigarettes, Shisha, or passive smoking) might have weakened the effect of the smoking profile variables during univariate and eventually the multivariate analysis.
### Table 5: Association between Smoking & risk level of CIMT (N=1425)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Average CIMT</th>
<th></th>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Risk N (%)</td>
<td>High risk N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td>960 (67.4)</td>
<td>465 (32.6)</td>
<td>0.412</td>
<td>6</td>
</tr>
<tr>
<td><strong>Smoking Cigarettes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>86 (64.2)</td>
<td>48 (35.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stopped smoking</td>
<td>426 (66.3)</td>
<td>217 (33.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occasional smoker</td>
<td>165 (71.4)</td>
<td>66 (28.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>267 (67.3)</td>
<td>130 (32.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Smoking Water pipe (shisha)</strong></td>
<td></td>
<td></td>
<td><strong>0.001</strong></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>320 (64.9)</td>
<td>173 (35.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>249 (77.6)</td>
<td>72 (22.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Passive smoking</strong></td>
<td></td>
<td></td>
<td><strong>0.945</strong></td>
<td>6</td>
</tr>
<tr>
<td>No</td>
<td>353 (69.1)</td>
<td>158 (30.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, 1 house member smokes</td>
<td>200 (70.4)</td>
<td>84 (29.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 or more house members smoke</td>
<td>117 (68.8)</td>
<td>53 (31.2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Average CIMT is the average value in mm., between right and left Carotid intima media thickness.
2. CIMT risk stratification is around 75th percentile, as per age and gender.
3. Smoking cigarettes: 2 missing data and 18 “Prefer Not to Answer”
4. Smoking Water pipe: 606 missing data and 5 “Prefer Not to Answer”
5. Passive smoking: 460 missing data and 5 “Prefer Not to Answer”
6. P value computed using chi-square test for trend

For cigarettes smokers, the risk was similar in the three sub-groups never, stopped and current smokers and slightly less in the occasional smokers. Such association was not statistically significant (P= 0.412). Also the risk was similar in the passive smoking subgroups. (Table 5)
Also the association between the CIMT level of risk and the different comorbidities in our population was studied. Comorbidities were associated with high risk CIMT with very high statistical significance \((P < 0.001)\) in case of hypertension, diabetes, and hypercholesterolemia. This association was seen but with less significance in case of myocardial infarction and stroke probably due to few number of observations in each variable (10 and 5 respectively. The comorbidities index were not found to be statistically significantly associated with high risk CIMT. (Table 6)

The association between each of the family history of hypertension and stroke and CIMT high risk was statistically significant \((P = 0.007\) and \(0.022\) respectively). This was not the case when the association between CIMT risk and the other different family comorbidities history was studied (e.g diabetes, Myocardial Infarction and obesity). Again the family comorbidities index which was developed was not associated significantly with CIMT high risk level \((P = 0.09)\) (Table 6)

Table 7 showed no association between CIMT risk levels and diet variables. The Fast-food diet was the only variable included in the multivariate analysis as \(P\)-value for its univariate regression was 0.26, close to the uni-variable cut-off \(P\)-value to shortlist variables for multivariable analyses.
Table 6: Association between comorbidities & risk level of CIMT (N=1425)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Average CIMT</th>
<th>Low Risk N (%)</th>
<th>High risk N (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>960 (67.4)</td>
<td>465 (32.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of Diabetes ³</td>
<td>105 (10.9)</td>
<td>100 (21.7)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>History of Hypercholesterolemia ⁴</td>
<td>292 (31.8)</td>
<td>196 (43.9)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>History of Hypertension ⁵</td>
<td>133 (13.9)</td>
<td>96 (20.8)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>History of Myocardial Infarction ⁶</td>
<td>4 (0.4)</td>
<td>6 (1.3)</td>
<td>0.062</td>
<td></td>
</tr>
<tr>
<td>History of Stroke ⁷</td>
<td>1 (0.1)</td>
<td>4 (0.9)</td>
<td>0.023</td>
<td></td>
</tr>
<tr>
<td>Comorbidities Index ⁸</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>No comorbidities</td>
<td>574 (71.4)</td>
<td>230 (28.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2 comorbidities</td>
<td>362 (64.9)</td>
<td>196 (35.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;= 3 comorbidities</td>
<td>24 (38.1)</td>
<td>39 (61.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of Hypertension</td>
<td>0.007</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paternal only</td>
<td>174 (72.5)</td>
<td>66 (27.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal Only</td>
<td>243 (61.5)</td>
<td>152 (38.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>224 (70.0)</td>
<td>96 (30.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of Myocardial Infarction</td>
<td>0.390</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paternal only</td>
<td>189 (65.4)</td>
<td>100 (34.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal Only</td>
<td>85 (60.3)</td>
<td>56 (39.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>31 (57.4)</td>
<td>23 (42.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of Stroke</td>
<td>0.022</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paternal only</td>
<td>109 (64.9)</td>
<td>59 (35.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal Only</td>
<td>38 (52.1)</td>
<td>35 (47.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>10 (40.0)</td>
<td>15 (60.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of Diabetes</td>
<td>0.544</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paternal only</td>
<td>201 (70.5)</td>
<td>84 (29.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal Only</td>
<td>215 (66.4)</td>
<td>109 (33.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>220 (68.3)</td>
<td>102 (31.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of Obesity</td>
<td>0.271</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paternal only</td>
<td>62 (68.1)</td>
<td>29 (31.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal Only</td>
<td>158 (66.1)</td>
<td>81 (33.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>44 (77.2)</td>
<td>13 (22.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family Comorbidities Index ⁹</td>
<td>0.090</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Family comorbidities</td>
<td>138 (74.2)</td>
<td>48 (25.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-4 Family comorbidities</td>
<td>658 (66.0)</td>
<td>339 (34.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;=5 Family comorbidities</td>
<td>164 (67.8)</td>
<td>78 (32.2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Average CIMT is the average value in mm., between right and left Carotid intima media thickness.
2. CIMT risk stratification is around 75th percentile, as per age and gender
3. Diabetes: 6 responses “Prefer Not to Answer”
4. Hypercholesterolemia: 59 responses “Do Not Remember” or “Prefer Not to Answer”
5. Hypertension: 2 missing data and 5 responses “Prefer Not to Answer”
6. Myocardial Infarction: 23 responses “Prefer Not to Answer”
7. Stroke: 23 responses “Prefer Not to Answer”
8. Index for the participant comorbidities (hypertension, diabetes, Myocardial Infarction, Stroke and Hypercholesterolemia)
9. Index for the family comorbidities (hypertension, diabetes, Myocardial Infarction, Stroke and obesity)
Table 7: Association between diet & risk level of CIMT (N=1425)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Average CIMT¹</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Risk N (%)</td>
<td>High risk N (%)</td>
<td>P value</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>960 (67.4)</td>
<td>465 (32.6)</td>
<td>0.412 6</td>
<td></td>
</tr>
<tr>
<td>Any special diet</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No special diet</td>
<td>729 (66.8)</td>
<td>363 (33.2)</td>
<td>0.412 6</td>
<td></td>
</tr>
<tr>
<td>Low fat diet</td>
<td>116 (68.2)</td>
<td>54 (31.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Another special diet</td>
<td>43 (79.6)</td>
<td>11 (20.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low calorie diet</td>
<td>42 (64.6)</td>
<td>23 (35.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No red meat diet</td>
<td>16 (80.0)</td>
<td>4 (20.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetarian diet ³</td>
<td>6 (60.0)</td>
<td>4 (40.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegan diet ⁴</td>
<td>3 (50.0)</td>
<td>3 (50.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low salt diet</td>
<td>3 (75.0)</td>
<td>1 (25.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fast Food</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never or rarely</td>
<td>318 (66.7)</td>
<td>159 (33.3)</td>
<td>0.262 7</td>
<td></td>
</tr>
<tr>
<td>Less than twice per week</td>
<td>495 (66.6)</td>
<td>248 (33.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Every day or almost every day</td>
<td>143 (72.2)</td>
<td>55 (27.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dairy Diet</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never or rarely</td>
<td>106 (68.4)</td>
<td>49 (31.6)</td>
<td>0.319 7</td>
<td></td>
</tr>
<tr>
<td>1 – 4 times per week</td>
<td>743 (67.9)</td>
<td>352 (32.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>One or more times per day</td>
<td>111 (63.4)</td>
<td>64 (36.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat Diet ⁵</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole fat diet</td>
<td>405 (68.2)</td>
<td>189 (31.8)</td>
<td>0.637 7</td>
<td></td>
</tr>
<tr>
<td>Reduced fat diet</td>
<td>431 (67.8)</td>
<td>205 (32.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat-free diet</td>
<td>76 (65.5)</td>
<td>40 (34.5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Average CIMT is the average value in mm., between right and left Carotid intima media thickness.
2. CIMT risk stratification is around 75th percentile, as per age and gender.
4. Vegan diet: No meat, fish, egg or dairy products.
5. Fat Diet: 79 responses were “Do Not Know” or “Prefer Not to Answer”.
7. P value computed using chi-square test for trend.
Clinical measure were studied with regards to possible association with the CIMT risk. Weight, BMI, Waist, Fat %, Systolic Blood Pressure, Diastolic Blood Pressure and Pulse Rate were all highly significantly associated with elevated risk of CIMT >75th percentile with P-value <0.001 for the Weight, BMI, Waist, Fat %, Systolic Blood Pressure and 0.02 for diastolic Blood Pressure and Pulse Rate. (Table 8)

Though Waist was highly associated with high level risk yet the Waist/Hip ratio was not (P = 0.8). It was clear that the possible association was masked by gender. A further stratified analysis by gender showed that the association was evident with good statistical significance (P = 0.012) in females but not in males (P = 0.322). Logistic regression of CIMT against Waist/Hip ratio in females showed that the odds of having CIMT above 75th percentile increases by 28 times for every 1 unit change in Waist/Hip ratio (OR= 28; 95%CI:5 – 158) while the increase in not evident in male (OR= 0.98; 95%CI:0.57- 1.68).

The biomedical laboratory markers also were mostly associated with increase in CIMT risk level except for homocysteine, HDL and LDL. The fact that 99.8% of the study population had high risk of LDL (above 0.77) rendered it statistically impossible to study the effect of LDL on CIMT levels. (Table 9)
### Table 8: Association between clinical measurements & risk levels of CIMT (N=1425)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Average CIMT&lt;sup&gt;1&lt;/sup&gt;</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Risk</td>
<td>High risk&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Median (min, max)</td>
</tr>
<tr>
<td>Height</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>163.2 ( 9.1)</td>
<td>163.0 (132.0, 186.0)</td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>76.4 (17.4)</td>
<td>75.3 ( 36.8, 150.8)</td>
</tr>
<tr>
<td>Adiposity Indicators</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>28.4 ( 5.8)</td>
<td>27.9 ( 14.8, 55.5)</td>
</tr>
<tr>
<td>Waist (cm)&lt;sup&gt;4&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>87.9 (14.9)</td>
<td>88.0 ( 0.0, 140.0)</td>
</tr>
<tr>
<td>Waist/Hip ratio&lt;sup&gt;5&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.8 ( 0.1)</td>
<td>0.8 ( 0.6, 1.1)</td>
</tr>
<tr>
<td>Fat %&lt;sup&gt;6&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>33.0 ( 9.7)</td>
<td>33.1 ( 1.7, 56.4)</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight &lt;18.5</td>
<td>25 (89.3)</td>
<td>3 (10.7)</td>
</tr>
<tr>
<td>Normal &gt;=18.5 - &lt;25</td>
<td>225 (73.5)</td>
<td>81 (26.5)</td>
</tr>
<tr>
<td>Overweight &gt;=25 - &lt;30</td>
<td>334 (70.1)</td>
<td>143 (29.9)</td>
</tr>
<tr>
<td>Obese &gt;=30</td>
<td>376 (61.2)</td>
<td>238 (38.8)</td>
</tr>
<tr>
<td>Average Systolic Blood Pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal &lt;120</td>
<td>704 (70.7)</td>
<td>292 (29.3)</td>
</tr>
<tr>
<td>Prehypertension &lt;140</td>
<td>218 (64.1)</td>
<td>122 (35.9)</td>
</tr>
<tr>
<td>Stage 1 hypertension &lt;160</td>
<td>34 (43.6)</td>
<td>44 (56.4)</td>
</tr>
<tr>
<td>Stage 2 hypertension &gt;=160</td>
<td>3 (30.0)</td>
<td>7 (70.0)</td>
</tr>
<tr>
<td>Average diastolic Blood Pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal &lt;80</td>
<td>681 (68.8)</td>
<td>309 (31.2)</td>
</tr>
<tr>
<td>Prehypertension &lt;90</td>
<td>208 (67.8)</td>
<td>99 (32.2)</td>
</tr>
<tr>
<td>Stage 1 hypertension &lt;100</td>
<td>65 (55.6)</td>
<td>52 (44.4)</td>
</tr>
<tr>
<td>Stage 2 hypertension &gt;=100</td>
<td>5 (50.0)</td>
<td>5 (50.0)</td>
</tr>
<tr>
<td>Average Pulse Rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent pulse for age</td>
<td>409 (70.4)</td>
<td>172 (29.6)</td>
</tr>
<tr>
<td>Average pulse for age</td>
<td>327 (66.9)</td>
<td>162 (33.1)</td>
</tr>
<tr>
<td>Poor pulse for age</td>
<td>224 (63.1)</td>
<td>131 (36.9)</td>
</tr>
</tbody>
</table>

1. Average CIMT is the average value in mm., between right and left Carotid intima media thickness.
2. CIMT risk stratification is around 75th percentile, as per age and gender
3. Weight: 3 missing data
4. Waist: 5 missing data
5. Waist hip ratio: 6 missing data
6. Fat %: 105 missing data
7. P value computed using t-student test of means
8. P value computed using chi-square test for trend
9. P value computed using Fisher exact test
Table 9: Association between biomedical laboratory tests & risk level of CIMT (N=1425)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Average CIMT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Risk</td>
<td>High risk</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Median (min, max)</td>
</tr>
<tr>
<td>A. Partial Thromboplast. Time (APTT)</td>
<td>34.8 (3.6)</td>
<td>34.4 (24.7, 60.6)</td>
</tr>
<tr>
<td>CRP ³</td>
<td>6.4 (4.1)</td>
<td>5.0 (2.0, 50.0)</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>4.9 (0.9)</td>
<td>4.9 (2.3, 8.7)</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>3.1 (0.7)</td>
<td>3.1 (0.4, 7.1)</td>
</tr>
<tr>
<td>Fasting Glucose</td>
<td>5.5 (1.9)</td>
<td>5.0 (3.1, 25.8)</td>
</tr>
<tr>
<td>HBA1C</td>
<td>5.7 (1.0)</td>
<td>0.5 (3.1, 15.0)</td>
</tr>
<tr>
<td>HDL</td>
<td>1.4 (0.4)</td>
<td>1.4 (0.5, 2.9)</td>
</tr>
<tr>
<td>LDL</td>
<td>2.9 (0.8)</td>
<td>3.0 (0.7, 6.0)</td>
</tr>
<tr>
<td>Triglycerides ⁴</td>
<td>1.3 (0.9)</td>
<td>1.1 (0.3, 9.3)</td>
</tr>
<tr>
<td>Homocysteine</td>
<td>8.7 (3.1)</td>
<td>8.2 (2.8, 45.1)</td>
</tr>
</tbody>
</table>

CRP ³: 0.721⁷
low to average risk
<=3 5 (62.5) 3 (37.5)
high risk >4 952 (67.4) 460 (32.6)

Cholesterol: 0.739⁶
optimal <5.3 648 (67.6) 311 (32.4)
intermediate 233 (67.3) 113 (32.7)
high >6.3 79 (65.8) 41 (34.2)

Fibrinogen: 0.328⁷
optimal <235 937 (67.2) 458 (32.8)
high risk >350 23 (76.7) 7 (23.3)

Fasting Glucose: 0.015⁶
optimal risk <4.8 358 (68.5) 165 (31.6)
Intermediate risk 474 (70.1) 202 (29.9)
high risk >6.1 128 (56.7) 98 (43.4)

HBA1C: <0.001⁶
optimal risk <6.5 815 (70.3) 344 (29.7)
Intermediate risk 63 (50.8) 61 (49.2)
high risk >9.6 82 (57.8) 60 (42.3)

HDL: 0.167⁶
optimal risk >1.6 198 (67.8) 94 (32.2)
Intermediate risk 477 (69.5) 209 (30.5)
high risk <1.1 285 (63.8) 162 (36.2)

LDL: 1.000⁷
Optimal/inter. risk <0.77 2 (100.0) 0 (0.0)
high risk >0.77 958 (67.32) 465 (32.7)

Triglycerides ⁴: 0.050⁶
optimal risk <1.13 483 (69.8) 209 (30.2)
Intermediate risk 255 (66.7) 127 (33.3)
high risk >1.69 218 (63.7) 124 (36.3)

---

1. Average CIMT is the average value in mm., between right and left Carotid intima media thickness.
2. CIMT risk stratification is around 75th percentile, as per age and gender.
3. CRP: 5 missing data
4. Triglycerides: 9 missing data
5. P value computed using t-student test of means
6. P value computed using chi-square test for trend
The univariate logistic regression analysis of different variables are displayed in table 10 along with the crude odds ratios (OR) estimates. Thirty five variables with statistically significant effects with \( P < 0.25 \), were included in the initial full model. After adjusting with a multivariate regression all variables lost their effect except the following variables: gender (Crude OR = 0.6; 95%CI:0.5 - 0.8, \( P < 0.001 \) and Adjusted OR= 0.3; 95%CI: 0.1 - 0.8, \( P =0.024 \)) and systolic blood pressure where (Crude OR = 1.6; 95%CI:1.3 – 1.9, \( P \) value =\(<0.001 \) and Adjusted OR= 2.0; 95%CI:1.4 – 2.7, \( P \) value =\(<0.001 \)). CPR kept the same effect with statistical significance (Crude OR = 1.0; 95%CI:1.0 - 1.1, \( P \) value =0.002, and Adjusted OR= 1.0; 95%CI:1.0 - 1.1, \( P \) value =0.022). (Table 10) A model that had systolic blood pressure (categorical variable), CRP (continuous variable), gender (Binary variable), as covariates was developed. Waist measure was added to the model as it appeared to confound gender \( \beta \) coefficient with more than 20% change. HDL level (continuous variable) was also added due to clinical and statistical significance.

