QATAR UNIVERSITY

COLLEGE OF HEALTH SCIENCE

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

BY

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A Thesis Submitted to the Faculty of

the College of Health Science

in Partial Fulfillment

of the Requirements

for the Degree of

Masters in

Public Health

June 2017

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ABSTRACT

NEGM ELDIN, REHAM, H.., Masters of Science : June : 2017:], Public Health

Title: CAROTID INTIMA MEDIA THICKNESS (CIMT) AND CARDIVASCULAR RISK ASSESMENT: 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

ACKNOWLEDGMENTS

Acknowledging the

College of Health Sciences –Public Health department faculty

- Dr. Lukman Thalib
- Dr. Manar AlHAssan
- Dr. Luis Kanamori
- Dr. Hanan Abdul Rahim, and

Qatar Biobank faculty and team, for all the professional support and dedicated efforts.

- Dr. Nahla Afifi
- Dr. Eleni Fthenou

And

- Dr. Abdellatif S. AlHusaini

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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
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.[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).[7]

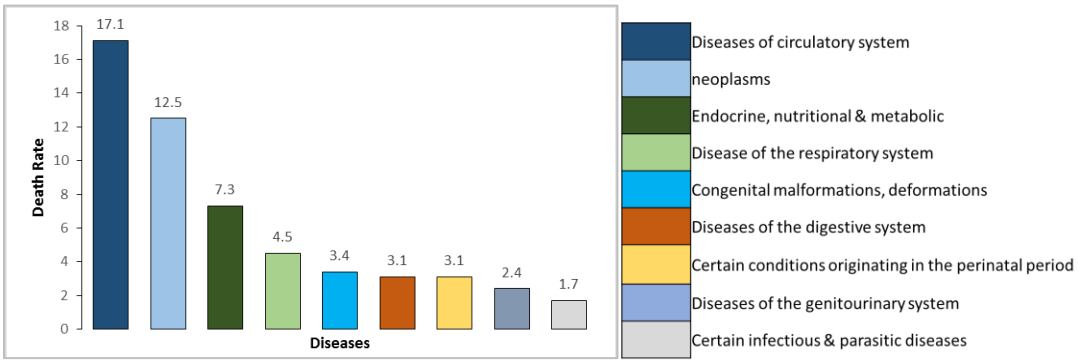

Figure 1. The most common diseases leading to death (Qatar – 2010) Death rate by 100,000 population [10]

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.[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.[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)

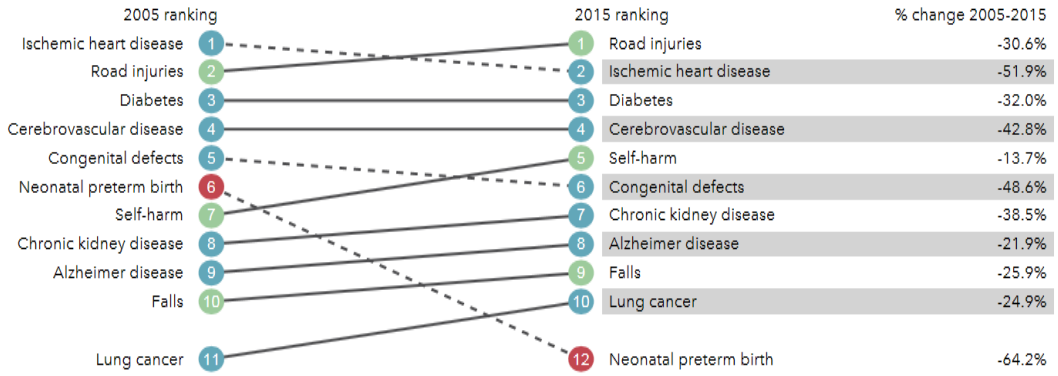

Figure 2: Top 10 causes of death by rate in 2015 and percent change, 2005-2015, by the Institute for Health Metrics and Evaluation (IHME)

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.[4] 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.[5]

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.

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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.[6] 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.[7] 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,.[8] 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,.[9]

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.4 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.[11] 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[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.[13] For instance, studies have shown higher prevalence of type 2 diabetes (15-18%) among adult populations[14,15] Obesity [16] and smoking [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.[18]

2.1.2. 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.[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.[22] Nonetheless, Framingham study has provided profound knowledge base on atherosclerosis and CVD disease risk factors that all subsequent risk assessment studies relied on.[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).[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]

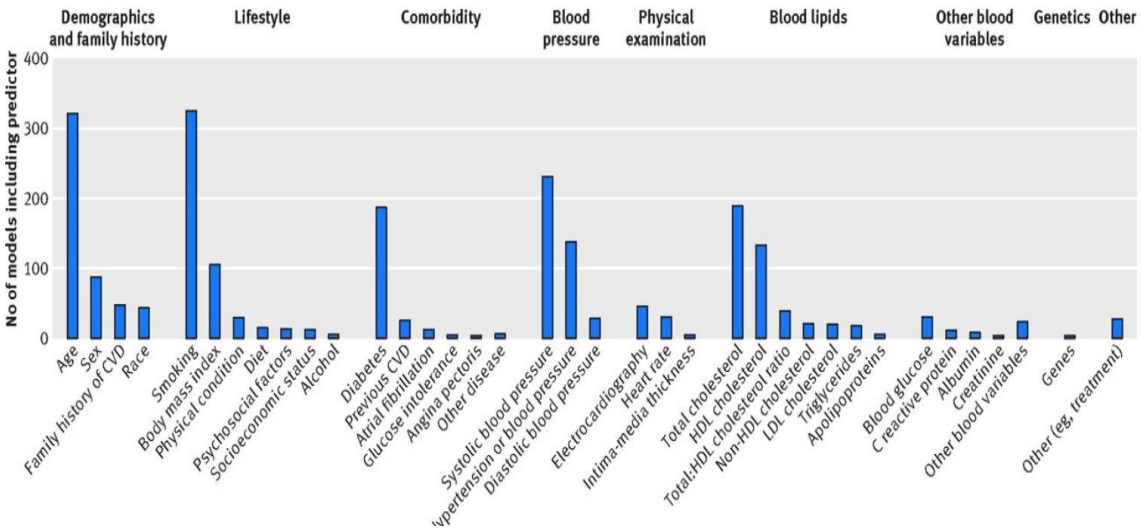

Figure 3 shows the Main categories of predictors included in several developed models[67]

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

Several studies also highlighted concerns about possible limitations of the FRS [27] 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.[28]

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. [29] 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. [28]

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 [30]

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.[36] 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.[36]

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, [33, 34, 37 38]

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.[39]

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.[40] 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.[41] Appendix A is a summary of the large studies focusing on the prognostic value of CIMT.[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.[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.[44] 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 [19]

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 [13, 18], 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.[36] 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.[46] 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.[47] 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.[48]

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 [49]