The final model showed that gender, CRP, HDL, systolic blood pressure, and waist measure were strong significant predictors of CIMT. The main effects model with the five covariates systolic blood pressure, C-reactive protein (CRP), gender, waist and high density lipoprotein (HDL) was then considered for all possible interactions between pairs of included covariates.
The interaction between systolic blood pressure & HDL variables and interaction between the waist measure in cm and HDL, resulted in a good to fit model by likelihood ratio test (P = 0.002 and 0.004 respectively) (Figure 7) (Table 11).

Hosmer-Lemeshow (P value= 0.611 >0.005) (>0.05) failing to reject the null hypothesis of goodness of fit of the model proved the goodness to fit of this model with no specification error (P value hatsq= 0.379) the model has all the relevant predictors and the linear combination of these predictors was sufficient, 71.35% were correctly classified, with Receiver operating characteristics (ROC) Area under the curve (AUC) 0.6574. (Figure 6)

*Figure 6:* Multivariate Model Receiver operating characteristics (ROC) Area under the curve (AUC)
Table 10: Logistic regression of risk factors and predictors of high risk level of CIMT (N=1425)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>OR (95% CI)</th>
<th>P value</th>
<th>Sig at &lt;0.2</th>
<th>OR (95% CI)</th>
<th>P value</th>
<th>Sig at &lt;0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18</td>
<td>Reference</td>
<td>&lt;0.001</td>
<td>0.731</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;35 – 55</td>
<td>1.2 (0.9 - 1.5)</td>
<td>0.212</td>
<td></td>
<td>0.9 (0.7 - 1.5)</td>
<td>0.947</td>
<td></td>
</tr>
<tr>
<td>&gt;55</td>
<td>2.3 (1.6 - 3.3)</td>
<td>&lt;0.001</td>
<td></td>
<td>1.2 (0.6 - 2.5)</td>
<td>0.529</td>
<td></td>
</tr>
<tr>
<td>Gender (Male)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than 50,000</td>
<td>0.6 (0.5 - 0.8)</td>
<td>&lt;0.001</td>
<td>0.3 (0.1 - 0.8)</td>
<td>0.024</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monthly Income in QR per month</td>
<td></td>
<td>0.018</td>
<td>0.113</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 10,000</td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Between 10,000 and 49,999</td>
<td>0.7 (0.5 - 0.9)</td>
<td>0.008</td>
<td>0.6 (0.3 - 1.0)</td>
<td>0.067</td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than 50,000</td>
<td>0.7 (0.4 - 1.4)</td>
<td>0.827</td>
<td>0.6 (0.2 - 1.5)</td>
<td>0.269</td>
<td></td>
<td></td>
</tr>
<tr>
<td>House ownership</td>
<td></td>
<td>0.039</td>
<td>0.622</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outright</td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortgage</td>
<td>0.7 (0.5 - 1.1)</td>
<td>0.097</td>
<td>1.5 (0.7 - 3.4)</td>
<td>0.283</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employer provided</td>
<td>0.6 (0.4 – 0.9)</td>
<td>0.022</td>
<td>omitted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rented</td>
<td>0.7 (0.4 - 1.4)</td>
<td>0.321</td>
<td>omitted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td>0.002</td>
<td>0.297</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary or less</td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary or technical</td>
<td>0.5 (0.3 - 0.8)</td>
<td>0.003</td>
<td>0.6 (0.3 - 1.3)</td>
<td>0.207</td>
<td></td>
<td></td>
</tr>
<tr>
<td>University or more</td>
<td>0.4 (0.3 - 0.7)</td>
<td>&lt;0.001</td>
<td>0.5 (0.2 - 1.0)</td>
<td>0.052</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Employment Status</td>
<td></td>
<td>0.002</td>
<td>0.789</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed or business owner</td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Housewife or Unemployed</td>
<td>1.4 (1.0 - 1.9)</td>
<td>0.037</td>
<td>0.6 (0.4 - 0.9)</td>
<td>0.040</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>1.9 (1.3 - 2.6)</td>
<td>0.001</td>
<td>1.3 (0.7 - 2.2)</td>
<td>0.427</td>
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<tr>
<td>Student or Trainee</td>
<td>0.9 (0.6 - 1.4)</td>
<td>0.626</td>
<td>0.8 (0.4 - 1.4)</td>
<td>0.406</td>
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<td>MET intensities</td>
<td></td>
<td>0.362</td>
<td>0.485</td>
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<tr>
<td>No Activity</td>
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<tr>
<td>Low MET (&lt;3)</td>
<td>0.9 (0.7 - 1.1)</td>
<td>0.323</td>
<td>0.9 (0.6 - 1.2)</td>
<td>0.432</td>
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<tr>
<td>Moderate MET (3-6)</td>
<td>1.1 (0.7 - 1.6)</td>
<td>0.705</td>
<td>1.5 (0.9 - 2.6)</td>
<td>0.117</td>
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<td>Vigorous MET (&gt;6)</td>
<td>0.8 (0.6 - 1.1)</td>
<td>0.141</td>
<td>1.1 (0.7 - 1.7)</td>
<td>0.702</td>
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<td>Time spent sitting in past week</td>
<td></td>
<td>0.103</td>
<td>0.180</td>
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<tr>
<td>Short, sitting &lt;5 hour/day</td>
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<tr>
<td>Moderate, sitting 5-12</td>
<td>0.8 (0.6 - 0.9)</td>
<td>0.039</td>
<td>0.7 (0.4 - 1.3)</td>
<td>0.266</td>
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<tr>
<td>Long, &gt;12 hours/day</td>
<td>0.7 (0.5 - 1.1)</td>
<td>0.149</td>
<td>0.6 (0.3 - 1.4)</td>
<td>0.248</td>
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<td>Hours of sleep in 24 hours</td>
<td></td>
<td>0.497</td>
<td>0.951</td>
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<tr>
<td>&lt; 5</td>
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<tr>
<td>5 - 8</td>
<td>1.1 (0.7 – 1.6)</td>
<td>0.616</td>
<td>1.1 (0.6 - 1.8)</td>
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<td>&gt;8</td>
<td>1.3 (0.8 - 2.0)</td>
<td>0.279</td>
<td>1.1 (0.6 - 1.9)</td>
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<td>Smoking Cigarettes</td>
<td></td>
<td>0.436</td>
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<td>Never smoker</td>
<td>Reference</td>
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<tr>
<td>Stopped smoking</td>
<td>0.9 (0.6 - 1.3)</td>
<td>0.645</td>
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<td>Occasional smoker</td>
<td>0.7 (0.5 - 1.1)</td>
<td>0.150</td>
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<td>Current smoker</td>
<td>0.9 (0.6 - 1.3)</td>
<td>0.515</td>
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<td>Smoking Water pipe (No)</td>
<td>1.9 (1.4 - 2.6)</td>
<td>&lt;0.001</td>
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<td>Passive smoking</td>
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<td>0.908</td>
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<tr>
<td>History of Diabetes (Yes)</td>
<td></td>
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<tr>
<td>History of Hypercholesterolemia (yes)</td>
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<tr>
<td>History of Hypertension (yes)</td>
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<tr>
<td>Category</td>
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<td>p-value</td>
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<td>Reference 3</td>
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<td>History of Myocardial Infarction (yes)</td>
<td>3.1 (0.9 - 11.1)</td>
<td>0.078</td>
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<td>History of Stroke (yes)</td>
<td>8.3 (0.9, 74.8)</td>
<td>0.028</td>
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<tr>
<td>Comorbidities Index</td>
<td>&lt;0.001</td>
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<tr>
<td>No comorbidities</td>
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<td>1-2 comorbidities</td>
<td>1.4 (1.1 - 1.7)</td>
<td>0.011</td>
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<td>&gt;= 3 comorbidities</td>
<td>4.1 (2.4 - 6.9)</td>
<td>&lt;0.001</td>
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<td>Family history of Hypertension</td>
<td>0.018</td>
<td>0.881</td>
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<td>Maternal Only</td>
<td>1.6 (1.1 - 2.3)</td>
<td>0.005</td>
<td>1.3 (0.8 - 2.1)</td>
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<td>Both</td>
<td>1.1 (1.0 - 1.6)</td>
<td>0.519</td>
<td>0.9 (0.6 - 1.6)</td>
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<td>Family history of Myocardial Infarction</td>
<td>0.392</td>
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<td>Maternal Only</td>
<td>1.2 (0.8 – 1.9)</td>
<td>0.301</td>
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<td>1.4 (0.8 – 2.5)</td>
<td>0.262</td>
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<td>Family history of Stroke</td>
<td>0.023</td>
<td>0.315</td>
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<td>Maternal Only</td>
<td>1.7 (0.9 - 2.9)</td>
<td>0.060</td>
<td>1.1 (0.5 - 2.3)</td>
<td>0.887</td>
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<td>2.7 (1.2 – 6.6)</td>
<td>0.020</td>
<td>1.5 (0.5 – 4.7)</td>
<td>0.476</td>
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<td>Family history of Diabetes</td>
<td>0.543</td>
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<td>1.2 (0.9 - 1.7)</td>
<td>0.270</td>
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<td>0.557</td>
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<td>Family history of Obesity</td>
<td>0.254</td>
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<td>Maternal Only</td>
<td>1.1 (0.6 – 1.8)</td>
<td>0.728</td>
<td>1.0 (0.5 – 2.0)</td>
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<td>Both</td>
<td>0.6 (0.3 – 1.3)</td>
<td>0.236</td>
<td>0.3 (0.1 – 0.9)</td>
<td>0.048</td>
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<td>Family Comorbidities Index</td>
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<td>No Family comorbidities</td>
<td>Reference</td>
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<tr>
<td>1-4 Family comorbidities</td>
<td>1.5 (1.0 - 2.1)</td>
<td>0.029</td>
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<td>&gt;=5 Family comorbidities</td>
<td>1.4 (0.9 - 2.1)</td>
<td>0.149</td>
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<td>Any special diet</td>
<td>0.410</td>
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<td>No special diet</td>
<td>Reference</td>
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<tr>
<td>Low fat diet</td>
<td>0.9 (0.7 – 1.3)</td>
<td>0.703</td>
<td>...</td>
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<tr>
<td>Another special diet</td>
<td>0.5 (0.2 – 1.0)</td>
<td>0.053</td>
<td>...</td>
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<td>Low calorie diet</td>
<td>1.1 (0.7 – 1.9)</td>
<td>0.722</td>
<td>...</td>
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<tr>
<td>No red meat diet</td>
<td>0.5 (0.2 – 1.5)</td>
<td>0.221</td>
<td>...</td>
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<tr>
<td>Vegetarian diet 4</td>
<td>1.3 (0.4 – 4.8)</td>
<td>0.653</td>
<td>...</td>
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<tr>
<td>Vegan diet 3</td>
<td>2.0 (0.4 – 9.9)</td>
<td>0.395</td>
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<td>Low salt diet</td>
<td>0.7 (0.1 – 6.5)</td>
<td>0.729</td>
<td>...</td>
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<td>Fast Food</td>
<td>0.291</td>
<td>0.483</td>
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<td>Never or rarely</td>
<td>Reference</td>
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<tr>
<td>Less than twice per week</td>
<td>1.0 (0.8 – 1.3)</td>
<td>0.987</td>
<td>1.6 (1.1 - 2.3)</td>
<td>0.010</td>
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<tr>
<td>Every day or almost every day</td>
<td>0.8 (0.5 – 1.1)</td>
<td>0.158</td>
<td>1.6 (0.9 - 2.7)</td>
<td>0.108</td>
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<td>Dairy Diet</td>
<td>0.496</td>
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<td>Never or rarely</td>
<td>Reference</td>
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<tr>
<td>1-4 times per week</td>
<td>1.0 (0.7 – 1.5)</td>
<td>0.894</td>
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<tr>
<td>One or more times per day</td>
<td>1.2 (0.8 – 1.9)</td>
<td>0.344</td>
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<td>Fat Diet</td>
<td>0.855</td>
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<td>Whole fat diet</td>
<td>Reference</td>
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<tr>
<td>Reduced fat diet</td>
<td>1.0 (0.8 – 1.3)</td>
<td>0.876</td>
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<td>Fat-free diet</td>
<td>1.1 (0.7 – 1.7)</td>
<td>0.575</td>
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<td>BMI</td>
<td>&lt;0.001</td>
<td>0.306</td>
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<td>Underweight &lt;18.5</td>
<td>Reference</td>
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<tr>
<td>Normal &gt;=18.5 - &lt;25</td>
<td>3.0 (0.9 - 10.2)</td>
<td>0.079</td>
<td>2.5 (0.6 - 9.7)</td>
<td>0.196</td>
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<td>Overweight &gt;=25 - &lt;30</td>
<td>3.6 (1.1 - 12.0)</td>
<td>0.040</td>
<td>3.1 (0.7 - 13.7)</td>
<td>0.133</td>
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<td>Obese &gt;=30</td>
<td>5.3 (1.6 - 17.7)</td>
<td>0.007</td>
<td>3.3 (0.6 - 17.3)</td>
<td>0.153</td>
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<td>Measure</td>
<td>Value 1</td>
<td>Value 2</td>
<td>p-value 1</td>
<td>p-value 2</td>
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<tr>
<td>Average Systolic Blood Pressure</td>
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<tr>
<td>Normal &lt;120</td>
<td>Reference</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
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<td>Prehypertension &lt;140</td>
<td>1.3 (1.0 - 1.8)</td>
<td>0.024</td>
<td>1.6 (1.0 - 2.5)</td>
<td>0.039</td>
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<td>Stage 1 hypertension &lt;160</td>
<td>&lt;0.001</td>
<td>4.8 (2.0 - 11.2)</td>
<td>&lt;0.001</td>
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<tr>
<td>Stage 2 hypertension &gt;=160</td>
<td>3.1 (1.9 - 4.9)</td>
<td>0.013</td>
<td>17.1 (1.4 - 212.0)</td>
<td>0.027</td>
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<td>Average Diastolic Blood Pressure</td>
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<tr>
<td>Normal &lt;80</td>
<td>Reference</td>
<td>0.25</td>
<td>0.107</td>
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<td>Prehypertension &lt;90</td>
<td>1.1 (0.8 - 1.3)</td>
<td>0.733</td>
<td>0.8 (0.5 - 1.2)</td>
<td>0.264</td>
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<tr>
<td>Stage 1 hypertension &lt;100</td>
<td>1.8 (1.2 - 2.6)</td>
<td>0.004</td>
<td>0.6 (0.3 - 1.2)</td>
<td>0.124</td>
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<td>Stage 2 hypertension &gt;=100</td>
<td>2.2 (0.6 - 7.7)</td>
<td>0.214</td>
<td>0.6 (0.1 - 5.1)</td>
<td>0.681</td>
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<td>Average Pulse Rate</td>
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<tr>
<td>Excellent pulse for age</td>
<td>Reference</td>
<td>1.25</td>
<td>1.0</td>
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<td>Average pulse for age</td>
<td>1.2 (0.9 - 1.5)</td>
<td>0.215</td>
<td>1.1 (0.8 - 1.5)</td>
<td>0.739</td>
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<td>Poor pulse for age</td>
<td>1.4 (1.2 - 1.8)</td>
<td>0.021</td>
<td>1.1 (0.7 - 1.6)</td>
<td>0.733</td>
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<td>Low to average risk &lt;=3</td>
<td>1.2 (0.3 - 5.2)</td>
<td>0.768</td>
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<td>High risk &gt;4</td>
<td>Reference</td>
<td>1.00</td>
<td>0.6</td>
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<tr>
<td>Cholesterol</td>
<td></td>
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<td>Optimal &lt;5.3</td>
<td>Reference</td>
<td>0.929</td>
<td>0.079</td>
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<tr>
<td>Intermediate</td>
<td>1.1 (0.8 - 1.3)</td>
<td>0.938</td>
<td>---</td>
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<tr>
<td>High &gt;6.3</td>
<td>1.1 (0.7 - 1.6)</td>
<td>0.702</td>
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<tr>
<td>Fasting Glucose</td>
<td>&lt;0.001</td>
<td>0.016</td>
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<tr>
<td>Optimal risk &lt;4.8</td>
<td>Reference</td>
<td>0.535</td>
<td>0.8 (0.5 - 1.1)</td>
<td>0.122</td>
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<td>Intermediate risk</td>
<td>0.9 (0.7 - 1.2)</td>
<td>0.525</td>
<td>0.6 (0.3 - 1.2)</td>
<td>0.167</td>
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<td>High risk &gt;6.1</td>
<td>1.7 (1.2 - 2.3)</td>
<td>0.002</td>
<td>1.5 (0.2 - 11.7)</td>
<td>0.683</td>
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<td>HBA1C</td>
<td>&lt;0.001</td>
<td>0.620</td>
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<td>Optimal risk &lt;6.5</td>
<td>Reference</td>
<td>0.01</td>
<td>0.1</td>
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<td>Intermediate risk</td>
<td>2.3 (1.6 - 3.3)</td>
<td>0.001</td>
<td>1.1 (0.4 - 2.7)</td>
<td>0.823</td>
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<td>High risk &gt;9.6</td>
<td>1.7 (1.2 - 2.5)</td>
<td>0.002</td>
<td>1.5 (0.2 - 11.7)</td>
<td>0.683</td>
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<tr>
<td>HDL</td>
<td>0.128</td>
<td>0.113</td>
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<tr>
<td>Optimal risk &gt;1.6</td>
<td>Reference</td>
<td>0.593</td>
<td>0.9 (0.6 - 1.4)</td>
<td>0.807</td>
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<td>Intermediate risk</td>
<td>0.9 (0.7 - 1.2)</td>
<td>0.258</td>
<td>1.4 (0.9 - 2.4)</td>
<td>0.157</td>
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<tr>
<td>Triglycerides</td>
<td>0.139</td>
<td>0.867</td>
<td></td>
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<tr>
<td>Optimal risk &lt;1.13</td>
<td>Reference</td>
<td>0.303</td>
<td>0.9 (0.6 - 1.4)</td>
<td>0.800</td>
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<td>Intermediate risk</td>
<td>1.2 (0.9 - 1.5)</td>
<td>0.050</td>
<td>1.1 (0.6 - 2.1)</td>
<td>0.775</td>
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<tr>
<td>Fat Percent</td>
<td>1.0 (1.0 - 1.1)</td>
<td>&lt;0.001</td>
<td>0.9 (0.9 - 1.0)</td>
<td>0.476</td>
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<tr>
<td>Waist</td>
<td>1.0 (1.0 - 1.1)</td>
<td>&lt;0.001</td>
<td>1.0 (0.9 - 1.0)</td>
<td>0.581</td>
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<tr>
<td>Weight</td>
<td>1.0 (1.0 - 1.0)</td>
<td>0.002</td>
<td>1.0 (0.9 - 1.0)</td>
<td>0.627</td>
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<td>BMI</td>
<td>1.0 (1.0 - 1.1)</td>
<td>&lt;0.001</td>
<td>1.0 (0.9 - 1.1)</td>
<td>0.982</td>
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<tr>
<td>CRP</td>
<td>1.0 (1.0 - 1.1)</td>
<td>0.002</td>
<td>1.0 (1.0 - 1.1)</td>
<td>0.022</td>
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</tr>
<tr>
<td>Fibrinogen</td>
<td>1.2 (1.0 - 1.5)</td>
<td>0.018</td>
<td>0.7 (0.6 - 1.0)</td>
<td>0.984</td>
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<td></td>
</tr>
<tr>
<td>Fasting Blood sugar</td>
<td>1.0 (1.0 - 1.2)</td>
<td>&lt;0.001</td>
<td>1.1 (0.9 - 1.2)</td>
<td>0.330</td>
<td></td>
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</tr>
<tr>
<td>Cholesterol</td>
<td>0.9 (1.0 - 1.1)</td>
<td>0.798</td>
<td>1.0 (0.9 - 1.2)</td>
<td>0.636</td>
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</tr>
<tr>
<td>HBA1C</td>
<td>1.3 (1.2 - 1.4)</td>
<td>&lt;0.001</td>
<td>1.0 (0.8 - 1.4)</td>
<td>0.843</td>
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<tr>
<td>Triglycerides</td>
<td>1.1 (0.9 - 1.3)</td>
<td>0.077</td>
<td>0.9 (0.7 - 1.3)</td>
<td>0.970</td>
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</table>

1. Observations omitted to 1026 with all variables available in full and short regression terms
2. Insignificant variable
3. Variable omitted as the outcome is a surrogate
4. Collinear with other variable(s)
Figure 7: Nomogram of the final logistic regression model

Table 11: Logistic Regression Model

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Odds Ratio</th>
<th>P value</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Binary CIMT</td>
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<tr>
<td>Gender</td>
<td>0.41</td>
<td>&gt;0.001</td>
<td>0.30 0.56</td>
</tr>
<tr>
<td>CRP</td>
<td>1.02</td>
<td>0.083</td>
<td>0.99 1.05</td>
</tr>
<tr>
<td>HDL</td>
<td>4.69</td>
<td>0.093</td>
<td>0.77 28.52</td>
</tr>
<tr>
<td>Waist</td>
<td>1.04</td>
<td>0.007</td>
<td>1.01 1.07</td>
</tr>
<tr>
<td>SBP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prehypertension</td>
<td>8.20</td>
<td>0.001</td>
<td>2.40 27.99</td>
</tr>
<tr>
<td>Stage 1</td>
<td>9.44</td>
<td>0.017</td>
<td>1.50 59.32</td>
</tr>
<tr>
<td>Stage 2</td>
<td>15.25</td>
<td>0.695</td>
<td>&lt;0.001 1.28e+07</td>
</tr>
<tr>
<td>SBP#HDL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prehypertension</td>
<td>0.25</td>
<td>0.004</td>
<td>0.09 0.63</td>
</tr>
<tr>
<td>Stage 1</td>
<td>0.41</td>
<td>0.179</td>
<td>0.11 1.49</td>
</tr>
<tr>
<td>Stage 2</td>
<td>0.72</td>
<td>0.943</td>
<td>&lt;0.001 5647.50</td>
</tr>
<tr>
<td>Waist#HDL</td>
<td>0.98</td>
<td>0.073</td>
<td>0.95 1.01</td>
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</table>
5. DISCUSSION

It has been established that people with CVD or who are at high risk for CVD, benefit significantly from early detection and management using counselling and medicines, as appropriate. Yet, any early detection and subsequent prevention relies heavily on the ability to accurately identify the individuals who are at high risk of developing CVD. Thus, there is a pressing need to diagnose subclinical atherosclerosis to facilitate optimum CVD risk stratification in asymptomatic individuals.

One of the first longitudinal studies of association between the carotid morphology with the risk of acute coronary events was based on the analysis of the population-based Kuoppio Ischaemic Heart Disease (KIHD) study, an extensive epidemiologic research project that was launched in the 1980s and involved around three thousand middle-aged males from the Eastern Finland. The study showed 11% increased risk of MI with each 0.1-mm incremental increase of CIMT and that the presence of intimal-medial thickening is associated with a 2.17-fold (95% confidence interval, 0.70-6.74; P value = Not significant) risk of acute myocardial infarction compared with men free of any structural changes in the carotid artery wall at baseline. Following this study, a number of important trials like the Atherosclerosis Risk In Communities study, the Cardiovascular Health Study, the Rotterdam Study, the Malmö Diet and Cancer Study, and the Carotid Atherosclerosis Progression Study showed results which were comparable.
Different studies findings are of different levels of significance with regards to adding CIMT to conventional cardiovascular risk scores such as Framingham,\textsuperscript{57} reaching to that Den et al meta-analysis found that there is no significant addition when CIMT was added to traditional risk scores.\textsuperscript{58} Also van den Oord et al concluded in his systematic review that the addition of CIMT to traditional CVD risk prediction models does not lead to a statistical significantly increase in performance of those models \textsuperscript{59}

The literature has stated that such contradicting results are probably stemming from the differences in study design, differences techniques in CIMT measurements, such as measuring the common or internal segment and whether plaques are included or excluded from analyses, as covered in a review by Naqvi \& Lee \textsuperscript{60} Another explanation to such phenomenon is that CIMT is correlated positively \& strongly with CVD risk, yet adding it to a prediction model with other CVD risk factors might not add to the score because of collinearity, specially that all the risk predictor in traditional risk are proven linear predictors of atherosclerosis and CIMT. It is evident that such multiple regression model with correlated predictors can indicate how well the entire bundle of predictors predicts the outcome variable, but it may not give valid results about any individual predictor.

Although CIMT has relatively less robust evidence base as compared to other noninvasive radiological modalities, it has the advantages of being less expensive, widely available, simpler to perform, and most importantly, being free from radiation exposure. These attributes make CIMT an attractive option for incorporation into routine clinical practice.
No large-scale study has so far provided the distribution of CIMT in the Qatari population. This might be a major factor limiting wider use of CIMT in clinical practice in Qatar. This study was conducted as an attempt to fill this knowledge gap. The strengths of this study is that it is one of the first to explore Qatari population CVD risk and describe the CIMT distribution. Using a fairly large study sample of males and females free from existing CVD, we derived age- and gender specific normative data for CIMT in Qatarsis. Similar studies were done on different populations such as the SCORE study on 1229 Indian subjects. Compared to the SCORE study, our population average CIMT was lower with statistically significant difference in average CIMT in males and females in age groups 0-39, 40-49, 50-59 and >60, except for age group 50-59 in males where the difference was not significant and females >60 where our study population had statistically non significant higher CIMT. (Appendix H)

A study of cross section study of 4394 who were grouped according to age and the present quantity and type of cardiovascular risk factors showed that hypertension was 79.4% correlated with the degree of severity carotid stenosis severity. The same study also showed that carotid atherosclerosis is related to the number of cardiovascular risk factors.

Our study further analyze the association of CIMT with different risk factors and attempt to model it as a regression outcome. In this study we found significant association between CIMT and various CVD risk factors such as age, gender, hypertension, diabetes, hypercholesterolemia, BMI, lipids profile. These findings are consistent with the existing literature on CIMT and provide an indirect validation of our data. The same SCORE study found significant relationship of CIMT with various CVD risk factors such as age, gender,
diabetes, hypertension, urine albumin concentration. A study from Sri Lanka on 68 type 2 diabetic mellitus (T2DM) patients proved a significant and positive association between CIMT with duration of T2DM and HbA1c level. In their study the other variables including age, total cholesterol, LDL, and TG too showed positive association even though they did not reach the statistical significance. A different study on 3789 low income Chinese subjects showed that male gender, old age, current smoking status, hypertension & high levels of systolic blood pressure, fasting blood sugar & LDL were independent determinants of mean CIMT, while a study from Egypt proved that CIMT was independently associated with male gender and was positively correlated with age, BMI, Waist Circumference, systolic blood pressure, Homeostasis model assessment of insulin resistance (HOMA-IR), TG, and LDL, and negatively correlated with insulin like growth factor-1 (IGF-1) in metabolically healthy obese subjects.

Such consistent findings with our study also validates the available risk scores for use with our population since the predictors were among the commonly used variables in available CVD risk scores. Yet in our study, there has been also statistically significant association between CIMT and various socio-economic factors such as income, employment status, education and house ownership.

Among the possible limitation of this study is that the recruitment of the QBB was done by convenience, which does not render the sample as a representative one, with evident selection bias and “healthy workers” bias. Thus the data was never used to describe prevalence, yet only establish associations.

The study population are relatively young (mean age 39 years) and almost two third
of the population were females (60%, versus only 40% males) when the outcome studied is evidently correlated with age and gender. This might have underestimated the studied effect or confounded the effect of some collinear variables.

Although the prognostic value of image detected subclinical atherosclerosis has proven to add significant value to FRS, especially in low and intermediate-risk categories. The question that rises for future research to answer would be “the value of carotid plaque presence?” . This is there is some evidence that plaque burden and the plaque phenotype (the amount, extent and composition of plaque) would likely contribute additional important prognostic information and would increase the sensitivity and specificity of noninvasive imaging for CVD risk. Another suggestion would be studying adding some measures beyond carotid arterial structure and focusing more on arterial function such as arterial compliance and vasodilator function.
6. CONCLUSION

The results shown allow for important comparative work with existing and future investigations in Middle Eastern countries. Also the study can be used to develop a simple, non-invasive yet sensitive risk-prediction tool to promptly identify those individuals at risk of CVD as valuable clinical strategy that can be more widely implemented in everyday primary care practice. There is need for prospective cohort follow up for this population of 1425 participants to capture the incidence of CVD in them.
7. REFERENCES