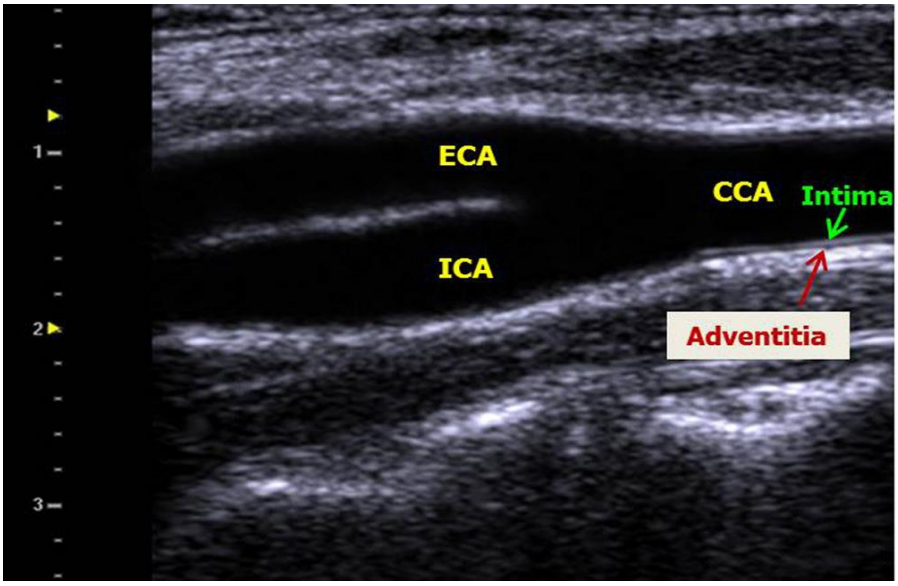

Figure 4: Longitudinal image of carotid bifurcation showing distal part of common carotid artery, carotid bifurcation and the proximal segment of external and internal carotid arteries. CIMT is defined as a double-line pattern visualized by echo 2D on both walls of the common carotid artery (CCA) in a longitudinal view. Two parallel lines (leading edges of two anatomical boundries) 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 1: Age- and gender-wise distribution of mean carotid intima-media thickness (CIMT) [1] in the study population. (N=1425)

	Men (N= 564)				Females (N= 861)			
	N	Mean (SD)	Median	75th percentile	N	Mean (SD)	Median	75th percentile
Age								
18 – 35	219	0.48 (0.06)	0.47	0.52	383	0.46 (0.04)	0.45	0.48
>35 – 55	280	0.54 (0.09)	0.53	0.59	367	0.54 (0.08)	0.53	0.58
>55	65	0.66 (0.13)	0.66	0.75	111	0.62 (0.09)	0.62	0.68

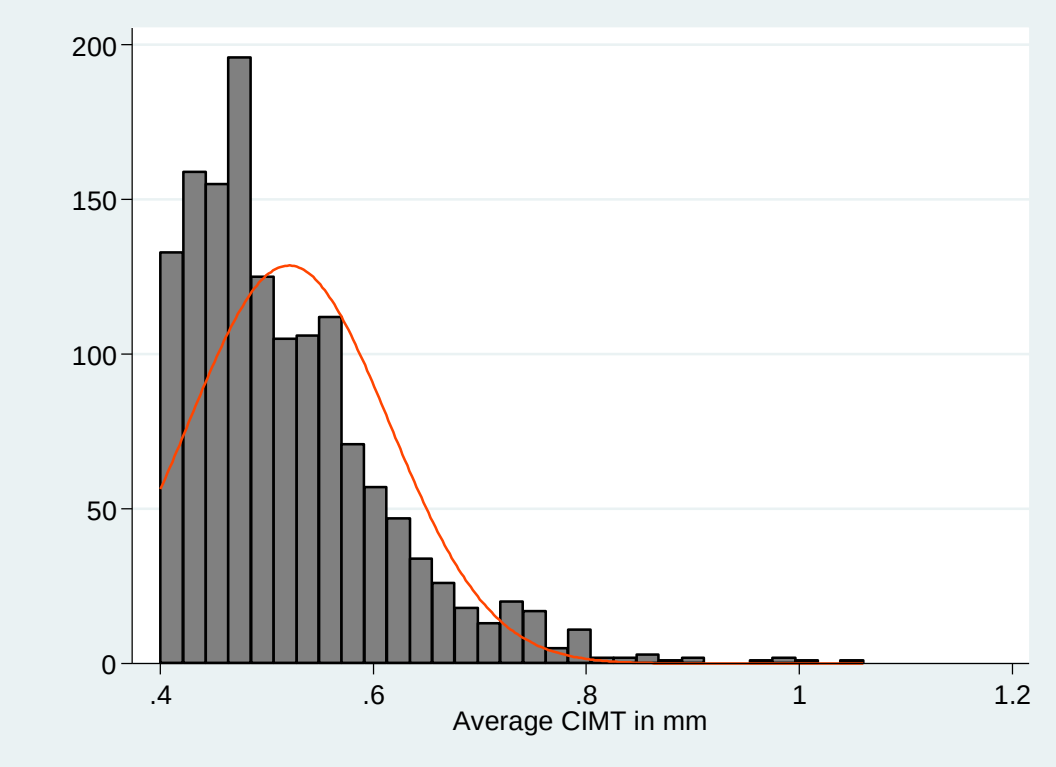

Figure 5: Histogram showing average CIMT distribution in the study population

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)

Predictors	Average CIMT[1]	
	Low Risk N (%)	**High risk[2] N (%)**
Overall	**960 (67.4)**	**465 (32.6)**
Age		
18 – 35	429 (71.3)	173 (28.7)
>35 – 55	440 (68.1)	207 (39.9)
>55	91 (51.7)	85 (48.3)
Gender		
Male	416 (73.8)	148 (26.2)
Female	544 (63.2)	317 (36.8)

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)

Predictors	Average CIMT[1]		
	Low Risk N (%)	High risk[2] N (%)	P value
Overall	**960 (67.4)**	**465 (32.6)**	
Monthly Income in QR per month [3]			**0.011 [7]**
Less than 10,000	682 (65.4)	360 (34.6)	
Between 10,000 and 49,999	185 (74.3)	64 (25.7)	
More than 50,000	32 (72.7)	12 (27.2)	
House ownership [4]			**0.045**
Rented	89 (76.1)	28 (23.9)	
Employer provided	32 (72.7)	12 (27.3)	
Mortgage	96 (72.7)	36 (27.3)	
Outright	682 (65.4)	360 (34.6)	
Level of education [5]			**0.002 [7]**
Primary or less	43 (50.0)	43 (50.0)	
Secondary or technical	301 (66.7)	150 (33.3)	
University or more	615 (69.4)	271 (30.6)	
Current Employment Status [6]			**0.001**
Employed or business owner	599 (69.9)	257 (30.1)	
Housewife or Unemployed	147 (62.8)	87 (37.2)	
Retired	84 (55.6)	67 (44.4)	
Student or trainee	88 (72.1)	34 (27.9)	

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)

Predictors	Average CIMT[1]		
	Low Risk N (%)	High risk[2] N (%)	P value
Overall	**960 (67.4)**	**465 (32.6)**	
MET intensities [3]			0.23 [6]
No Activity	340 (65.5)	179 (34.5)	
Low MET (<3)	357 (68.4)	165 (31.6)	
Moderate MET (3-6)	79 (63.7)	45 (36.3)	
Vigorous MET (>6)	184 (70.8)	76 (29.2)	
Time spent sitting in the past week [4]			**0.05** [6]
Short, sitting <5 hour/day	191 (62.8)	113 (37.2)	
Moderate, sitting 5-12	643 (69.2)	286 (30.8)	
Long, >12 hours/day	85 (70.2)	36 (29.8)	
Hours of sleep in 24 hours [5]			0.49 [6]
< 5	95 (69.9)	41 (30.2)	
5 - 8	707 (67.7)	337 (32.3)	
>8	144 (64.3)	80 (35.7)	

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 18-35years 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)