<table>
<thead>
<tr>
<th>Study [Reference #]</th>
<th>Sample Size</th>
<th>Age of Subjects</th>
<th>Follow-up</th>
<th>Carotid Ultrasound Parameters</th>
<th>Plaque</th>
<th>Endpoints</th>
<th>CIMT, RR (95% CI)</th>
<th>NRI</th>
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<tr>
<td>AFSRE [67]</td>
<td>598</td>
<td>69-7yrs</td>
<td>Median, 3yrs</td>
<td>Max left CCA-IMT, far wall</td>
<td>Not specified</td>
<td>CV death, MI, revascularization</td>
<td>INT: 0.98mm; RR: 0.78 (0.60-1.01); for CV death or MI; RR: 1.07 (0.78-1.46) for revascularization</td>
<td>INT: 0.98mm; RR: 0.78 (0.60-1.01) for CV death or MI; RR: 1.07 (0.78-1.46) for revascularization</td>
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<td>AREC [68]</td>
<td>12,421</td>
<td>45-64yrs</td>
<td>Mean follow-up 15.1yrs</td>
<td>Mean for wall IMT at 6 sites (CCA, bifurc., ICA, bilateral)</td>
<td>Plaque included</td>
<td>MI, CV death</td>
<td>RR: 0.87 (0.72-1.06); for ICA-IMT: RR: 0.78 (0.60-1.00); for CCA-IMT: RR: 0.78 (0.60-1.00); for ICA-IMT: RR: 0.78 (0.60-1.00)</td>
<td>7.1</td>
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<td>CAPS [69]</td>
<td>7,056</td>
<td>49.0-66yrs</td>
<td>Mean follow-up 2yrs</td>
<td>Mean for wall IMT bilaterally at CCA, carotid bif, ICA bif</td>
<td>Not specified</td>
<td>MI, stroke, death</td>
<td>RR: 0.74 (0.52-1.08) for CCA-IMT; RR: 0.74 (0.52-1.08) for CCA-IMT; RR: 0.74 (0.52-1.08) for ICA-IMT</td>
<td>-4.4</td>
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<td>CCOCC [70]</td>
<td>2,190</td>
<td>&gt; 35yrs</td>
<td>Median, 10.5yrs</td>
<td>Maximal CCA-IMT, far wall, bilaterally</td>
<td>Plaque excluded</td>
<td>MI, CV death, PCI, CARG</td>
<td>RR: 1.39 (1.02-1.92)</td>
<td>16.8</td>
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<td>Charlottesville Study [71]</td>
<td>727</td>
<td>14-54yrs</td>
<td>Mean, 46.3yrs</td>
<td>Mean Carotid IMT, both IMT, ICA-IMT, near and far wall bilaterally</td>
<td>Plaque included</td>
<td>MI, stroke, death, all-cause mortality</td>
<td>RR: 1.39 (1.02-1.92)</td>
<td>16.8</td>
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<td>CHS [72]</td>
<td>5,020</td>
<td>72.6-5.5yrs</td>
<td>5 days to 12 yrs (median 11 yrs)</td>
<td>CCA and ICA-IMT, mean of maximum IMT, near and far wall bilaterally</td>
<td>Plaque included</td>
<td>MI, stroke/CVA, death, all-cause mortality</td>
<td>RR: 1.39 (1.02-1.92)</td>
<td>16.8</td>
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<td>Cournu et al. [73]</td>
<td>2,563</td>
<td>51.6-105.5yrs</td>
<td>2-10yrs</td>
<td>Mean Carotid IMT, ICA-IMT bilaterally</td>
<td>Plaque excluded</td>
<td>CV death, MI, angina</td>
<td>INT &gt; 0.65mm; RR: 2.28 (1.52-3.76)</td>
<td>16.8</td>
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<tr>
<td>FAST [74]</td>
<td>1,574</td>
<td>49.4-69.6yrs</td>
<td>Mean, 7.2yrs</td>
<td>Right CCA-IMT</td>
<td>Plaque excluded</td>
<td>CV death, MI, stroke, all-cause mortality</td>
<td>RR: 1.45 (1.15-1.81)</td>
<td>11.6</td>
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<td>Framingham Offspring Study [75]</td>
<td>2,465</td>
<td>38-101yrs</td>
<td>Average, 7.2yrs</td>
<td>Mean Carotid IMT, or maximal CCA-IMT, maximal ICA-IMT, bilaterally</td>
<td>Plaque included</td>
<td>MI, stroke/CVA, death, all-cause mortality</td>
<td>RR: 1.45 (1.15-1.81)</td>
<td>11.6</td>
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<td>IMPROVE [76]</td>
<td>3,730</td>
<td>54.9-59.9yrs</td>
<td>Median, 36.2 months</td>
<td>Maximal and mean CCA, ICA, BF, bilaterally</td>
<td>Plaque included</td>
<td>MI, SCD, angina, stroke, TIA, heart failure, revascularization</td>
<td>RR: 1.45 (1.15-1.81)</td>
<td>11.6</td>
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<td>KIID [77]</td>
<td>1,257</td>
<td>42-69yrs</td>
<td>1 mos-2.5yrs</td>
<td>CCA-IMT, mean of max IMT, near and far wall bilaterally</td>
<td>Plaque excluded</td>
<td>CV death, MI, stroke, revascularization</td>
<td>INT &gt; 0.65mm; RR: 2.28 (1.52-3.76)</td>
<td>16.8</td>
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<td>LILAC [78]</td>
<td>298</td>
<td>Median, 79.69ys</td>
<td>Mean, 112.95ys</td>
<td>Average of CCA bilaterally, near and far wall bilaterally</td>
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<td>All-cause mortality</td>
<td>RR: 1.45 (1.15-1.81)</td>
<td>11.6</td>
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<td>MESA [79]</td>
<td>8,146</td>
<td>45-84yrs</td>
<td>Median, 7.6yrs</td>
<td>Max of max right CCA-IMT, far wall</td>
<td>Plaque excluded</td>
<td>CV death, MI, SCD, angina, stroke, TIA, heart failure, revascularization</td>
<td>INT &gt; 0.65mm; RR: 2.28 (1.52-3.76)</td>
<td>16.8</td>
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<td>MDCS [79]</td>
<td>5,165</td>
<td>46-64yrs</td>
<td>Median, 7yrs</td>
<td>Mean for wall distal CCA</td>
<td>Plaque included</td>
<td>MI, CV death</td>
<td>RR: 1.45 (1.15-1.81)</td>
<td>11.6</td>
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<td>OSACOG [80]</td>
<td>574</td>
<td>65.3-95.5yrs</td>
<td>Mean, 26yrs</td>
<td>Mean minimal CCA-IMT, ICA-IMT, ICA-IMT, near and far wall bilaterally</td>
<td>Plaque included</td>
<td>MI, SCD, angina, stroke, TIA, heart failure, revascularization</td>
<td>INT &gt; 0.65mm; RR: 2.28 (1.52-3.76)</td>
<td>16.8</td>
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<td>Rotterdam Study [81]</td>
<td>6,389</td>
<td>59.3-92.9yrs</td>
<td>7-10 years</td>
<td>Avg of max CCA-IMT or near and far wall bilaterally</td>
<td>Not specified</td>
<td>MI, SCD, angina, stroke, TIA, heart failure, revascularization</td>
<td>INT &gt; 0.65mm; RR: 2.28 (1.52-3.76)</td>
<td>16.8</td>
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<td>The Edinburgh Artery Study [72]</td>
<td>1,087</td>
<td>69.4yrs</td>
<td>12yrs</td>
<td>Max for wall CCA-IMT bilaterally</td>
<td>Not specified</td>
<td>MI, stroke, angina, revascularization</td>
<td>RR: 1.45 (1.15-1.81)</td>
<td>11.6</td>
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<tr>
<td>Three-City Study [82]</td>
<td>5,895</td>
<td>65-85yrs</td>
<td>Median, 5yrs</td>
<td>Mean Carotid IMT bilaterally, near and far wall bilaterally</td>
<td>Plaque excluded</td>
<td>MI, SCD, angina, stroke, TIA, heart failure, revascularization</td>
<td>INT &gt; 0.65mm; RR: 2.28 (1.52-3.76)</td>
<td>16.8</td>
</tr>
<tr>
<td>Tromsø Study [83]</td>
<td>6,226</td>
<td>25-84yrs</td>
<td>6yrs</td>
<td>Max of near and far wall CCA-IMT and far wall of the bulb</td>
<td>Plaque included</td>
<td>MI, SCD, angina, stroke, TIA, heart failure, revascularization</td>
<td>INT &gt; 0.65mm; RR: 2.28 (1.52-3.76)</td>
<td>16.8</td>
</tr>
</tbody>
</table>
APPENDIX B: CARDIOVASCULAR PREDICTION MODELS DEVELOPED IN GENERAL POPULATIONS (50)

Table 2  Cardiovascular risk models developed in general populations with diabetes as risk factor

<table>
<thead>
<tr>
<th>Reference</th>
<th>Development population</th>
<th>n events/</th>
<th>Type of model</th>
<th>Outcomes</th>
<th>Predicted years</th>
<th>Number of predictors</th>
<th>Apparent discrimination (AUC)</th>
<th>Apparent calibration (p value)</th>
<th>Method of internal validation</th>
<th>Presentation of risk model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen 2010</td>
<td>Chinese GP</td>
<td>240/502</td>
<td>Cox</td>
<td>Stroke</td>
<td>10</td>
<td>8</td>
<td>0.73</td>
<td>NR</td>
<td>Cross-validation</td>
<td>Original model, scoring chart, reclassification</td>
</tr>
<tr>
<td>Hippikoski-Cox 2010 (ABIDAG)</td>
<td>British GP</td>
<td>121/67/1 /126/799</td>
<td>Cox</td>
<td>CVD, MI, Stroke</td>
<td>14</td>
<td>14</td>
<td>0.94</td>
<td>0.81</td>
<td>Good</td>
<td>Split sample</td>
</tr>
<tr>
<td>Melgarman 2011 (HMERS)</td>
<td>GP from 57 countries</td>
<td>12 416/374</td>
<td>Logistic</td>
<td>MI</td>
<td>NR</td>
<td>6</td>
<td>0.71</td>
<td>0.004</td>
<td>Split sample</td>
<td>Original model</td>
</tr>
<tr>
<td>Arora 2009</td>
<td>Japanese GP</td>
<td>211/276</td>
<td>Cox</td>
<td>CVD</td>
<td>14</td>
<td>7</td>
<td>0.81*</td>
<td>0.04*</td>
<td>Split sample</td>
<td>Original model, scoring chart</td>
</tr>
<tr>
<td>Akahira 2009 (JAS cohort study)</td>
<td>Japanese GP</td>
<td>125/1239</td>
<td>Cox</td>
<td>Stroke</td>
<td>10</td>
<td>5</td>
<td>MI</td>
<td>NR</td>
<td>NA</td>
<td>Scoring chart</td>
</tr>
<tr>
<td>Mathurman 2009 (JAMS cohort study)</td>
<td>Japanese GP</td>
<td>52/32</td>
<td>Cox</td>
<td>MI</td>
<td>10</td>
<td>6</td>
<td>MI</td>
<td>NR</td>
<td>NA</td>
<td>Scoring chart</td>
</tr>
<tr>
<td>Fennone 2019 (Frankingham)</td>
<td>USA GP</td>
<td>641/4026</td>
<td>Cox</td>
<td>CVD</td>
<td>30</td>
<td>0</td>
<td>0.80, 0.89*</td>
<td>p = 0.81, p = 0.64*</td>
<td>Cross-validation</td>
<td>Original model</td>
</tr>
<tr>
<td>D’Agostino 2001 (Frankingham)</td>
<td>US GP</td>
<td>841/469</td>
<td>Cox</td>
<td>CVD</td>
<td>10</td>
<td>7</td>
<td>MI</td>
<td>0.70</td>
<td>0.001</td>
<td>NA</td>
</tr>
<tr>
<td>Hippokoski-Cox 2010 (ABIDAG)</td>
<td>British GP</td>
<td>125/115</td>
<td>Cox</td>
<td>CVD</td>
<td>10</td>
<td>14</td>
<td>0.91</td>
<td>0.01</td>
<td>Good</td>
<td>Split sample</td>
</tr>
<tr>
<td>Asvanyan 2007 (PREDIAM)</td>
<td>German GP</td>
<td>566/3105</td>
<td>Cox</td>
<td>CVD</td>
<td>10</td>
<td>0</td>
<td>0.81</td>
<td>0.01</td>
<td>NR</td>
<td>NA</td>
</tr>
<tr>
<td>Fiddler 2009 (Ramsey health score)</td>
<td>US GP</td>
<td>1934/528</td>
<td>Cox</td>
<td>CVD</td>
<td>10</td>
<td>0</td>
<td>0.81</td>
<td>0.01</td>
<td>NR</td>
<td>NA</td>
</tr>
<tr>
<td>Woodward 2007 (ASSiD)</td>
<td>GP from Scotland</td>
<td>420/1327</td>
<td>Cox</td>
<td>CVD</td>
<td>10</td>
<td>0</td>
<td>0.33</td>
<td>0.77</td>
<td>NR</td>
<td>NA</td>
</tr>
<tr>
<td>Asia-Pacific Cohort Studies Collaboration 2006</td>
<td>Asian GP</td>
<td>2303/3645</td>
<td>Cox</td>
<td>CVD</td>
<td>8</td>
<td>6</td>
<td>MI</td>
<td>NR</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Lee 2005 (Korean Heart Study)</td>
<td>American Indian GP</td>
<td>784/397</td>
<td>Cox</td>
<td>CVD</td>
<td>10</td>
<td>9</td>
<td>0.73</td>
<td>0.001</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Malirca 2007 (Personal HEART™)</td>
<td>USA GP</td>
<td>1109/91434</td>
<td>Cox</td>
<td>CVD</td>
<td>10</td>
<td>0</td>
<td>0.37</td>
<td>0.72</td>
<td>NR</td>
<td>Split sample</td>
</tr>
<tr>
<td>Wu 2006</td>
<td>Chinese GP</td>
<td>742/893</td>
<td>Cox</td>
<td>CVD</td>
<td>10</td>
<td>7</td>
<td>0.60</td>
<td>0.29</td>
<td>NR</td>
<td>0.73</td>
</tr>
<tr>
<td>Ferrone 2005 (CURE)</td>
<td>Italian men</td>
<td>312/885</td>
<td>Cox</td>
<td>CHD</td>
<td>10</td>
<td>0</td>
<td>0.75</td>
<td>0.24</td>
<td>NA</td>
<td>0.05</td>
</tr>
<tr>
<td>Merletti 2010 (Rekard)</td>
<td>Italian GP</td>
<td>1362/176</td>
<td>Cox</td>
<td>CVD</td>
<td>5, 10, 15</td>
<td>0</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NA</td>
</tr>
<tr>
<td>Decode study Group 2006</td>
<td>European GP</td>
<td>371/254</td>
<td>Cox</td>
<td>CVD</td>
<td>5, 10, 15</td>
<td>0</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NA</td>
</tr>
<tr>
<td>Liu 2001 (CINOS)</td>
<td>Chinese GP</td>
<td>616/200</td>
<td>Cox</td>
<td>CVD</td>
<td>10</td>
<td>6</td>
<td>0.73</td>
<td>0.00</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Figsman 2004</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>Stroke</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NA</td>
</tr>
<tr>
<td>Schnee 2003</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>Stroke</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NA</td>
</tr>
</tbody>
</table>

Continued
<table>
<thead>
<tr>
<th>Reference</th>
<th>Development population</th>
<th>n events/total</th>
<th>Type of model</th>
<th>Outcome</th>
<th>Predicted years</th>
<th>Number of predictors</th>
<th>Apparent discrimination (AUC)</th>
<th>Apparent calibration (p value)</th>
<th>Method of internal validation</th>
<th>Presentation of risk model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assmann 2002 (PROCAM)²⁵</td>
<td>German men</td>
<td>325/5345</td>
<td>Cox</td>
<td>CHD</td>
<td>10</td>
<td>8</td>
<td>0.83</td>
<td>P &gt; 0.02</td>
<td>NA</td>
<td>Original model and scoring chart</td>
</tr>
<tr>
<td>Lumley 2002 (CHS)²⁶</td>
<td>GP of elderly</td>
<td>399/5868</td>
<td>Cox</td>
<td>Stroke</td>
<td>5</td>
<td>10</td>
<td>0.65 (men)*</td>
<td>NR</td>
<td>Split sample, bootstrapping</td>
<td>Original model, scoring chart, risk software</td>
</tr>
<tr>
<td>Merletti 2002 (Riskcard 2002)²⁷</td>
<td>Italian SP</td>
<td>944/1771</td>
<td>Cox</td>
<td>CHD and CVA and CVD</td>
<td>5</td>
<td>9</td>
<td>CHD: 0.76</td>
<td>NR</td>
<td>NA</td>
<td>Original model, risk software</td>
</tr>
<tr>
<td>EuroSCORE²⁸</td>
<td>European GP</td>
<td>219/698</td>
<td>Logistic</td>
<td>Stroke</td>
<td>7</td>
<td>6</td>
<td>0.69*</td>
<td>&gt; 0.50</td>
<td>Bootstrapping</td>
<td>Original model</td>
</tr>
<tr>
<td>Thomsen 2001 (Copenhagen Risk Score)²⁹</td>
<td>European GP</td>
<td>50524/108</td>
<td>Cox</td>
<td>MI</td>
<td>5, 10, 20</td>
<td>9</td>
<td>NR</td>
<td>NA</td>
<td>NA</td>
<td>Original model, risk software</td>
</tr>
<tr>
<td>Knuitman 1998 (Framingham)³⁰</td>
<td>Australian SP</td>
<td>516/2248</td>
<td>Cox</td>
<td>Mortality or CHD</td>
<td>10</td>
<td>10</td>
<td>NR</td>
<td>NR</td>
<td>NA</td>
<td>Original model</td>
</tr>
<tr>
<td>Wilson 1998 (Framingham)³¹</td>
<td>US GP</td>
<td>510/5345</td>
<td>Cox</td>
<td>CHD</td>
<td>10</td>
<td>7</td>
<td>NR</td>
<td>NR</td>
<td>NA</td>
<td>Original model and score sheet</td>
</tr>
<tr>
<td>Wood 1998 (JBSRC)³²</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>CHD</td>
<td>10</td>
<td>7</td>
<td>NR</td>
<td>NR</td>
<td>NA</td>
<td>Risk chart</td>
</tr>
<tr>
<td>Zodpey 1998 (³³</td>
<td>Indian SP</td>
<td>154/308</td>
<td>Logistic</td>
<td>CHD</td>
<td>NR</td>
<td>5</td>
<td>NR</td>
<td>NR</td>
<td>NA</td>
<td>Scoring chart</td>
</tr>
<tr>
<td>Anderson 1991 (Framingham)³⁴</td>
<td>US GP</td>
<td>NR/575</td>
<td>Cox</td>
<td>CHD, stroke, CVD, mortality</td>
<td>Variable</td>
<td>7</td>
<td>NR</td>
<td>NR</td>
<td>NA</td>
<td>Original model</td>
</tr>
<tr>
<td>Anderson 1991 (Framingham)³⁵</td>
<td>US GP</td>
<td>558/537</td>
<td>Cox</td>
<td>CHD</td>
<td>5, 10</td>
<td>8</td>
<td>NR</td>
<td>NR</td>
<td>NA</td>
<td>Original model, scoring chart</td>
</tr>
</tbody>
</table>

Displayed are the type of model, the outcome, predicted risk period, population in which it was developed and the apparent (i.e., as quantified in the original development study) discrimination and calibration.

For details on risk factors included in the models, see online appendix.

*After correction.
†Values of the simplified risk or sum score.
AUC, area under the curve; CHD, coronary heart disease; CVA, cerebrovascular accident; CVD, cardiovascular disease; GP, general population; MI, myocardial infarction; NR, not reported.
APPENDIX C: QATAR BIOBANL ETHICAL APPROVAL AND MUTUAL NON-DISCLOSURE AGREEMENT

QATAR BIOBANK
MUTUAL NON-DISCLOSURE AGREEMENT (APPENDIX C)

THIS MUTUAL NON-DISCLOSURE AGREEMENT (hereinafter the “Agreement”) is made and entered into this 26th of December, 2016, by and between DR. REHAM NEGM ELDIN - HAMAD HEALTHCARE QUALITY INSTITUTE HMC & DR. TALIB LUKMAN FROM THE PUBLIC HEALTH DEPARTMENT COLLEGE OF HEALTH SCIENCE QATAR UNIVERSITY and Qatar Biobank, a member of Qatar Foundation for Education, Science and Community Development, a private institution for public benefit established under the laws of the State of Qatar located at PO Box 5825, Doha (hereinafter referred to as “QF”), represented by Dr. Nabil Affifi in his capacity as Acting Director of Qatar Biobank (hereinafter referred to as “QBIB”).

For purposes of this Agreement “DR. REHAM NEGM ELDIN - HAMAD HEALTHCARE QUALITY INSTITUTE HMC & DR. TALIB LUKMAN FROM THE PUBLIC HEALTH DEPARTMENT AND QBIB” shall collectively be referred to as the “Parties.”

PREAMBLE

WHEREAS, in order to facilitate the Purpose of this Agreement and to prevent the dissemination of Confidential Information (as hereinafter defined), the Parties have agreed to enter into this Agreement and be bound by the terms and conditions hereinafter set forth governing the disclosure, use and protection of the Confidential Information;

THEREFORE, THE PARTIES HEREBY AGREE AS FOLLOWS:

Article 1 - Purpose

1.1 The Parties agree to enter into a confidential relationship with respect to the mutual disclosure of certain proprietary and confidential information of each party in connection to a study on “Qatar Biobank data analysis: Lifestyle, biological factors and clinical biomarkers as risk factors of cardiovascular diseases burden in Qatar”. The proprietary and confidential information is to be disseminated only to DR. REHAM NEGM ELDIN & DR. TALIB LUKMAN FROM THE PUBLIC HEALTH DEPARTMENT AND QBIB on a need to know basis.

Article 2 - Definitions

2.1 “Affiliate” shall mean any corporation, company, or other entity, which: (i) is Controlled by a party hereto; or (ii) Controls a party hereto; or (iii) is under common Control with a party hereto. For this purpose “Control” means that more than fifty percent (50%) of the controlled entity’s shares or ownership interest representing the right to make decisions for such entity are owned or controlled, directly or indirectly, by the controlling entity. An entity is considered an Affiliate only so long as such ownership or control exists.

2.2 “Confidential Information” means all information and/or material disclosed by the Disclosing Party to the Receiving Party or which is otherwise communicated to or comes to the attention of the Receiving Party whether such information is in writing, oral or in any other form or media and whether such disclosure, communication or coming to the attention of the Receiving Party occurs prior to or during this Agreement.

2.2.1 Confidential Information includes, but is not limited to, the following:

2.2.1.1 any and all knowledge, information or materials relating to the Disclosing Party’s proprietary business strategies, business that: (a) has its origin or is related to the Purpose of this Agreement and (b) is specifically marked as confidential upon disclosure, including information, inventions, developments, concepts, improvements, designs, discoveries, software, samples, know-how, trademarks, or trade secrets, whether or not patentable or registrable under intellectual property or similar laws, whether or not data provided in hardcopy or electronic or other form, media forecasts, proposals, human resources and personnel information, marketing and sales information, product and/or pricing information, customer and/or potential customer lists and information, customer orders and related documentation and information relating to vendors or potential vendors, whether of technical or
QATAR BIOBANK
MUTUAL NON-DISCLOSURE AGREEMENT
(APPENDIX C)

Research Application No. QF-OBB-RES-ACC-0051

financial nature or otherwise relating in any manner to the business affairs of the Disclosing Party or any parent, subsidiary or associated company of the Disclosing Party,

2.2.1.2 any and all information which can be obtained by examination, testing or analysis of any hardware, any component part thereof, software or material samples provided to the Receiving Party by the Disclosing Party;

2.2.1.3 any and all information disclosed by one Party to any of the other Parties relating directly or indirectly to the Purpose;

2.2.1.4 the fact that the Parties are interested in and/or are assessing the Purpose and/or are discussing the Purpose with each other;

2.2.1.5 the terms of any and all agreements reached by the Parties or proposed by any of the Parties.

2.2.2 Confidential Information shall not include information which the Receiving Party can show is:

2.2.2.1 already published or otherwise available to the public at the time of disclosure to the Receiving Party by the Disclosing Party, other than by a breach of a confidentiality obligation;

2.2.2.2 rightfully disclosed to the Receiving Party from a third party with rights of use and disclosure;

2.2.2.3 proven to be known by the Receiving Party on a non-confidential basis prior to disclosure hereunder;

2.2.2.4 disclosed in compliance with applicable law or a valid administrative or court order, provided that the Receiving Party first gives (as long as this notice does not contravene any legal obligation condition) the Disclosing Party reasonable notice of such law or order and allows the Disclosing Party to assert the privileged and confidential nature of the Confidential Information against the third party seeking disclosure;

2.2.2.5 independently developed by or for the Receiving Party, as evidenced by documentation, without any reliance, reference, or access to the Disclosing Party’s Confidential Information; or

2.2.2.6 the Disclosing Party has agreed in writing that it is free of such restrictions.

2.3 “Disclosing Party” means any Party, its Affiliates, and or its Representatives disclosing Confidential Information to the other Party.

2.4 “Employee” means the employees, officers, directors, and professional or technical advisors of the Receiving Party. Without limitation, the reference to professional advisors shall be deemed to include third-party legal, accounting and auditing parties.

2.5 “Receiving Party” means any Party, its Affiliates, and or its Representatives receiving Confidential Information from the other Party.

Article 3 – Obligations of the Parties

3.1 In consideration of the disclosure of Confidential Information by the Disclosing Party, the Receiving Party agrees:

3.1.1 to hold Confidential Information in strict confidence and not to disclose any part of such information to any third party without prior written consent of the Disclosing Party;

3.1.2 not to communicate or contact with parties subject of the Confidential Information.

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3.1.3 to employ all affirmative steps necessary to protect the Confidential Information from unauthorized access, disclosure or use exercising at all times commercially reasonable degree of care, and at least to the same extent and manner as the Receiving Party protects its own Confidential Information;

3.1.4 to assist Subcontractor(s) compliance with this Non-Disclosure Agreement regarding Confidential Information;

3.1.5 not to reproduce or use Confidential Information disclosed to it under this Agreement for any purpose other than the Purpose set forth in this Agreement; and

3.1.6 to restrict access to the Confidential Information within its own organization to its researchers or employees having a need-to-know strictly for the Purpose of this Agreement.

3.2 The parties hereto recognize that they are each part of an organization of multiple legal entities in several jurisdictions and that it may be necessary for either party to provide Confidential Information to or disclose Confidential Information of its Affiliate in connection with the Purpose. For this purpose, each of the parties agrees (both as disclosing party and as receiving party hereunder) that:

3.2.1 each of the parties may disclose Confidential Information to its Affiliates and their respective employees, but only to the extent that such Affiliate has a need to know for the purpose of carrying out the Purpose and is made aware of its obligations under this Agreement; and

3.2.2 disclosure of any Affiliate of a party hereto in connection with the Purpose shall be deemed to be disclosure made by or to, respectively, that party and subject to this Agreement.

3.3 Nothing in this Agreement shall be construed as:

3.3.1 creating an obligation on any of the Parties to disclose particular information;

3.3.2 creating an obligation on the parties to negotiate;

3.3.3 a representation as to the accuracy, completeness, quality or reliability of the information;

3.4 Within five (5) days of the receipt of the Disclosing Party’s written request, the Receiving Party will return to the Disclosing Party or destroy all documents containing Confidential Information. For purposes of this Section, the term “documents” includes any medium, including paper, digital media, and any other means of recording information. The Receiving Party will, upon request, certify in writing that it has complied with this Section.

Article 4 - Term and Termination

4.1 This Agreement shall be effective as of the date first written above and shall be valid for a period of twenty four (24) months from the date. The Confidential Information shall thereafter remain confidential for three (3) years from the date of termination or expiration of this Agreement.

4.2 This Agreement may be renewed by a written agreement between the Parties.

4.3 Either Party may terminate this Agreement on fifteen (15) days written notice to the other Party subject to the provisions of Article 4.1.

Article 5 - General Provisions

5.1 Nothing contained in this Agreement shall be construed as creating, conveying, transferring, granting, or conferring upon the Receiving Party any right, license, or authority in or title to Confidential Information received by it from the Disclosing Party, other than as expressly provided in this Agreement.
QATAR BIOBANK
MUTUAL NON-DISCLOSURE AGREEMENT
(APPENDIX C)

Research Application No. QF-OB-RES-ACC-0051

5.2 Assignment. Neither Party may assign its rights and/or obligations pursuant to this Agreement, without the prior written consent of the other Party, and any attempt to do so is void.

5.3 Amendment. No amendment to this Agreement shall be valid or binding unless set forth in writing and duly executed by both Parties.

5.4 Governing Law and Dispute Resolution.

5.4.1 This Agreement shall be governed by and construed in accordance with the substantive laws of the State of Qatar.

5.4.2 All disputes arising in connection with this Agreement shall be dealt with in accordance with the following procedure:

i. the Parties shall, in the first instance, attempt to settle the dispute by mutual agreement between the Parties. The dispute resolution process shall be initiated by one Party giving written notice ("Initial Notice") to the other Party setting out the nature and basis of the dispute and requiring the Parties to act reasonably and in good faith to resolve the dispute.

ii. If the Parties are unable to resolve the Dispute within fifteen (15) business days after the date of the Initial Notice, either Party may, by notice to the other Party ("Escalation Notice") require the dispute to be referred to a two members of senior management (or nominees) representing each of the Parties.

iii. If the senior managers are unable to resolve the dispute by agreement within ten (10) business days of the date of the Escalation Notice, either Party may require that the Dispute is referred to binding arbitration.

5.4.3 Where a Party wishes to refer a matter to arbitration, it shall be conclusively settled in accordance with the rules then in force of the United Nations Commission on International Trade Law (UNCITRAL) Arbitration Rules. The seat of the arbitration shall be Qatar, in the English language. There shall be a sole arbitrator, with reasonable knowledge of the subject matter of this Agreement, appointed by the mutual agreement of the parties as set in article 8 of the UNCITRAL Arbitration Rules (as revised in 2010).

WHEREOF, the Parties have executed this Agreement by their duly authorized representatives.

SIGNED for and on behalf of ICL

[Signature]

Print Name: Dr. Reham Negm El Din
Hamad Health Care Quality Institute
HMC &

[Signature]

Print Name: Dr. Thaib Lukan
From the Public Health Department

Designation: Acting Director QBB

Phone:

Date: 26/12/2016

SIGNED for Qatar Biobank

[Signature]

Print Name: Dr. Nahla Affifi

Title/Position: Acting Director QBB

Phone:

Date: 26/12/2016

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MATERIAL TRANSFER AGREEMENT

This Agreement is made between

QATAR BIOBANK, A MEMBER OF QATAR FOUNDATION FOR EDUCATION, SCIENCE AND COMMUNITY, P.O. BOX 5825,
DOHA, QATAR ("QBB"),
(the "Provider")

- and -

DR. REHAM NEGMI EL DIN - HAMAD HEALTH CARE QUALITY INSTITUTE HMC & DR. THALIB ALI KAMAN FROM
QATAR UNIVERSITY UNDER THE LAWS OF QATAR WHOSE REGISTERED OFFICE IS SITUATED AT P. O. BOX 3050 & PO BOX
2713 DOHA QATAR,
(the "Recipient")

Effective the last date of execution below (the "Effective Date").

Purpose

The purpose of this Material Transfered Agreement is to regulate the obligations between the parties in order to protect the data transferred from the provider to the recipient.

1.0 Definitions

The following words have the following meanings in this Agreement:

a) "Commercial Purpose" means the sale, lease, license, or other transfer of the Material or Modifications for any commercial purpose or for the direct benefit of any for-profit entity, including use of the Material or Modifications by any organization, including Recipient, to perform research for third parties who obtain rights in research results, to screen compounds, to produce or manufacture products for general sale, or to conduct any research activities that result in the sale, lease, license, or transfer of the Material to a for-profit entity.

b) "Confidential Information" means information that a party identifies in writing at the time of transmission as confidential, but does not include information that:

i. is already known by the party to which it is disclosed;
ii. is or becomes part of the public domain without breach of this Agreement;
iii. is obtained from third parties that have no obligation to keep confidential to the parties to this Agreement;
iv. is independently developed by the receiving party or its parent corporation or their respective subsidiaries and/or affiliates without the aid, application or use of the Confidential Information (and such independent development can be properly demonstrated by the receiving party); or,
QATAR BIOBANK
MATERIAL TRANSFER
AGREEMENT (APPENDIX D)

Research Application No. QF-OBB-RES-ACC-0051

V. is required by law, regulation, rule, act or order of any governmental authority or agency to be disclosed by the receiving party, provided, however, that such receiving party (A) gives the disclosing party sufficient advance written notice to permit it to seek a protective order or other similar order with respect to such Confidential Information and (B) thereafter discloses only the minimum information required to be disclosed in order to comply, whether or not a protective order or other similar order is obtained by such disclosing party.

c) “Material” means Original Material, data samples and Unmodified Derivatives, but does not include Modifications or other substances created by the Recipient through the use of the Material.

d) “Modifications” means substances created by the Recipient which contain or incorporate the Material.

e) “Patent Rights” means any patents, patent applications, trade secrets or other proprietary rights of the Provider having claims relating to the Original Material, including any altered forms of the Material made by the Provider, and any substitutions, divisions, continuations, continuations-in-part, reissues, renewals, registrations, confirmations, re-examinations, extensions, supplementary protection certificates or the like, or provisional applications of any such patents and patent applications, or foreign equivalents thereof.

f) “Provider’s Scientist” means Dr. Naula Alfi of the Department of Qatar Biobank.

g) “Research” means the research project described in Appendix – Titled “Qatar Biobank data analysis: Lifestyle, biological factors and clinical biomarkers as risk factors of cardiovascular diseases burden in Qatar”.

h) “Researcher” means DR. REHAM NEG M ELDIN & DR. THALIB LUKMAN of the Recipient.

i) “Unmodified Derivatives” means substances created by the Recipient which constitute an unmodified functional subunit or product expressed by the Original Material, including subclones of unmodified cell lines, purified or fractionated subsets of the Original Material, proteins expressed by plasmids supplied by the Provider, or monoclonal antibodies secreted by a hybridoma cell line.