Predictors	Average CIMT[1]		
	Low Risk N (%)	High risk[2] N (%)	P value
Overall	**960 (67.4)**	**465 (32.6)**	
Smoking Cigarettes [3]			0.412 [6]
Never smoker	86 (64.2)	48 (35.8)	
Stopped smoking	426 (66.3)	217 (33.7)	
Occasional smoker	165 (71.4)	66 (28.6)	
Current smoker	267 (67.3)	130 (32.7)	
Smoking Water pipe (shisha) [4]			**0.001**
No	320 (64.9)	173 (35.1)	
Yes	249 (77.6)	72 (22.4)	
Passive smoking [5]			0.945 [6]
No	353 (69.1)	158 (30.9)	
Yes, 1 house member smokes	200 (70.4)	84 (29.6)	
2 or more house members smoke	117 (68.8)	53 (31.2)	

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 sub-groups. (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)

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

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 response " 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)

Predictors	Average CIMT[1]		
	Low Risk N (%)	High risk[2] N (%)	P value
Overall	**960 (67.4)**	**465 (32.6)**	
Any special diet			0.412 [6]
No special diet	729 (66.8)	363 (33.2)	
Low fat diet	116 (68.2)	54 (31.8)	
Another special diet	43 (79.6)	11 (20.4)	
Low calorie diet	42 (64.6)	23 (35.4)	
No red meat diet	16 (80.0)	4 (20.0)	
Vegetarian diet [3]	6 (60.0)	4 (40.0)	
Vegan diet [4]	3 (50.0)	3 (50.0)	
Low salt diet	3 (75.0)	1 (25.0)	
Fast Food			0.262 [7]
Never or rarely	318 (66.7)	159 (33.3)	
Less than twice per week	495 (66.6)	248 (33.4)	
Every day or almost every day	143 (72.2)	55 (27.8)	
Dairy Diet			0.319 [7]
Never or rarely	106 (68.4)	49 (31.6)	
1 – 4 times per week	743 (67.9)	352 (32.2)	
One or more times per day	111 (63.4)	64 (36.6)	
Fat Diet [5]			0.637 [7]
Whole fat diet	405 (68.2)	189 (31.8)	
Reduced fat diet	431 (67.8)	205 (32.2)	
Fat-free diet	76 (65.5)	40 (34.5)	

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. Vegetarian diet: allows dairy products
4. Vegan diet: No meat, fish, egg or dairy products
5. Fat Diet: 79 responses were "Do Not Know" or "Prefer Not to Answer"
6. P value computed using Fisher exact test
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)

Predictors	Average CIMT[1]				
	Low Risk		High risk[2]		P value
	Mean (SD)	Median (min,max)	Mean (SD)	Median (min,max)	
Height	163.2 (9.1)	163.0 (132.0, 186.0)	161.5 (8.8)	161.0 (136.0, 188.0)	**0.001** [7]
Weight [3]	76.4 (17.4)	75.3 (36.8 , 150.8)	79.6 (18.1)	78.4 (38.6, 148.2)	**0.001** [7]
Adiposity Indicators					
BMI (Kg/m2)	28.4 (5.8)	27.9 (14.8, 55.5)	29.9 (5.9)	29.4 (16.6, 53.8)	**<0.001** [7]
Waist (cm) [4]	87.9 (14.9)	88.0 (0.0, 140.0)	90.9 (15.1)	90.0 (59.0, 155.0)	**<0.001** [7]
Waist/Hip ratio [5]	0.8 (0.1)	0.8 (0.6, 1.1)	0.8 (0.1)	0.8 (0.6, 1.2)	0.821 [7]
Fat % [6]	33.0 (9.7)	33.1 (1.7, 56.4)	36.2 (8.7)	37.0 (7.1, 56.2)	**<0.001** [7]
	N (%)		**N (%)**		
BMI					**<0.001** [8]
Underweight <18.5	25 (89.3)		3 (10.7)		
Normal >=18.5 - <25	225 (73.5)		81 (26.5)		
Overweight >=25 - <30	334 (70.1)		143 (29.9)		
Obese >=30	376 (61.2)		238 (38.8)		
Average Systolic Blood Pressure					**<0.001** [9]
Normal <120	704 (70.7)		292 (29.3)		
Prehypertension <140	218 (64.1)		122 (35.9)		
Stage 1 hypertension <160	34 (43.6)		44 (56.4)		
Stage 2 hypertension >=160	3 (30.0)		7 (70.0)		
Average diastolic Blood Pressure					**0.021** [9]
Normal <80	681 (68.8)		309 (31.2)		
Prehypertension <90	208 (67.8)		99 (32.2)		
Stage 1 hypertension <100	65 (55.6)		52 (44.4)		
Stage 2 hypertension >=100	5 (50.0)		5 (50.0)		
Average Pulse Rate					**0.020** [8]
Excellent pulse for age	409 (70.4)		172 (29.6)		
Average pulse for age	327 (66.9)		162 (33.1)		
Poor pulse for age	224 (63.1)		131 (36.9)		

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)

Predictors	Average CIMT[1]				
	Low Risk		High risk[2]		P value
	Mean (SD)	Median (min, max)	Mean (SD)	Median (min, max)	
A. Partial Thromboplast. Time (APTT)	34.8 (3.6)	34.4 (24.7, 60.6)	34.5 (3.8)	34.4 (23.2, 55.0)	0.152 [5]
CRP [3]	6.4 (4.1)	5.0 (2.0, 50.0)	7.3 (5.9)	5.0 (2.0, 55.0)	**0.001** [5]
Cholesterol	4.9 (0.9)	4.9 (2.3, 8.7)	5.0 (1.0)	4.9 (2.1, 9.7)	0.06 [5]
Fibrinogen	3.1 (0.7)	3.1 (0.4, 7.1)	3.2 (0.7)	3.2 (0.5, 6.0)	**0.012** [5]
Fasting Glucose	5.5 (1.9)	5.0 (3.1, 25.8)	6.1 (3.1)	0.5 (3.3, 26.1)	**<0.001** [5]
HBA1C	5.7 (1.0)	0.5 (3.1, 15.0)	6.1 (1.5)	0.5 (4.2, 14.2)	**<0.001** [5]
HDL	1.4 (0.4)	1.4 (0.5, 2.9)	1.4 (0.4)	1.3 (0.6, 2.7)	1 [5]
LDL	2.9 (0.8)	3.0 (0.7, 6.0)	2.9 (0.9)	3.0 (0.9, 6.3)	1 [5]
Triglycerides [4]	1.3 (0.9)	1.1 (0.3, 9.3)	1.4 (0.9)	1.2 (0.4, 5.8)	**0.05** [5]
Homocysteine	8.7 (3.1)	8.2 (2.8, 45.1)	8.6 (2.6)	8.1 (2.3, 23.6)	0.557 [5]
	N (%)		**N (%)**		
CRP [3]					0.721 [7]
low to average risk <=3		5 (62.5)		3 (37.5)	
high risk >4		952 (67.4)		460 (32.6)	
Cholesterol					0.739 [6]
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					0.328 [7]
optimal <235		937 (67.2)		458 (32.8)	
high risk >350		23 (76.7)		7 (23.3)	
Fasting Glucose					**0.015** [6]
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					**<0.001** [6]
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					0.167 [6]
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					
Optimal/inter. risk <0.77		2(100.0)		0 (0.0)	1.000 [7]
high risk >0.77		958 (67.32)		465 (32.7)	
Triglycerides [4]					**0.050** [6]
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 β 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)