2.0 Material Transfer

2.1 License. Subject to the terms and conditions herein, the Provider grants to the Recipient a royalty-free, non-exclusive license to use the Material solely in performance of the Research. The Recipient agrees that the Material:

a) will not be used for Commercial Purposes;

b) will not be used in human subjects, in clinical trials, or for diagnostic purposes involving human subjects without the Provider’s prior written consent;

c) will be used only at the Recipient organization and only in the Researcher’s laboratory under the direction of the Researcher or others working under his or her direct supervision, and;

d) will not be further transferred without the Provider’s prior written consent.
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MATERIAL TRANSFER
AGREEMENT (APPENDIX D)

Research Application No. QF-OBB-RES-ACC-0051

e) Will not be transferred outside Qatar.

f) The Approved User shall use the Research Data and Material only for the purpose of conducting the Research in accordance with the Access Application Form and the terms and conditions of this Agreement. Use of the Research Data and/or Material for a different purpose or research project shall require a new application and approval.

2.2 Replication of Research. The Recipient will refer any request for the Material from anyone other than those persons working under the Researcher’s direct supervision to the Provider’s Scientist. To the extent supplies are available, the Provider may make the Material available, under a separate agreement, to other scientists at non-profit organizations who wish to replicate the Research. In no event shall the Recipient transfer the Material to any third party without prior consent of the Provider.

2.3 Research Results. The Recipient will provide a summary the results of the Research to the Provider’s Scientist annually during the term of this Agreement.

2.4 Fee. The license to use the Material for the Research is provided for a fee of 000.00

2.5 Payment. Upon receipt by the Provider of the fee stipulated in 2.4, which will be payable by cheque made payable to 00000000 and addressed to 00000000, the Material will be transferred to the Recipient.

2.6 Compliance with Laws. The Recipient will use the Material and Modifications in compliance with Qatari Law.

2.7 Delivery. Upon delivery of the original materials to the Recipient, the Recipient must sign and acknowledge the receipt of receiving the delivered materials. Upon signing Section agrees to be fully responsible for the custody and protection of the materials and all associated risks.

2.8 Access and Audit. the Recipient agrees to provide access to the provider “QBB” to audit and inspect the sample data and materials during the period of the Agreement.

2.9 Recipient’s Personnel. The Recipient shall ensure that the Recipient’s employees, students and agents using the Material and Modifications agree to be bound by the terms of this Agreement.

3.0 Intellectual Property

3.1 Ownership. The Provider retains ownership of the Material, including any Material contained or incorporated in Modifications. The Recipient will own (a) Modifications (except that the Provider retains ownership of Material included therein), and (b) substances created through the use of the Material or Modifications, but which are not Progeny, Unmodified Derivatives or Modifications (i.e., do not contain the Original Material, Progeny, Unmodified Derivatives). If either 3.1(a) or (b) result from the collaborative efforts of the Provider and the Recipient, joint ownership may be negotiated.

3.2 Further Distribution. The Recipient may distribute substances created by the Recipient through the use of the Original Material only if those substances are not Progeny, Unmodified Derivatives, or Modifications with prior written notice to the Provider.
3.3 Patent Rights. The Recipient acknowledges that the Material is or may be the subject of the Patent Rights. Except as provided in this Agreement, no express or implied licenses or other rights are provided to the Recipient under the Patent Rights. In particular, no express or implied licenses or other rights are provided to use the Material, Modifications, or any related patents of the Provider for Commercial Purposes.

3.4 Commercial Use. If the Recipient wishes to use the Material or Modifications for profit-making or Commercial Purposes, the Recipient will, in advance of such use, negotiate in good faith with the Provider to establish the terms of a commercial license. The Recipient acknowledges that the Provider has no obligation to grant such a license to the Recipient, and may grant commercial licenses to others, or sell or assign all or part of the rights in the Material to any third party, subject to any pre-existing rights held by others. However, nothing in this paragraph shall prevent the Recipient from granting commercial licenses under intellectual property rights claiming Modifications, or methods of their manufacture or their use, that are solely owned by the Recipient.

3.5 Patent Applications. The Recipient may file patent application(s) claiming inventions made by the Recipient through the use of the Material, but will give at least thirty (30) days written notice to Provider before filing a patent application claiming Modifications or method(s) of manufacture or use(s) of the Material.

3.6 Publications. Recipient’s Scientist will provide appropriate acknowledgement of Provider’s Scientist in all publications involving the Material, and will send a copy of any such publications to the Provider at least thirty (30) days prior to submission for publication.

3.7 Confidential Information. The parties may disclose Confidential Information one to another to facilitate the performance of the Research. Confidential Information will be safeguarded and not disclosed to third parties by the receiving party. The Recipient may disclose the Provider’s Confidential Information to the Recipient’s parent corporations, affiliates and subsidiaries only if such parent corporations, affiliates and subsidiaries agree to be bound by confidentiality and non-use provisions at least as protective of the Provider’s rights as those contained in this Agreement.

3.8 “Nothing in this Agreement shall be interpreted or construed to provide the Approved User or the Approved Institution with any rights in or to the Research Data or the Material except as explicitly set out in this Agreement. The Approved User shall have intellectual property rights in the Research results (including subsequent innovations and downstream discoveries) arising from the Research Data or the Material, in accordance with the Intellectual Property Policy. The Approved User shall implement licensing policies that will not obstruct further research and shall follow the OECD Guidelines for the Licensing of Genetic Inventions.”

4.0 Limitation of Liability

4.1 Limitation of Liability. Except to the extent prohibited by law, the Recipient assumes all liability for damages which may arise from its use, storage or disposal of the Material and Modifications. The Provider will not be liable to the Recipient for any loss, claim or demand made by the Recipient, or made against the Recipient by any other party, due to or arising from the use of the Material or Modifications by the Recipient, except to the extent permitted by law when caused by the gross negligence or willful misconduct of the Provider.
QATAR BIOBANK
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4.2 Indemnity. To the extent permitted by law, the Recipient shall indemnify, defend and hold harmless the Provider, and its employees, officers, governors and agents from and against any and all liability, loss, damage, cost, and expense (including reasonable attorneys’ fees), which they may incur, suffer or be required to pay resulting from or arising in connection with the use, handling or storage of Material or Modifications by the Recipient or the Recipient’s personnel, or the breach of any obligation of the Recipient hereunder.

4.3 No Warranties. The Material is experimental in nature and is provided without warranty, term or condition of merchantability or fitness for a particular purpose, or any other warranty, express or implied. The Provider makes no representation or warranty that the use of the Material will not infringe any patent, copyright, trademark or other proprietary rights.

5.0 Term and Termination

5.1 Termination. This Agreement will enter into force as of the Effective Date and will terminate on the earliest of the following dates:

a) when the Material becomes generally available from third parties, for example, through reagent catalogues or public depositories;

b) on completion of the Research;

c) on thirty (30) days written notice by either party to the other; or

d) immediately by Provider if the Recipient has not cured a breach of this Agreement within seven (7) days of being notified of such breach.

5.2 Effect of Termination. If termination occurs:

a) under paragraph 5.1(a), the Recipient shall be bound to the Provider by the least restrictive terms applicable to the Material obtained from the then-available sources; or,

b) under paragraph 5.1(b) or (c), upon the effective date of termination, or if deferred under subsection 5.2, such deferred date of termination of this Agreement, the Recipient will discontinue its use of the Material and will, upon direction of the Provider, return or destroy any remaining Material. The Recipient, at its discretion, will also either destroy any Modifications or remain bound by the terms of this Agreement as they apply to Modifications.

5.3 Survival. The provisions of sections 3, 4, 5, and 6, together with any necessary definitions, will survive termination or expiration of this Agreement.

6.0 Miscellaneous

6.1 Notices. Communication between the parties shall be given in writing and may be given by personal delivery, express delivery service, certified or registered mail, postage prepaid, or facsimile transmission, addressed to:

(a) if to the Provider:

Name: Dr. Nahla Afifi
Department: Scientific & Education
Address: Qatar Biobank, PO Box 5825

(b) if to the Recipient:

Name: Dr. Nahla Afifi
Department: Scientific & Education
Address: Qatar Biobank, PO Box 5825

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5/1/11
6.2 No Assignment. The Recipient shall not assign any or all of its rights and obligations under this Agreement without the Provider’s prior written consent, which may not be unreasonably withheld.

6.3 Dispute. If any difference or dispute arise as to the interpretation of this Agreement or as to any matter arising out of or in connection with this Agreement then either party may give notice in writing informing the other party of the details of the difference or dispute. The parties shall then work together in good faith to resolve their difference or dispute, and senior Sidra and QBB’s representatives shall, within fourteen (14) working days of a written request from either party to the other, meet in good faith in an effort to resolve the difference or dispute.

6.4 Governing law: This Agreement shall be governed by and construed in accordance with the Laws of the State of Qatar.

6.5 Successors. This Agreement will bind and enure to the benefit of the parties and their respective heirs, successors and permitted assigns.

6.6 Entire Agreement. This Agreement is the entire agreement of the parties and no change or modification will be valid unless it is in writing and signed by all parties.

6.7 Headings. Paragraph headings in this Agreement are for purposes of convenience only and will not be used to interpret this Agreement.

6.8 Counterparts. This Agreement may be executed in one or more counterparts, each of which shall be deemed to be an original and all of which, together, shall constitute one and the same instrument. For the purposes of this Agreement, the signature of any party hereto evidenced by a facsimile showing such signature shall constitute conclusive proof for all purposes of the signature of such party to this Agreement.
WHEREOF the parties agree to be bound by the terms and conditions of this Agreement.

**QATAR BIOBANK**

**NAME:** DR. NAHLA AFIFI

**TITLE:** SCIENTIFIC & EDUCATION MANAGER/ ACTING DIRECTOR

**DATE:** 26/12/2016

**RECIPIENT RESEARCHER:**

I agree to be bound by the terms and conditions of this Agreement, and further agree to ensure that the Recipient's employees, students and agents using the Material and Modifications agree to be bound by the terms of this Agreement.

**NAME:** DR. REHAM NEGMELDIN- HMC

**DATE:** 26/12/2016
APPENDIX E NORMAL RIGHT (A) AND LEFT (B) CIMT VALUES – 50TH , 25TH AND 75TH PERCENTILE CIMT VALUES AT DIFFERENT AGE CATEGORIES FOR MEN AND WOMEN \((35) (43) (51)\)

### A right

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<tr>
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<td>Female</td>
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APPENDIX F STATA DO FILE

1 use "C:|\users\hassan\desktop\masters\Spring 2017\thesis\bickbank\State\Thesis data March.dta", clear
2 encode Gender, generate(GenderCode)
3 label define GenderCode 2 "Male" 1 "Female", modify
4 label list GenderCode
5 generate age-
6 replace age = 1 if (Age<=10 & Age>=30)
7 replace age = 2 if (Age>10.1 & Age<=30)
8 replace age = 3 if (Age>35.1 & Age>=55)
9 replace age = 4 if (Age>55)
10 label variable age "Age coded"
11 label define age 1 "16 - 35" 2 "35.1 - 55" 3 "55" 4 ">55", modify
12 label value age age
13 label list age
14 tab age
15
tab LoCIMT
16 tab RoCIMT
17 replace RoCIMT=LoCIMT if RoCIMT==0
18 replace LoCIMT=RoCIMT if LoCIMT==0
19 gen AverageCIMT= (LoCIMT+ RoCIMT)/2
20 sum AverageCIMT
21 histogram AverageCIMT
22
gen Cматериалцимт-=
23 replace Cматериалцимт = 1 if ( GenderCode==2 & Age<30 & AverageCIMT)=0.455)
24 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>30 & Age<50 &
25 AverageCIMT)=0.515)
26 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.59)
27 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.615)
28 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.645)
29 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.67)
30 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.7)
31 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.715)
32 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.745)
33 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.775)
34 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.8)
35 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.835)
36 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.865)
37 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.895)
38 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.925)
39 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.955)
40 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=0.985)
41 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=1)
42 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=1.1)
43 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=1.2)
44 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=1.3)
45 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=1.4)
46 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=1.5)
47 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=1.6)
48 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=1.7)
49 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=1.8)
50 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & AverageCIMT)=1.9)
51 replace Cматериалцимт = 1 if ( Cматериалцимт==1 & RoCIMT =0 & RoCIMT ==0)
52 label define Cматериалцимт 1 "above 50th percentile" 0 "below 50th percentile"
53
gen Cматериалцимт=
54 replace Cматериалцимт = 1 if ( GenderCode==2 & Age<30 & Cматериалцимт==0.455)
55 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>30 & Cматериалцимт==0.515)
56 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & Cматериалцимт==0.59)
57 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & Cматериалцимт==0.615)
58 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & Cматериалцимт==0.645)
59 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & Cматериалцимт==0.67)
60 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & Cматериалцимт==0.7)
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70 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & Cматериалцимт==0.985)
71 replace Cматериалцимт = 1 if ( Cматериалцимт==1 & Cматериалцимт =0 & Cматериалцимт ==0)
72 label define Cматериалцимт 1 "above 75th percentile" 0 "below 75th percentile"
73
gen Cматериалцимт=
74 replace Cматериалцимт = 1 if ( GenderCode==2 & Age<30 & Cматериалцимт==0.455)
75 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>30 & Cматериалцимт==0.515)
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89 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & Cматериалцимт==0.955)
90 replace Cматериалцимт = 1 if ( GenderCode==2 & Age>50 & Cматериалцимт==0.985)
91 replace Cматериалцимт = 1 if ( Cматериалцимт==1 & Cматериалцимт =0 & Cматериалцимт ==0)
replace CatCINT = 0 if (CatCINT == .)
replace CatCINT = 1 if (CatCINT==1 & CatRtCINT==1)
replace CatCINT = 0 if (CatCINT==0 & CatRtCINT==0)
replace CatCINT = 2 if (CatCINT==1 & CatRtCINT==0)
replace CatCINT = 3 if (CatCINT==0 & CatRtCINT==1)
label define CatCINT 1 "above 75th percentile" 0 "below 75th percentile"
label value CatCINT CatRtCINT
tab CatCINT
gen CatCINT=
replace CatCINT = 1 if ( CatLoCINT==1 & CatRtCINT==1)
replace CatCINT = 0 if ( CatLoCINT==0 & CatRtCINT==0)
replace CatCINT = 3 if ( CatLoCINT==1 & CatRtCINT==0)
replace CatCINT = 2 if ( CatLoCINT==0 & CatRtCINT==1)
label define CatCINT 1 "above 75th percentile" 0 "below 75th percentile" 3 "discrepancy", modify
label value CatCINT CatCINT
tab CatCINT

label variable levelofeducation "What is the highest level of education that you have completed?"
label define levelofeducation 1 "Primary school" 2 "Secondary school" 3 "Technical or professional school (but less than University)" 4 "University" 5 "Postgraduate degree" 9999 "Prefer not to answer" 7777 "None of the above", modify
label list levelofeducation
label value levelofeducation levelofeducation
sum levelofeducation
tabulate levelofeducation CatAverageCINT
tab sleep
replace sleep = 1 if (sleep == 0)
replace sleep = 2 if (sleep==2 & sleep <=3)
replace sleep = 3 if (sleep ==4)
replace sleep = 5 if (sleep ==999)
label define sleep 1 "Less than 5 hours" 2 "Between 5 and less than 8 hours" 3 "8 hours or more" 5 "Prefer not to answer", modify
label value sleep sleep
tab sleep
gen educationtrend=
replace educationtrend = 1 if ( levelofeducation >1 & levelofeducation<2)
replace educationtrend = 2 if ( levelofeducation >2 & levelofeducation <4)
replace educationtrend = 3 if ( levelofeducation >4 & levelofeducation <6)
replace educationtrend = 4 if ( levelofeducation >6)
label define educationtrend 1 "Primary or less" 2 "Technical or Secondary" 3 "University or more" 4 "MBA or PhD", modify
label list educationtrend
label value educationtrend educationtrend
tab educationtrend

label variable employment "During the last 12 months, what has been your employment status?"
label define employment 1 "In paid employment" 2 "Self employed" 3 "Business / Company Owner" 4 "Retired" 5 "Housewife" 6 "Unemployed" 7 "Student or trainee" 9999 "Prefer not to answer" 7777 "None of the above", modify
label list employment
label value employment employment
tab employment
gen employmenttrend=
replace employmenttrend = 1 if ( employment >=1 & employment<3)
replace employmenttrend = 2 if ( employment >3 & employment <=6)
replace employmenttrend = 3 if ( employment ==6)
replace employmenttrend = 4 if ( employment ==7)
replace employmenttrend = 5 if (employment >7000)
label define employmenttrend 1 "Employed or business owner" 2 "Housewife or Unemployed" 3 "Retired" 4 "Student or Trainee" 5 "Job or FNA", modify
label list employmenttrend
label value employmenttrend employmenttrend
tab employmenttrend
label variable income "total approximate monthly income for you as an individual? (Indicate the closest category in Qatari Riyal. Include salary, rental income, investments and government transfers)"

label define income 1 "Less than 10,000 per month" 2 "Between 10,000 and 19,999 per month" 3 "Between 20,000 and 49,999 per month" 4 "Between 50,000 and 79,999 per month" 5 "More than 70,000 per month" 9999 "Prefer not to answer" 9880 "do not know"

label list income
label value income income
label value incommetrend incommetrend
label list incommetrend
label value incommetrend incommetrend
label list incommetrend
label variable homeownership "Can you tell us about the ownership status of your home?"