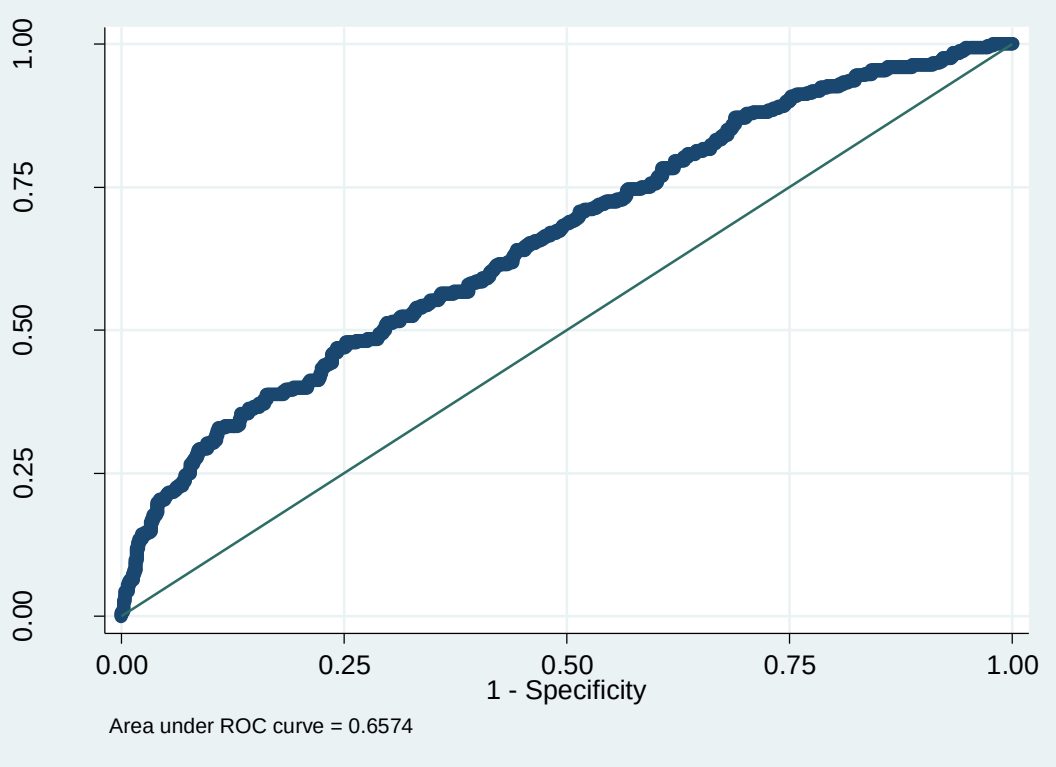

Figure 6: Multivariate Model Receiver operating characteristics (ROC) Area under the curve (AUC)

Table 10 : Logistic regression of risk factors and predictors of high risk level of CIMT (N=1425)

Predictors	OR (95% CI)			
	Univariate analysis OR	P value Sig at <0.2	Multivariate analysis OR	P value Sig at <0.05
Age		**<0.001**		0.731
<18	Reference			
>35 – 55	*1.2 (0.9 - 1.5)*	*0.212*	*0.9 (0.7 - 1.5)*	*0.947*
>55	*2.3 (1.6 - 3.3)*	*<0.001*	*1.2 (0.6 - 2.5)*	*0.529*
Gender (Male)	0.6 (0.5 - 0.8)	**<0.001**	**0.3 (0.1 - 0.8)**	**0.024**
Monthly Income in QR per month		**0.018**		0.113
Less than 10,000	Reference			
Between 10,000 and 49,999	*0.7 (0.5 - 0.9)*	*0.008*	*0.6 (0.3 - 1.0)*	*0.067*
More than 50,000	*0.7 (0.4 - 1.4)*	*0.827*	*0.6 (0.2 - 1.5)*	*0.269*
House ownership		**0.039**		0.622
Outright	Reference			
Mortgage	*0.7 (0.5 - 1.1)*	*0.097*	*1.5 (0.7 - 3.4)*	*0.283*
Employer provided	*0.6 (0.4 – 0.9)*	*0.022*	*omitted*	---
Rented	*0.7 (0.4 - 1.4)*	*0.321*	*omitted*	---
Level of education		**0.002**		0.297
Primary or less	Reference			
Secondary or technical	*0.5 (0.3 - 0.8)*	*0.003*	*0.6 (0.3 - 1.3)*	*0.207*
University or more	*0.4 (0.3 - 0.7)*	*<0.001*	*0.5 (0.2 - 1.0)*	*0.052*
Current Employment Status		**0.002**		0.789
Employed or business owner	Reference			
Housewife or Unemployed	*1.4 (1.0 - 1.9)*	*0.037*	*0.6 (0.4 - 0.9)*	*0.040*
Retired	*1.9 (1.3 – 2.6)*	*0.001*	*1.3 (0.7 - 2.2)*	*0.427*
Student or Trainee	*0.9 (0.6 - 1.4)*	*0.626*	*0.8 (0.4 - 1.4)*	*0.406*
MET intensities		0.362		0.485
No Activity	Reference			
Low MET (<3)	*0.9 (0.7 - 1.1)*	*0.323*	*0.9 (0.6 - 1.2)*	*0.432*
Moderate MET (3-6)	*1.1 (0.7 - 1.6)*	*0.705*	*1.5 (0.9 - 2.6)*	*0.117*
Vigorous MET (>6)	*0.8 (0.6 - 1.1)*	*0.141*	*1.1 (0.7 - 1.7)*	*0.702*
Time spent sitting in past week		**0.103**		0.180
Short, sitting <5 hour/day	Reference			
Moderate, sitting 5-12	*0.8 (0.6 - 0.9)*	*0.039*	*0.7 (0.4 - 1.3)*	*0.266*
Long, >12 hours/day	*0.7 (0.5 - 1.1)*	*0.149*	*0.6 (0.3 - 1.4)*	*0.248*
Hours of sleep in 24 hours		0.497		0.951
< 5	Reference			
5 - 8	*1.1 (0.7 – 1.6)*	*0.616*	*1.1 (0.6 - 1.8)*	*0.79*
>8	*1.3 (0.8 – 2.0)*	*0.279*	*1.1 (0.6 - 1.9)*	*0.83*
Smoking Cigarettes		0.436		
Never smoker	Reference		---	--- [2]
Stopped smoking	*0.9 (0.6 - 1.3)*	*0.645*	---	--- [2]
Occasional smoker	*0.7 (0.5 - 1.1)*	*0.150*	---	--- [2]
Current smoker	*0.9 (0.6 - 1.3)*	*0.515*	---	--- [2]
Smoking Water pipe (No)	1.9 (1.4 - 2.6)	**<0.001**	---	--- [2]
Passive smoking		0.908		
No	Reference		---	--- [2]
1 house member smokes	0.9 (0.7 - 1.3)	0.694	---	--- [2]
>=2 house members smoke	1.0 (0.7 - 1.5)	0.719	---	--- [2]
History of Diabetes (Yes)	*2.2 (1.7 - 3.0)*	**<0.001**	*1.1 (0.6 - 2.0)*	0.836
History of Hypercholesterolemia (yes)	*1.7 (1.3 - 2.1)*	**<0.001**	*1.1 (0.8 - 1.6)*	0.109
History of Hypertension (yes)	*1.6 (1.2 - 2.2)*	**0.001**	*0.9 (0.6 - 1.6)*	0.948

History of Myocardial Infarction (yes)	*3.1 (0.9 - 11.1)*	**0.078**	---	--- [3]	
History of Stroke (yes)	*8.3 (0.9, 74.8)*	**0.028**	---	--- [3]	
Comorbidities Index		**<0.001**			
No comorbidities	Reference				
1-2 comorbidities	*1.4 (1.1 - 1.7)*	*0.011*	---	--- [4]	
>= 3 comorbidities	*4.1 (2.4 - 6.9)*	*<0.001*	---	--- [4]	
Family history of Hypertension		**0.018**			0.881
Paternal history	Reference				
Maternal Only	*1.6 (1.1 - 2.3)*	*0.005*	*1.3 (0.8 - 2.1)*		0.266
Both	*1.1 (0.8 - 1.6)*	*0.519*	*0.9 (0.6 - 1.6)*		0.988
Family history of Myocardial Infarction		0.392			
Paternal history	Reference				
Maternal Only	*1.2 (0.8 – 1.9)*	*0.301*	---	--- [2]	
Both	*1.4 (0.8 – 2.5)*	*0.262*	---	--- [2]	
Family history of Stroke		**0.023**			0.315
Paternal history	Reference				
Maternal Only	*1.7 (0.9 – 2.9)*	*0.060*	*1.1 (0.5 - 2.3)*		*0.887*
Both	*2.7 (1.2 – 6.6)*	*0.020*	*1.5 (0.5 - 4.7)*		*0.476*
Family history of Diabetes		0.543			
Paternal history	Reference				
Maternal Only	*1.2 (0.9 - 1.7)*	*0.270*	---	--- [2]	
Both	*1.1 (0.8 - 1.6)*	*0. 557*	---	--- [2]	
Family history of Obesity		**0.254**			0.734
Paternal history	Reference				
Maternal Only	*1.1 (0.6 – 1.8)*	*0.728*	*1.0 (0.5 - 2.0)*		*0.976*
Both	*0.6 (0.3 – 1.3)*	*0.236*	*0.3 (0.1 - 0.9)*		*0.048*
Family Comorbidities Index					
No Family comorbidities	Reference				
1-4 Family comorbidities	*1.5 (1.0 - 2.1)*	*0.029*	---	--- [4]	
>=5 Family comorbidities	*1.4 (0.9 - 2.1)*	*0.149*	---	--- [4]	
Any special diet		0.410			
No special diet	Reference		---	--- [2]	
Low fat diet	*0.9 (0.7 – 1.3)*	*0.703*	---	--- [2]	
Another special diet	*0.5 (0.2 - 1.0)*	*0.053*	---	--- [2]	
Low calorie diet	*1.1 (0.7 - 1.9)*	*0.722*	---	--- [2]	
No red meat diet	*0.5 (0.2 - 1.5)*	*0.221*	---	--- [2]	
Vegetarian diet [4]	*1.3 (0.4 - 4.8)*	*0.653*	---	--- [2]	
Vegan diet [3]	*2.0 (0.4 - 9.9)*	*0.395*	---	--- [2]	
Low salt diet	*0.7 (0.1 - 6.5)*	*0.729*	---	--- [2]	
Fast Food		**0.291**			0.483
Never or rarely	Reference				
Less than twice per week	*1.0 (0.8 - 1.3)*	*0.987*	*1.6 (1.1 - 2.3)*		*0.010*
Every day or almost every day	*0.8 (0.5 - 1.1)*	*0.158*	*1.6 (0.9 - 2.7)*		*0.108*
Dairy Diet		0.496			
Never or rarely	Reference		---	--- [2]	
1 – 4 times per week	*1.0 (0.7 - 1.5)*	*0.894*	---	--- [2]	
One or more times per day	*1.2 (0.8 - 1.9)*	*0.344*	---	--- [2]	
Fat Diet		0.855			
Whole fat diet	Reference		---	--- [2]	
Reduced fat diet	*1.0 (0.8 - 1.3)*	*0.876*	---	--- [2]	
Fat-free diet	*1.1 (0.7 - 1.7)*	*0.575*	---	--- [2]	
BMI		**<0.001**			0.306
Underweight <18.5	Reference				
Normal >=18.5 - <25	*3.0 (0.9 - 10.2)*	*0.079*	*2.5 (0.6 - 9.7)*		*0.196*
Overweight >=25 - <30	*3.6 (1.1 - 12.0)*	*0.040*	*3.1 (0.7 - 13.7)*		*0.133*
Obese >=30	*5.3 (1.6 - 17.7)*	*0.007*	*3.3 (0.6 - 17.3)*		*0.153*

Average Systolic Blood Pressure		**<0.001**		**<0.001**
Normal <120	Reference			
Prehypertension <140	*1.3 (1.0 - 1.8)*	*0.024*	***1.6 (1.0 - 2.5)***	***0.039***
Stage 1 hypertension <160	*3.1 (1.9 - 4.9)*	*<0.001*	***4.8 (2.0 - 11.2)***	***<0.001***
Stage 2 hypertension >=160	*5.6 (1.4 - 21.9)*	*0.013*	***17.1 (1.4 - 212.0)***	***0.027***
Average Diastolic Blood Pressure		**0.025**		0.107
Normal <80	Reference			
Prehypertension <90	*1.1 (0.8 -1.3)*	*0.733*	*0.8 (0.5 - 1.2)*	*0.264*
Stage 1 hypertension <100	*1.8 (1.2 - 2.6)*	*0.004*	*0.6 (0.3 - 1.2)*	*0.124*
Stage 2 hypertension >=100	*2.2 (0.6 -7.7)*	*0.214*	*0.6 (0.1 - 5.1)*	*0.681*
Average Pulse Rate		**0.067**		0.803
Excellent pulse for age	Reference			
Average pulse for age	*1.2 (0.9 – 1.5)*	*0.215*	*1.1 (0.8 - 1.5)*	*0.739*
Poor pulse for age	*1.4 (1.2 – 1.8)*	*0.021*	*1.1 (0.7 - 1.6)*	*0.733*
CRP		0.769		
Low to average risk <=3	*1.2 (0.3 - 5.2)*	*0.768*	---	--- [2]
High risk >4	Reference			
Cholesterol		0.929		
Optimal <5.3	Reference			
Intermediate	*1.1 (0.8 - 1.3)*	*0.938*	---	--- [2]
High >6.3	*1.1 (0.7 - 1.6)*	*0.702*	---	--- [2]
Fasting Glucose		**<0.001**		0.079
Optimal risk <4.8	Reference			
Intermediate risk	*0.9 (0.7 - 1.2)*	*0.535*	*0.8 (0.5 - 1.1)*	*0.122*
High risk >6.1	*1.7 (1.2 - 2.3)*	*0.002*	*0.6 (0.3 - 1.2)*	*0.167*
HBA1C		**<0.001**		0.620
Optimal risk <6.5	Reference			
Intermediate risk	*2.3 (1.6 - 3.3)*	*<0.001*	*1.1 (0.4 - 2.7)*	*0.823*
high risk >9.6	*1.7 (1.2 - 2.5)*	*0.002*	*1.5 (0.2 - 11.7)*	*0.683*
HDL		**0.128**		0.113
Optimal risk >1.6	Reference			
Intermediate risk	*0.9 (0.7 - 1.2)*	*0.593*	*0.9 (0.6 - 1.4)*	*0.807*
high risk <1.1	*1.2 (0.9 - 1.6)*	*0.258*	*1.4 (0.9 - 2.4)*	*0.157*
Triglycerides		**0.139**		0.867
Optimal risk <1.13	Reference			
Intermediate risk	*1.2 (0.9 - 1.5)*	*0.303*	*0.9 (0.6 - 1.4)*	*0.800*
high risk > 1.69	*1.3 (0.9 - 1.7)*	*0.050*	*1.1 (0.6 - 2.1)*	*0.775*
Fat Percent	1.0 (1.0 - 1.1)	**<0.001**	0.9 (0.9 - 1.0)	0.476
Waist	1.0 (1.0 - 1.1)	**<0.001**	1.0 (0.9 - 1.0)	0.581
Weight	1.0 (1.0 - 1.0)	**0.002**	1.0 (0.9 - 1.0)	0.627
BMI	1.0 (1.0 - 1.1)	**<0.001**	1.0 (0.9 - 1.1)	0.982
CRP	1.0 (1.0 - 1.1)	**0.002**	1.0 (1.0 - 1.1)	**0.022**
Fibrinogen	1.2 (1.0 - 1.5)	**0.018**	0.7 (0.6 – 1.0)	0.084
Fasting Blood sugar	1.0 (1.0 - 1.2)	**<0.001**	1.1 (0.9 - 1.2)	0.330
Cholesterol	0.9 (1.0 - 1.1)	0.798	1.0 (0.9 - 1.2)	0.636
HBA1C	1.3 (1.2 - 1.4)	**<0.001**	1.0 (0.8 - 1.4)	0.843
Triglycerides	1.1 (0.9 - 1.3)	**0.077**	0.9 (0.7 - 1.3)	0.970