label define homeownership 1 "It is owned outright" 2 "It is owned with a mortgage (by you or someone in your household)" 3 "It is rented" 4 "It is provided by an employment institution" 7777 "None of the above" 9999 "Prefer not to answer"

label list homeownership
label value homeownership homeownership

label variable timeyouhavepentasinging "time you have spent sitting per day in the last 7 days? watching T.V or using computer, during weekdays and weekends (Do not include time spent at work)"

label define timeyouhavepentasinging 1/4=1 5/12=2 13/25=3

label define timeyouhavepentasinging 1 "Short, sitting <5 hours/day" 2 "Moderate, sitting 5-12 hours per day" 3 "Long,>12 hours/day", modify

label list timeyouhavepentasinging
label value timeyouhavepentasinging timeyouhavepentasinging

gen noactivity =
replace noactivity =0 if ( lowMETS ==0 & modMETS ==0 & vigMETS ==0)
replace noactivity =0 if (noactivity ==.)

label define noactivity 1 "No activity" 0 "activity", modify

label value noactivity noactivity

gen PA -
replace PA =2 if ( lowMETS ==1)
replace PA =3 if ( modMETS ==1)
replace PA =4 if ( vigMETS ==1)
replace PA =5 if ( noactivity ==)

label define PA 2 "lowMETS" 3 "modMETS" 4 "vigMETS" 1 "Noactivity", modify

label value PA PA

gen housemembers 0=0 1/5=1 6/10=2 10/100=3

label define housemembers 0 "alone" 1 "1-5 house members" 2 "6-10 house members" 3
label define householdsmembers "5-10 household members" 1 "11-20 household members" 2 "21-30 household members" 3 "31-40 household members" 4 "41-50 household members" 5 "51-60 household members" 6 "61-70 household members" 7 "71-80 household members" 8 "81-90 household members" 9 "91-100 household members" . tab householdsmembers

label define workingnightshifts "Never overworked" 1 "No, never worked at night" 2 "Yes, less than 2 nights per month" 3 "Yes, 3 nights per month or more" 9999 "FNA", modify

label define workingnightshifts workingnightshifts

recode smoking 1=1 2=3 3=3 4=2

label define smoking 1 "Never smoker" 2 "Occasional smoker" 3 "Stopped smoking" 4 "Current smoker" 9999 "FNA", modify

label define Waterpipe 1 "yes" 0 "No" 9999 "FNA", modify

label define Waterpipe Waterpipe

label define passivesmoker "Does anyone in your household smoke cigarettes, cigars or pipes? "

label define passivesmoker 1 "Yes, 1 household member smokes" 2 "Yes, 2 or more household members smoke" 0 "No" 9999 "FNA", modify

label define passivesmoker passivesmoker

label define HDM "History of Diabetes"

label define HDM 1 "yes" 0 "No" 9999 "FNA", modify

label define HDM HDM

label define HOC "History of hypercholesteremia"

label define HOC 1 "yes" 0 "No" 9999 "FNA", modify

label define HOC HOC

label define HKP "History of Hypertension"

label define HKP 1 "yes" 0 "No" 9999 "FNA", modify

label define HKP HKP

label define HOMA "History of MI"

label define HOMA 1 "yes" 0 "No" 9999 "FNA", modify

label define HOMA HOMA

label define HOS "History of Stroke"

label define HOS 1 "yes" 0 "No" 9999 "FNA", modify

label define HOS HOS

replace FHBP = 0 if ( FHBP == 7777)
replace FHBP = 0 if ( FHBP == 9999)
replace FMB = 0 if ( FMB == 7777)
replace FMB = 0 if ( FMB == 9999)
replace FMH = 0 if ( FMH == 7777)
replace FMH = 0 if ( FMH == 9999)
replace FS = 0 if ( FS == 7777)
replace FS = 0 if ( FS == 9999)
replace FD = 0 if ( FD == 7777)
replace FD = 0 if ( FD == 9999)
replace HBMB = 0 if ( HBMB == 7777)
replace HBMB = 0 if ( HBMB == 9999)
replace MMH = 0 if ( MMH == 7777)
replace MMH = 0 if ( MMH == 9999)
replace MS = 0 if ( MS == 7777)
replace MS = 0 if ( MS == 9999)
replace MD = 0 if ( MD == 7777)
replace MD = 0 if ( MD == 9999)
replace MO = 0 if ( MO == 7777)
replace MO = 0 if ( MO == 9999)
replace FHBP= 1 if (FHBP==1 & MHB==.)
replace FHBP= 1 if (FHBP==1 & MHB==0)
replace FHBP= 2 if (FHBP==1 & MHB==1)
replace FHBP= 3 if (FHBP==1 & MHB==1)
label variable FHBP "family history of hypertension"
label define FHBP 1 "Paternal HBP" 2 "maternal HBP" 3 "Both"
label value FHBP FHBP

tab FHBP

gen FHMI=
replace FHMI= 1 if (FHMI==1 & MNI==.)
replace FHMI= 1 if (FHMI==1 & MNI==0)
replace FHMI= 2 if (FHMI==1 & MNI==1)
replace FHMI= 2 if (FHMI==1 & MNI==1)
replace FHMI= 3 if (FHMI==1 & MNI==1)
label variable FHMI "family history of MI"
label define FHMI 1 "Paternal MI" 2 "maternal MI" 3 "Both"
label value FHMI FHMI

tab FHMI

gen FS=
replace FS= 1 if (FS==1 & MS ==.)
replace FS= 1 if (FS==1 & MS==0)
replace FS= 2 if (FS==1 & MS==1)
replace FS= 2 if (FS==1 & MS==1)
replace FS= 3 if (FS==1 & MS==1)
label variable FS "family history of Stroke"
label define FS 1 "Fathernal History of Stroke" 2 "maternal History of stroke" 3 "Both", modify
label value FS FS

tab FS

gen FD=
replace FD= 1 if (FD==1 & MD ==.)
replace FD= 1 if (FD==1 & MD==0)
replace FD= 2 if (FD==1 & MD==1)
replace FD= 2 if (FD==1 & MD==1)
replace FD= 3 if (FD==1 & MD==1)
label variable FD "family history of diabetes"
label define FD 1 "Fathernal History of Diabetes" 2 "maternal History of diabetes" 3 "Both", modify
label value FD FD

tab FD

gen FO=
replace FO= 1 if (FO==1 & MO ==.)
replace FO= 1 if (FO==1 & MO==0)
replace FO= 2 if (FO==1 & MO==1)
replace FO= 2 if (FO==1 & MO==1)
label variable FO "family history of Obesity"
label define FO 1 "Fathernal History of Obesity" 2 "maternal History of Obesity" 3 "Both", modify
label value FO FO

tab FO

tab FHBP CataverageCIMT if CataverageCIMT <=1, chi2 col
tab FHMI CataverageCIMT if CataverageCIMT <=1, chi2 col
tab FS CataverageCIMT if CataverageCIMT <=1, chi2 col
tab FD CataverageCIMT if CataverageCIMT <=1, chi2 col
tab FO CataverageCIMT if CataverageCIMT <=1, chi2 col

label variable vegandiet "no meat, fish, eggs, dairy products"
label variable Vegetariandiet "allows dairy products"
replace lowcaloriediet =0 if ( lowcaloriediet ==9999)
replace lowsaltdiet =0 if ( lowsaltdiet ==9999)
replace lowfatdiet =0 if ( lowfatdiet ==9999)
replace vegdiet = 0 if ( vegdiet == 9999)
replace Vegetariandiet = 0 if ( Vegetariandiet == 9999)
replace noredmeat = 0 if ( noredmeat == 9999)
replace anotherspecialdiet = 0 if ( anotherspecialdiet == 9999)
replace Hospediet = 0 if ( Hospediet == 9999)
gen specialdiet =
replace specialdiet = 1 if ( lowcaloriediet == 1)
replace specialdiet = 2 if ( lowsaltdiet == 1)
replace specialdiet = 3 if ( lowfatdiet == 1)
replace specialdiet = 4 if ( vegdiet == 1)
replace specialdiet = 5 if ( Vegetariandiet == 1)
replace specialdiet = 6 if ( noredmeat == 1)
replace specialdiet = 7 if ( anotherspecialdiet == 1)
replace specialdiet = 8 if ( Hospediet == 1)
label define specialdiet 1 "lowcalorie" 2 "lowsalt" 3 "lowfat" 4 "vegdiet" 5 "vegetariandiet" 6 "noredmeat" 7 "anotherspecialdiet" 8 "hospediet", modify
label value specialdiet specialdiet
tab specialdiet

label variable fastfood "Foods from home delivery, take-away, or fast food restaurants"
replace fastfood = 1 if ( fastfood == 1)
replace fastfood = 2 if ( fastfood == 2 & fastfood < 3)
replace fastfood = 3 if ( fastfood == 3 & fastfood < 5)
label define fastfood 1 "Never or rarely" 2 "Less than twice per week" 3 "Every day or almost every day" 9999 "prefer not to answer", modify
label value fastfood fastfood
tab fastfood

label variable Dairydiet "Dairy Diet"
replace Dairydiet = 1 if ( Dairydiet == 1 & Dairydiet < 5)
replace Dairydiet = 2 if ( Dairydiet == 5 & Dairydiet < 10)
replace Dairydiet = 3 if ( Dairydiet == 10 & Dairydiet < 15)
replace Dairydiet = 4 if ( Dairydiet == 15 & Dairydiet < 100)
label define Dairydiet 1 "Never or rarely" 2 "1-4 times per week" 3 "Once or more times per day" 9999 "prefer not to answer", modify
label value Dairydiet Dairydiet
tab Dairydiet

label variable fatdiet "Fat intake as evident from type of milk you consumed most often during the last year, whole, reduced or fat-free milk"
label define fatdiet 1 "Whole fat diet" 2 "Reduced fat diet" 3 "Fat-free diet" 4 "Balanced fat diet" 5 "Other" 9999 "prefer not to answer", modify
label value fatdiet fatdiet
tab fatdiet

label variable SBPCat "Average SBP of 3 readings?"
label variable SBPCat "Average SBP of 3 readings?"
recode SBPCat 77/119.999999 = 1 120/139.999999 = 2 140/159.999999 = 3 160/280 = 4
label define SBPCat 1 "Normal <120" 2 "Prehypertension <140" 3 "Stage 1 hypertension <160" 4 "Stage 2 hypertension >=160"
label value SBPCat SBPCat
tab SBPCat
recode SBPCat 30/79.999999 = 1 80/89.999999 = 2 90/99.999999 = 3 100/280 = 4
label define SBPCat 1 "Normal <120" 2 "Prehypertension <140" 3 "Stage 1 hypertension <160" 4 "Stage 2 hypertension >=160"
label value SBPCat SBPCat
tab SBPCat
gen CatAveragepulse =
replace CatAveragepulse = 0 if ( Age<26 & Averagepulse <65)
replace CatAveragepulse = 0 if ( Age<35 & Averagepulse<65)
replace CatAveragepulse = 0 if ( Age<45 & Averagepulse<65)
replace CatAveragepulse = 0 if ( Age<55 & Averagepulse<65)
replace CatAveragepulse = 0 if ( Age<65 & Averagepulse<65)
replace CatAveragepulse = 0 if ( Age>65 & Averagepulse<65)
78
```stata
446  gen HDLcode =.  
447  replace HDLcode = 0 if (HDL >=1.6838)  
448  replace HDLcode = 1 if (HDL <1.6884) & (HDL >1.1688)  
449  replace HDLcode = 2 if (HDL <=1.1688)  
450  label define HDLcode 0 "optimal > 1.6" 1 "intermediate risk <1.1"  
451  label value HDLcode HDLcode  
452  tab HDLcode  
453  
454  gen LDLcode =.  
455  replace LDLcode = 0 if (LDL <=0.777)  
456  replace LDLcode = 1 if (LDL >0.777)  
457  label define LDLcode 0 "optimal/intermediate risk <0.77" 1 "high risk >0.77"  
458  label value LDLcode LDLcode  
459  tab LDLcode  
460  
461  gen TSCode =.  
462  replace TSCode = 0 if (TS <=1.129)  
463  replace TSCode = 1 if (TS >1.129) & (TS <=1.6899)  
464  replace TSCode = 2 if (TS >1.6899)  
465  label define TSCode 0 "optimal <1.12" 1 "intermediate risk >1.69"  
466  label value TSCode TSCode  
467  tab TSCode  
468  
469  replace comorbidity = 1 if (comorbidity > 0 & comorbidity < 3)  
470  replace comorbidity = 2 if (comorbidity > 3)  
471  label define comorbidity 0 "no comorbidity" 1 "1-2 comorbidity" 2 ">3 comorbidity"  
472  label value comorbidity comorbidity  
473  label list comorbidity  
474  
475  replace Fcomorbidity = 1 if (Fcomorbidity > 0 & Fcomorbidity < 5)  
476  replace Fcomorbidity = 2 if (Fcomorbidity > 5)  
477  label define Fcomorbidity 0 "no Fcomorbidity" 1 "1-4 Fcomorbidity" 2 ">5 Fcomorbidity"  
478  label value Fcomorbidity Fcomorbidity  
479  label list Fcomorbidity  
480  
481  keep if CataverageCI1MT==2  
482  
483  **Table 1  
484  by age, sort : summarize AverageCI1MT if Gender==1, detail  
485  by age, sort : summarize AverageCI1MT if Gender==2, detail  
486  
487  **Table 2  
488  tab age CataverageCI1MT, chi2 row  
489  tab GenderCode CataverageCI1MT, chi2 row  
490  
491  **Table 3  
492  tab incometrend CataverageCI1MT, chi2 row  
493  tabdods CataverageCI1MT incometrend if incometrend==4  
494  tab homeownership CataverageCI1MT if homeownership <=4 , chi2 row  
495  tabdods CataverageCI1MT homeownership  
496  tab housemembers, ncol  
497  tabdods CataverageCI1MT housemembers if housemembers<=3  
498  
499  tab educationtrend  
500  tab educationtrend, ncol  
501  tab educationtrend CataverageCI1MT if educationtrend==4 , chi2 row  
502  tabdods CataverageCI1MT educationtrend if educationtrend==4  
503  
504  tab employmenttrend  
505  tab employmenttrend CataverageCI1MT if employmenttrend <=4 , chi2 row  
506  
507  **Table 4  
508  tab PA  
509  tabdods CataverageCI1MT PA  
510  tab PA CataverageCI1MT, chi2 row  
511  
512  
513  
514  
515  
79
```
80
81
82