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

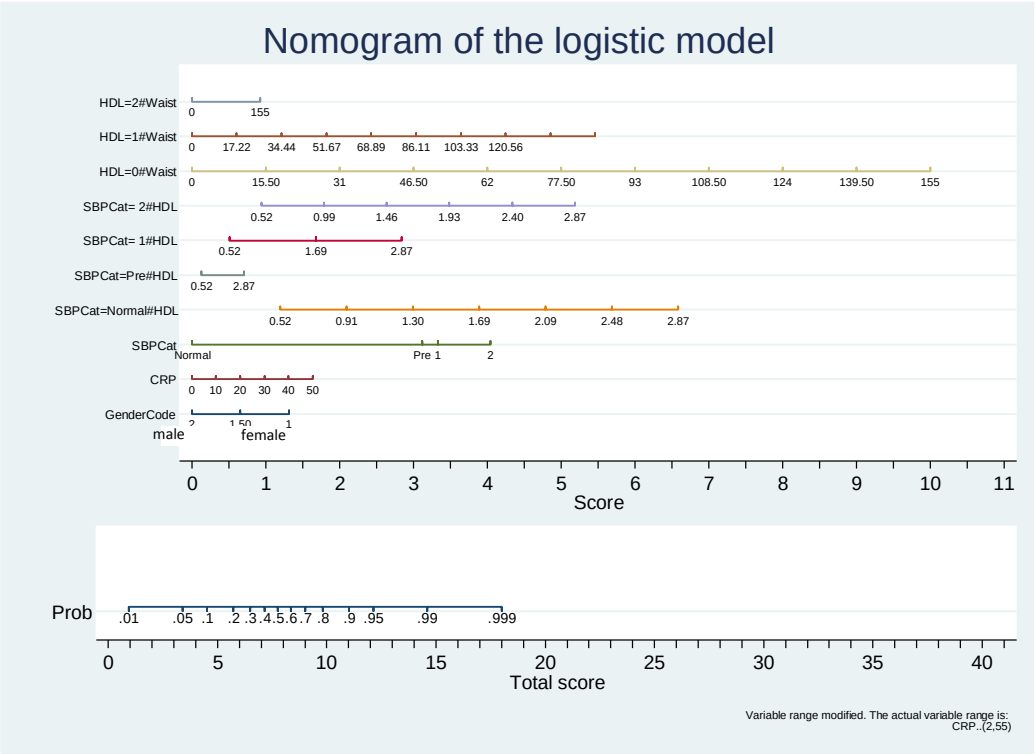

Figure 7: Nomogram of the final logistic regression model

Table 11: Logistic Regression Model

Predictors			Confidence Interval	
Binary CIMT	**Odds Ratio**	**P value**		
Gender	0.41	>0.001	0.30	0.56
CRP	1.02	0.083	0.99	1.05
HDL	4.69	0.093	0.77	28.52
Waist	1.04	0.007	1.01	1.07
SBP				
Prehypertension	8.20	0.001	2.40	27.99
Stage 1	9.44	0.017	1.50	59.32
Stage 2	15.25	0.695	<0.001	1.28e+07
SBP#HDL				
Prehypertension	0.25	0.004	0.09	0..63
Stage 1	0.41	0.179	0.11	1.49
Stage 2	0.72	0.943	<0.001	5647.50
Waist#HDL	0.98	0.073	0.95	1.01

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[52] Following this study, a number of important trials like the Atherosclerosis Risk In Communities study,[47] the Cardiovascular Health Study,[53] the Rotterdam Study,[54] the Malmö Diet and Cancer Study,[55] and the Carotid Atherosclerosis Progression Study[56] 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,[57] reaching to that Den et al meta-analysis found that there is no significant addition when CIMT was added to traditional risk scores.[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 [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 [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 Qataris. Similar studies were done on different populations such as the SCORE study on 1229 Indian subjects.[61] 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.[62]

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.[61] 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.[26] 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,[63] 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.[64]

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 [31]. 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.[65] 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.[66]

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.

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APPENDIX A .STUDIES ASSESSING THE PROGNOSTIC VALUE OF CIMT

Study [Reference #]	Sample Size	Age of Subjects	Follow-up	Carotid Ultrasound Parameters	Plaque	Endpoints	CIMT, RR (95% CI)	NRI
APSIS [67]	558	60 + 7 yrs	Median, 3.0 yrs	Max left CCA-IMT, far wall	Not specified	CV death, MI, revascularization	IMT>1.02mm, RR: 0.78 (0.36-1.70) for CV death or MI; RR: 1.07 (0.56-2.04) for revascularization	
ARIC [68]	12,841	45-64 yrs	Mean follow-up 15.1 yrs	Mean far wall IMT at 6 sites (CCA, bulb, ICA, bilateral)	Plaque included	MI, CV death	IMT > 1.0mm: women HR: 5.07 (3.08-8.36); men 1.85 (1.28-2.69)	7.1
CAPS [69]	5,056	19-90yrs	Mean follow-up 4.2 yrs	Mean far wall IMT bilaterally at CCA, carotid BIF, ICA bulb	Not specified	MI, stroke, death	RR for 1 SD: RR 1.17(1.08-1.26) for CCA-IMT; RR 1.14 (1.05-1.24), for carotid bulb-IMT; RR 1.09 (1.01-1.18) for ICA-IMT.	-1.4
CCCC [70]	2,190	> 35 yrs	Median, 10.5 yrs	Maximal CCA-IMT, far wall, bilateral	Plaque excluded	MI, CV death, PCI, CABG	RR: 1SD; 1.38 (1.12-1.70)	
Charlottesville Study [71]	727	16-85 yrs	Mean, 4.78 yrs	Mean CCA-IMT, bulb-IMT, ICA-IMT, near and far wall bilaterally	Plaque included	MI, revascularization, stroke, TIA	OR for highest quartile of carotid bulb IMT: 5.8 (1.3-26.6)	
CHS [72]	5,020	72.6+5.5 yrs	5 days to 12 yrs (median, 11 yrs)	CCA and ICA-IMT; mean of maximal IMT, near and far wall bilaterally	Plaque included	MI, stroke, CV death, all-cause mortality	Highest tertile: RR: 1.84 (1.54-2.20)	
Cournot, et al. [73]	2,561	51.6 + 10.5 yrs	2-10 yrs	CCA-IMT, ICA-IMT bilaterally	Plaque excluded	CV death, MI, angina	IMT >0.63mm; HR: 2.26 (1.35-3.79)	
FATE [74]	1,574	49.4 + 9.9yrs	Mean, 7.2 yrs	Right CCA-IMT	Plaque excluded	CV death, revascularization, MI, angina, stroke	HR: 1.45 (1.15-1.83)	11.6%
Framingham Offspring Study [75]	2,965	58 + 10yrs	Average, 7.2yrs	Mean CCA-IMT, or maximal CCA-IMT, maximal ICA-IMT, bilaterally	Plaque excluded	MI, angina, CV death, stroke, claudication, heart failure	HR for 1-SD mean CCA-IMT: 1.13 (1.02-1.24); HR for 1-SD maximal CCA-IMT: 1.21 (1.13-1.29); HR for 1-SD maximal ICA-IMT: 1.21 (1.13-1.29)	CCA: 0% ICA: 7.6%
IMPROVE [76]	3,703	Median 64.4yrs	Median 36.2 months	Maximal and mean CCA, ICA, BIF, bilaterally	Plaque included	MI, SCD, angina, stoke, TIA, heart failure, revascularization	HR for 1-SD increase: mean CCA-IMT: 1.33 (1.18-1.50); mean BIF-IMT: 1.28 (1.12-1.47); mean ICA-IMT: 1.34 (1.18-1.51)	FRF+fCCAD+IMT mean-max 12.1%
KIHD [77]	1,257	42-60 yrs	1 mo- 2.5yrs	CCA-IMT, mean of max IMT, near and far wall bilaterally	Focal calcified plaque not included	AMI	CCA-IMT increment, 0.1mm; RR: 2.14 (1.08-4.26)	
LILAC [78]	298	Mean, 79.6yrs	Mean 1,152 days	Average of CCA bilaterally, near and fall wall	Not specified	All-cause mortality	For 0.5mm increase in left IMT, RR: 1.65 (1.08-2.5); right IMT, RR: 3.3 (1.4-1.7)	
MESA [20]	6,814	45-84 yrs	Median, 7.6yrs	Mean of max right CCA-IMT, far wall	Plaque excluded	MI, revascularization, SCD, CV death	HR: 1.17 (0.95-1.45)	Mean-max IMT 7.0% Max-IMT 6.8%
MDCS [79]	5,163	46-68 yrs	Median 7yrs	Mean far wall right distal CCA	Plaque included	MI, CV death	RR for highest tertile: 1.50 (0.81-2.59)	
OSAACA2 [80]	574	65.3 + 9.5yrs	Mean, 2.6yrs	Mean maximal CCA-IMT, BIF-IMT, ICA-IMT, near and far wall bilaterally	Plaque included	MI, CABG, angioplasty, PAD, stroke	For 1-SD increase, RR: 1.57 (1.11-2.20)	
Rotterdam Study [81]	6,389	69.3 + 9.2 yrs	7-10 years	Avg of max CCA-IMT or near and far wall bilaterally	Not specified	MI	RR: 1.95 (1.19-3.19)	CAD, Stroke Men: 0.2, 3.9 Women: 8.2, 8.0
The Edinburg Artery Study [82]	1,007	Mean 69.4 yrs	12 years	Max far wall CCA-IMT bilaterally	Not specified	MI, stroke, angina, claudication	IMT > 0.9mm, OR: 1.59 (1.07-2.37)	
Three-City Study [83]	5,895	65-85 yrs	Median 5.4yrs	Mean CCA-IMT bilaterally, near and far wall	Plaque measured separately	MI, angina, CV death, revascularization	HR for fifth quintile: 0.8 (0.5-1.2)	Carotid plaque 13.7%
Tromso Study [84]	6,226	25-84yrs	6 years	Mean of near and far wall right CCA-IMT and far wall of the bulb	Plaque included	MI	Highest IMT quartile, 1.73 (0.98-3.06) in men and 2.86 (1.07-7.65) in women	

APPENDIX B: CARDIOVASCULAR PREDICTION MODELS DEVELOPED IN GENERAL POPULATIONS [50]

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

Reference	Development population	n events/ n total	Type of model	Outcome	Predicted years	Number of predictors	Apparent discrimination (AUC)	Apparent calibration (p value Hosmer–Lemeshow)	Method of internal validation	Presentation of risk model
Chien 2010[34]	Chinese GP	240/3602	Cox	Stroke	10	8	0.77	NR	Cross-validation	Original model, scoring chart, nomogram
Hippisley-Cox 2010 (QRISK)[35]	British GP	121 623/ 1 267 159	Cox	CVD	Lifetime	14	Women: 0.84* Men: 0.83*	Good*	Split sample	Original model
McGorrian 2011 (IHMRS)[36]	GP from 52 countries	12 438/27 043	Logistic	MI	NR	6	0.71	0.0004	Split sample	Original model
Arima 2009[37]	Japanese GP	216/2742	Cox	CVD	14	7	0.81*	0.60*	Split sample	Original model, scoring chart
Ishikawa 2009 (JMS cohort study)[38]	Japanese GP	255/12 276	Cox	Stroke	10	5	NR	NR	NA	Scoring chart
Matsumoto 2009 (JMS cohort study)[39]	Japanese GP	92/12 323	Cox	MI	10	6	NR	NR	NA	Scoring chart
Pencina 2009 (Framingham)[40]	USA GP	671/4506	Cox	CVD	30	8	0.80, 0.80*	p=0.913, p=0.894*	Cross-validation	Original model
D'Agostino 2008 (Framingham)[41]	US GP	641/8491	Cox	CVD	10	7	Men: 0.76 Women: 0.79 Men: 0.75† Women: 0.79†	p=0.14–0.56	NA	Original model, simplified model, scoring chart
Hippisley-Cox 2008 (QRISK2)[42]	British GP	140 115/ 1 535 583	Cox	CVD	10	14	Women: 0.82 Men: 0.79	Good*	Split sample	Original model
Assmann 2007[43] (PROCAM)	German GP	596/35 100	CHD: Weibull Stroke: Cox	CHD and stroke	10	CHD: 8 Stroke: 5	CHD: 0.81, Stroke: 0.71	NR	NA	Original model, scoring chart
Ridker 2007 (Reynolds risk score)[44]	US GP	504/24 558	Cox	CVD	10	9	0.81, 0.81*	p=0.38, p=0.62*	Split sample	Original model, simplified model
Woodward 2007 (ASSIGN)[45]	GP from Scotland	422/13 297	Cox	CVD	10	9	Men: 0.73 Women: 0.77	NR	NA	Original model
Asia-Pacific Cohort Studies Collaboration 2006[46]	Asian GP	2265/364 566	Cox	CHD mortality	8	6	NR	NR	NA	Original model
Lee 2006 (Strong Heart Study)[47]	American Indian GP	724/4372	Cox	CHD	10	9	Men: 0.73 Women: 0.71 Men: 0.70* Women: 0.72*	Men p=0.45 Women p=0.51	Bootstrap	Original model
Mainous 2007 (Personal HEART)[48]	USA GP	1108/14 343	Cox	CHD	10	9	Men: 0.65* Women: 0.79*	NR	Split sample	Original model, scoring chart
Wu 2006[49]	Chinese GP	742/9903	Cox	Ischaemic CVD	10	7	Men: 0.80 Women: 0.79	Men: p=0.733 Women: p=0.274	NA	Original model, simplified model, scoring chart
Ferrario 2005 (CUORE)[50]	GP Italian men	312/6865	Cox	CHD	10	8	0.75, 0.74*	>0.05	Bootstrap and split sample	Original model
Menotti 2005 (Riskard 2005)[51]	Italian GP	1382/17 153	Weibull	CVD	5, 10, 15	9	NR	NR	NA	Original model, risk chart, risk software
Decode study Group 2004[52]	European GP	791/25 413	Cox	CVD death	5, 10	6	NR	NR	NA	Original model
Liu 2004 (CMCS)[53]	Chinese GP	816/30 121	Cox	CHD and mortality	10	6	0.73	0.08	NA	Original model
Pignone 2004[54]	NR	NR	NR	CHD	10	8	NR	NR	NA	Risk software
Schau 2003[55]	NR	NR	NR	Stroke	NR	8	NR	NR	NA	Risk software