**Appendix:**

```
* table 10
tab age, nol
logistic CaraverageCIMT 1.age
test 2. age 3.age
**0.0069

* gender code
tab GenderCode
logistic CaraverageCIMT 1. GenderCode
**0.0069

* income trend
tab income trend, nol
logistic CaraverageCIMT 1. income trend if income trend<4
**0.02

* homeownership
tab homeownership, nol
logistic CaraverageCIMT 1. homeownership if homeownership <=4
test 2. homeownership 3. homeownership 4. homeownership
**0.04

* education trend
tab education trend, nol
logistic CaraverageCIMT 1. education trend if education trend <4
**0.0015

* employment trend
tab employment trend, nol
logistic CaraverageCIMT 1. employment trend if employment trend <=4
test 2. employment trend 3. employment trend 4. employment trend
** 0.0015
```
729  tab PA
730  tab PA, nol
731  logistic CaraverageCIMT 1.PA
732  logistic CaraverageCIMT 1.PA
733  test 2.PA 3.PA 4.PA
734  ** 0.34
735
736  tab sitting
737  tab sitting, nol
738  logistic CaraverageCIMT 1.sitting if sitting>=1
739  logistic CaraverageCIMT 1b2.1.sitting
740  test 2.sitting 3.sitting
741  **0.51
742
743  tab sleep
744  tab sleep, nol
745  logistic CaraverageCIMT 1.sleep if sleep <4
746  test 2.sleep 3.sleep
747  **0.494
748
749  tab smoking
750  tab smoking, nol
751  logistic CaraverageCIMT 1.smoking if smoking <3
752  logistic CaraverageCIMT 1.smoking
753  test 2.smoking 3.smoking 4.smoking
754  **0.44
755
756  logistic CaraverageCIMT 1b1.1.Waterpipe if Waterpipe <=1
757  logistic CaraverageCIMT 1.Waterpipe
758  **<0.001
759
760  tab passivesmoker
761  tab passivesmoker, nol
762  logistic CaraverageCIMT 1b1.1.passivesmoker if passivesmoker <=1
763  logistic CaraverageCIMT 1.passivesmoker
764  **<0.5
765
766
767
768  logistic CaraverageCIMT 1.HGDM if HGDM <=1
769  logistic CaraverageCIMT 1.HCC if HCC <=1
770  logistic CaraverageCIMT 1.HGBP if HGBP <=1
771  logistic CaraverageCIMT 1.HGHA if HGHA <=1
772  logistic CaraverageCIMT 1.HOS if HOS <=1
773
774  logistic CaraverageCIMT 1.FHRP
775  **<0.007
776  logistic CaraverageCIMT 1.FHMI if FHMI<4
777  test 2.FHRP 3.FHRP
778  ** 0.59
779
780  logistic CaraverageCIMT 1.FS if FS<4
781  logistic CaraverageCIMT 1.FD if FD<4
782  logistic CaraverageCIMT 1.FG if FG <4
783
784
785
786  logistic CaraverageCIMT 1b1.1.specialdiet
787  logistic CaraverageCIMT 1.fastfood if fastfood <=3
788  logistic CaraverageCIMT 1.Dairydist
789  logistic CaraverageCIMT 1.fatdiet if fatdiet<4
790
791  logistic CaraverageCIMT 1.SBPCat
792  logistic CaraverageCIMT 1.SBPCat
793  logistic CaraverageCIMT 1.SMPCat
794  logistic CaraverageCIMT 1.Cataveragepulse
795
796  logistic CaraverageCIMT 1b2.1.CBPcode
797  logistic CaraverageCIMT 1.Cholesterolcode
798  logistic CaraverageCIMT 1b1.1.Fibrinogencode
799  logistic CaraverageCIMT 1.glucosecode
800  logistic CaraverageCIMT 1.BA1code
m1: stepwise, pr(.1) pr(.2): logistic CathaverageCIMT (1.age) (1.GenderCode) (1.income traveld) (1.education trend) (1.employment trend) (1.FDG) (1.FBP) (1.FS) (1.HOM) (1.HOC) (1.HOB) (1.1.fastfood) (1.SBPcat) (1.DBPcat) (1.CatAveragePulse) (1.BMIcat) (Fatpercent) (weight) (Waist) (1.Glucosecode) (1.HBAlcCode) (1.HDLcode) (FBS) (TG) (HBAlc) (1.TGcode) (CRP) (Cholesterol) (Fibrinogen) (BMI) (sitting) (1.PA) (APTT) (1.sleep)

xi: stepwise, pr(.2): logistic CathaverageCIMT (1.age) (1.GenderCode) (1.income traveld) (1.education trend) (1.employment trend) (1.FDG) (1.FBP) (1.FS) (1.HOM) (1.HOC) (1.HOB) (1.1.fastfood) (1.SBPcat) (1.DBPcat) (1.CatAveragePulse) (1.BMIcat) (Fatpercent) (weight) (Waist) (1.Glucosecode) (1.HBAlcCode) (1.HDLcode) (FBS) (TG) (HBAlc) (1.TGcode) (CRP) (Cholesterol) (Fibrinogen) (BMI) (sitting) (1.PA) (APTT) (1.sleep)

**full model ( based on univariate P value <.02 )

estimates store full
test 1.fastfood 1.slowfood
logistic CathaverageCIMT 1.age 1.income traveld 1.homes owership 1.GenderCode education trend employment trend FBP FS FO HOB HOM HOC fastfood SBPcat DBPcat CatAveragePulse BMIcat Glucosecode HBAlcCode HDLcode weight BMI CRP Fibrinogen FBS HBAlc TG sitting PA sleep Waist Fatpercent APTT Cholesterol TGcode

**shorter model ( based on Wald test P value <.05 )
gen sample=m(sample)
logistic CathaverageCIMT 1.GenderCode 1.SBPcat CRP if sample==1
list full.
*0.1563


logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP
logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP if sample==1
*coefficients have changed >20 % (confounders)
logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP 1.age if sample==1
logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP 1.income traveld if sample==1
logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP 1.homes owership if sample==1
logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP 1.education trend if sample==1
logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP 1.employment trend if sample==1
logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP 1.FBP if sample==1
logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP 1.FS if sample==1
logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP 1.FO if sample==1
logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP 1.HOB if sample==1
logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP 1.HOM if sample==1
logit CathaverageCIMT 1.GenderCode 1.SBPcat CRP 1.HOC if sample==1
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logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.SBPc Cat if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.CatAveragepulse if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.RMTCat if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.Glucone if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.HBA1Ccode if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.HDLcode if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.weight if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.BMI if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.FBS if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.HBA1C if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.TG if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.sitting if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.DA if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.sleep if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP Waist if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP Fatpercent if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP APIT if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP Cholesterol if sample=1
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP 1.TGcode if sample=1

"waist confounded gender"
logit CatarativeCINT i.GenderCode 1.SBPc Cat CRP Waist if sample=1

"significant individual covariates excluded in univariate analysis"

** Interaction: main effects model

**Interaction:

logistic CatarativeCINT i.GenderCode 1.SBPc Cat CRP Waist HDL
estat store main
logistic CatarativeCINT i.GenderCode##1.SBPc Cat CRP Waist HDL
estat main
"**.01
logistic CatarativeCINT i.GenderCode##1.SBPc Cat CRP Waist HDL 1.SBPc Cat
estat main
"**.73
logistic CatarativeCINT i.GenderCode##1.SBPc Cat CRP Waist HDL 1.SBPc Cat
estat main
"**.52
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estat main
"**.39
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estat main
"**.09
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estat main
"**.57
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estat main
"**.02
logistic CatarativeCINT i.GenderCode##1.SBPc Cat CRP##1.SBPc Cat CRP if sample=1
estat main
"**.49
logistic CatarativeCINT i.GenderCode##1.SBPc Cat CRP##1.SBPc Cat CRP if sample=1
estat main
"**.07
logistic CatarativeCINT i.GenderCode##1.SBPc Cat CRP##1.SBPc Cat CRP if sample=1
estat main
"**.004**
**Logistic model for Categorization, goodness-of-fit test**

logit Categorization i.GenderCode CRP i.SBPCat##c.HDL c.Waist##c.HDL if sample ==1
estat gof, group(5)
ifit, group(5) table
**P Value 0.6107, good fit**

**Specification error (hetero sig 0.379, not sig, we don’t reject null, and there is no specification error)**

linktest, nolog

*Classification table, Correctly classified 71.38%*

ltest

*ROC ( AUC 0.66)*
lroc

logit Categorization GenderCode CRP SBP Cat##c.HDL c.Waist##c.HDL

collin Categorization i.GenderCode CRP i.SBP Cat##c.HDL c.Waist##c.HDL if sample ==1

nomolog, title(Nomogram of the logistic model ) vline(CRF,2,55,30,0) hvline(HDL,0.58,1.335,1.6)
**APPENDIX G QBB DATA AND BIOLOGICAL SAMPLE RECEIPT FORM**

### 1. PROJECT DETAILS

<table>
<thead>
<tr>
<th><strong>Project Title</strong></th>
<th>Qatar Biobank data analysis: Lifestyle, biological factors and clinical biomarkers as risk factors of cardiovascular diseases burden in Qatar</th>
</tr>
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<tbody>
<tr>
<td><strong>Project Duration</strong></td>
<td>8 months</td>
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<tr>
<td><strong>Proposed Start Date</strong></td>
<td>01/10/2016</td>
</tr>
<tr>
<td><strong>Grant Source</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Grant Number</strong></td>
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### 2. PRINCIPAL INVESTIGATOR’S DETAILS

<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>Dr.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surname</strong></td>
<td>Negm Eldin</td>
</tr>
<tr>
<td><strong>Forename</strong></td>
<td>Reham</td>
</tr>
<tr>
<td><strong>Designation</strong></td>
<td>Program Manager, MPH student</td>
</tr>
<tr>
<td><strong>Department</strong></td>
<td>Education &amp; Training Institution</td>
</tr>
<tr>
<td><strong>Institution</strong></td>
<td>Hamad Healthcare Quality Institute HMC.</td>
</tr>
<tr>
<td><strong>Telephone Number</strong></td>
<td>974 40253357</td>
</tr>
<tr>
<td><strong>Institution Address</strong></td>
<td>PO Box. 3650, Doha Qatar</td>
</tr>
<tr>
<td><strong>Email Address</strong></td>
<td><a href="mailto:rhassan@hamad.qa">rhassan@hamad.qa</a></td>
</tr>
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### 4. CO-APPLICANT’S DETAILS

<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>Dr.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surname</strong></td>
<td>Thalib</td>
</tr>
<tr>
<td><strong>Forename</strong></td>
<td>Lukman</td>
</tr>
<tr>
<td><strong>Designation</strong></td>
<td>Head of Public Health Department</td>
</tr>
<tr>
<td><strong>Department</strong></td>
<td>Public Health Department</td>
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<tr>
<td><strong>Institution</strong></td>
<td>College of Health Sciences, Qatar University</td>
</tr>
<tr>
<td><strong>Telephone Number</strong></td>
<td>974 44034815</td>
</tr>
<tr>
<td><strong>Institution Address</strong></td>
<td>P.O. Box 4815</td>
</tr>
<tr>
<td><strong>Email Address</strong></td>
<td><a href="mailto:lthalib@qu.edu.qa">lthalib@qu.edu.qa</a></td>
</tr>
</tbody>
</table>
### Data and Biological Sample Receipt Form

**Main Questionnaire**
- 1. Ethnicity
- 2. Occupation
- 3. Health screening
- 4. Cancer
- 5. Other medical conditions
- 6. Surgery
- 7. Family medical history
- 8. Medications
- 9. Pregnancy and contraception

**Diet Questionnaire**
- 1. Memory test
- 2. Speed of reaction test

**Mode of data provision:**

**USB Number:** CQU.21-DR. Reham

Any other comments:
**QATAR BIOPHARM ACCESS RECEIPT FORM (APPENDIX G)**

Research Application No. QF-QBB-RES-ACC-0051

**Laboratory Data**

1. Blood Count, including:
   - Haemoglobin, Haematocrit, Red Cell Count, White Cell Count (total), Differential white cell count, Platelet count, Mean corpuscular volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), Mean Platelet Volume (MPV)

2. Clinical Chemistry, including:
   - Sodium, Potassium, Chloride, Bicarbonate, Urea, Creatinine, Random Glucose, Bilirubin (total), Protein (total), Albumin, Alkaline Phosphatase, Alanine Transaminase (ALT), Aspartate Transaminase (AST), Gamma Glutamyl Transferase (GGT), Total cholesterol, LDL Cholesterol, Triglycerides, Calcium, Phosphate, Uric acid, Creatinine Kinase, Iron, Total Iron binding capacity, Magnesium

3. Coagulation tests, including:
   - Prothrombin Time (PT), International Normalised Ratio (INR), Partial Thromboplastin Time (PTT), Fibrinogen

4. Endocrinology tests, including:
   - Vitamin D, T3, T4, TSH, Ferritin, Folate, Vitamin B12, C Peptide, Insulin, Testosterone, Estradiol, Sex Hormone Binding Globulin

5. Immunology tests, including:
   - Rheumatoid Factor, ANA, ANCA

6. Cardiac Markers, including:
   - Myoglobin, Brain Natriuretic Peptide

7. Trace Elements, including:
   - Copper, Zinc

8. Others such as HbA1C, Homocysteine

**Medical tests and anthropometrics**

- Systolic and diastolic blood pressure
- Respiratory test
- Body fat content
- Height
- Weight
- Waist
- Hip measurement
- Waist to Hip Ratio
- Heart activity
- Blood flow?
QATAR BIOBANK ACCESS RECEIPT FORM  
(APPENDIX G)  

Research Application No. _QF-QBB-RES-ACC-0051_

<table>
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<tr>
<td>Body fat content</td>
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<tr>
<td>Carotid artery scan</td>
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<td>Fitness test</td>
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<td>Retina test</td>
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Mode of data provision:

USB Number:

Any other comments:

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<tr>
<th>PI Signature and Date</th>
<th>IT Manager Signature and Date</th>
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5. BIOLOGICAL SAMPLE PROVIDED  
Please mention the type and quantity of samples provided  
To be filled by Laboratory Supervisor

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</tr>
<tr>
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</tr>
<tr>
<td>Serum</td>
<td></td>
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</tr>
<tr>
<td>DNA from Buffy coats</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine</td>
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<tr>
<td>Saliva</td>
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<thead>
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**QATAR BIOBANK RESEARCH**  
**DATA AND BIOLOGICAL SAMPLE RECEIPT FORM**  
(APPENDIX G)

Research Application No. QF-QBB-RES-ACC-0051

<table>
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<th>IT Manager Signature and Date</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Naela Alwi</td>
</tr>
<tr>
<td></td>
<td>26/12/2016</td>
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### APPENDIX H AGE- AND GENDER-WISE DISTRIBUTION OF AVERAGE CIMT
IN THE SCORE INDIAN STUDY AND OUR STUDY POPULATIONS

<table>
<thead>
<tr>
<th>Age group</th>
<th>N- Indian</th>
<th>Mean - I</th>
<th>SD - I</th>
<th>N- Qatari</th>
<th>mean - Q</th>
<th>SD-Q</th>
<th>P- Value</th>
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</thead>
<tbody>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39 years</td>
<td>186</td>
<td>0.53</td>
<td>0.06</td>
<td>165</td>
<td>0.5</td>
<td>0.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>40–49 years</td>
<td>170</td>
<td>0.58</td>
<td>0.08</td>
<td>162</td>
<td>0.55</td>
<td>0.09</td>
<td>0.001</td>
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<tr>
<td>50–59 years</td>
<td>149</td>
<td>0.64</td>
<td>0.13</td>
<td>79</td>
<td>0.62</td>
<td>0.12</td>
<td>0.26</td>
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<tr>
<td>≥60 years</td>
<td>119</td>
<td>0.73</td>
<td>0.14</td>
<td>36</td>
<td>0.67</td>
<td>0.12</td>
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<tr>
<td>30–39 years</td>
<td>153</td>
<td>0.51</td>
<td>0.06</td>
<td>201</td>
<td>0.48</td>
<td>0.05</td>
<td>&lt;0.001</td>
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<tr>
<td>Females</td>
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<tr>
<td>40–49 years</td>
<td>138</td>
<td>0.58</td>
<td>0.11</td>
<td>196</td>
<td>0.53</td>
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<tr>
<td>50–59 years</td>
<td>129</td>
<td>0.61</td>
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<td>0.08</td>
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<tr>
<td>≥60 years</td>
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<td>0.64</td>
<td>0.11</td>
<td>45</td>
<td>0.67</td>
<td>0.09</td>
<td>0.12</td>
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