Continued

Table 2 Continued

Reference	Development population	n events/ n total	Type of model	Outcome	Predicted years	Number of predictors	Apparent discrimination (AUC)	Apparent calibration (p value Hosmer–Lemeshow)	Method of internal validation	Presentation of risk model
Assmann 2002 (PROCAM)[56]	German men	325/5345	Cox	CHD	10	8	0.83 0.82 scoring chart	P>0.03	NA	Original model and scoring chart
Lumley 2002 (CHS)[57]	GP of elderly	399/5888	Cox	Stroke	5	10	0.65 (men)* 0.77 (women)*	NR	Split sample, Bootstrap	Original model, scoring chart, risk software
Menotti 2002 (Riscard 2002)[58]	Italian GP	544/9771	Weibull	CHD and CVA and CVD	5	9	CHD: 0.76 CVA: 0.86	NR	NA	Original mode, risk software
Moons 2002 (EUROSTROKE)[59]	European GP	219/698	Logistic	Stroke	7	6	0.69*	>0.50	Bootstrap	Original model
Thomsen 2001 (Copenhagen Risk Score)[60]	European GP	509/24 508	Cox	MI	5, 10, 20	9	NR	NR	NA	Original model, risk software
Knuiman 1998[61]	Australian GP	519/2258	Cox	Mortality or CHD	10	10	NR	NR	NA	Original model
Wilson 1998 (Framingham)[62]	US GP	610/5345	Cox	CHD	10	7	Men: 0.74 Women: 0.76 Men: 0.68† Women: 0.71†	NR	NA	Original model and score sheet
Wood 1998 (JBSRC)[63]	NR	NR	NR	CHD	10	7	NR	NR	NA	Risk chart
Zodpey 1994[64]	Indian GP	154/308	Logistic	CHD	NR	5	NR	NR	NA	Scoring chart
Anderson 1991 (Framingham)[65]	US GP	NR/5573	Weibull	CHD, stroke, CVD, CVD mortality	Variable	7	NR	NR	NA	Original model
Anderson 1991(2) (Framingham)[66]	US GP	626/5573	Weibull	CHD	5, 10	8	NR	NR	NA	Original model scoring chart

Displayed are the type of model, the outcome, predicted risk period, population in which it was developed and the apparent (ie, 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)

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

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 HEALTH CARE QUALITY INSTITUTE HMC & DR THALIB LUKMAN FROM THE PUBLICH 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. Nahla Afifi in his capacity as Acitng Director of Qatar Biobank (hereinafter referred to as "QBB"),

For purposes of this Agreement "**DR. REHAM NEGM ELDIN- HAMAD HEALTH CARE QUALITY INSTITUTE HMC & DR THALIB LUKMAN FROM THE PUBLICH HEALTH DEPARTMENT AND** "QBB" 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 THALIB LUKMAN FROM THE PUBLICH HEALTH DEPARTMENT AND** QBB 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

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) to 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 on/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 **"Employees"** 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;

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 that the Receiving Party protects its own Confidential Information;

3.1.4 to ensure 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 by or to an Affiliate of a party hereto in connection with the Purpose shall be deemed to be a disclosure 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-QBB-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 be settled the dispute by mutual agreement between the Parties. The dispute resolution process shall be instituted 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 nominee) 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 ELDIN-
HAMAD HEALTH CARE QUALITY INSTITUTE
HMC &

DR THALIB LUKMAN FROM THE PUBLICH
HEALTH DEPARTMENT DR. THALIB LUKMAN

Designation:

Phone:

Date: 26/12/2016

SIGNED for Qatar BioBank

Nahla Afifi

Signature:

Print Name: Dr. Nahla Afifi

Title/Position: Acting Director QBB

Phone:

Date: 26/12/2016

APPENDIX D MATERIAL TRANFER AGREEMENT

QATAR BIOBANK
MATERIAL TRANSFER
AGREEMENT (APPENDIX D)

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

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 NEGM ELDIN- HAMAD HEALTH CARE QUALITY INSTITUTE HMC & DR THALIB LUKMAN 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 Transferred 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 Purposes"** 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 any 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 transmittal 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,

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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. Nahla Afifi** 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 NEGM 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 dna/rna 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
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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 xxxx

2.5 **Payment.** Upon receipt by the Provider of the fee stipulated in 2.4, which will be payable by cheque made payable to xxxxxx and addressed to xxxxxxxx, 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 Sidra 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 or 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.

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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 wilful misconduct of the Provider.

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

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City, Province/State:	Doha, Qatar	Doha, Qatar
Postal/Zip Code,		
Country:		
Tel:		
Email:	974-44548356 nafifi@qf.org.qa	974-44548356 nafifi@qf.org.qa
(a) if to the Recipient		
	For Legal and Administrative Materials	*For Technical and Scientific Matters*
Name:	DR. REHAM NEGM ELDIN-	DR THALIB LUKMAN
Department:	Education & Trianing Institution	Public Health Department
Address:	Hamad Health Care Quality Institute Hmc	Qatar Universtiy
City, Province/State:	Doha Qatar	Doha Qatar
Postal/Zip Code, Country	3050	2713
PO Box:		
Tel:	974 40253357	9744 4034815
Email:	rhassan@hamad.qa	lthalib@qu.edu.qa

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 serve 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 telecopy showing such signature shall constitute conclusive proof for all purposes of the signature of such party to this Agreement.

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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

NAME: DR. REHAM NEGM ELDIN- HMC

DR THALIB LUKMAN- QU

TITLE:

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 NEGM ELDIN- HMC

DR THALIB LUKMAN- QU

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

Age	P25	P50	P75
Men <30	0.39	0.43	0.48
Men 31-40	0.42	0.46	0.50
Men 41-50	0.46	0.50	0.57
Men >50	0.46	0.52	0.62
Women <30	0.39	0.40	0.43
Women 31-40	0.42	0.45	0.49
Women 41-50	0.44	0.48	0.53
Women >50	0.50	0.54	0.59

B left

Age	P25	P50	P75
Men <30	0.39	0.43	0.48
Men 31-40	0.42	0.46	0.50
Men 41-50	0.46	0.50	0.57
Men >50	0.46	0.52	0.62
Women <30	0.39	0.40	0.43
Women 31-40	0.42	0.45	0.49
Women 41-50	0.44	0.48	0.53
Women >50	0.50	0.54	0.59

	Right common carotid artery							
	Male				Female			
Age, y/percentile	**≤30**	**31-40**	**41-50**	**>50**	**≤30**	**31-40**	**41-50**	**>50**
25th	0.39	0.42	0.46	0.46	0.39	0.42	0.44	0.50
50th	0.43	0.46	0.50	0.52	0.40	0.45	0.48	0.54
75th	0.48	0.50	0.57	0.62	0.43	0.49	0.53	0.59

	Left common carotid artery							
	Male				Female			
Age, y/percentile	**≤30**	**31-40**	**41-50**	**>50**	**≤30**	**31-40**	**41-50**	**>50**
25th	0.42	0.44	0.50	0.53	0.30	0.44	0.46	0.52
50th	0.44	0.47	0.55	0.61	0.44	0.47	0.51	0.59
75th	0.49	0.57	0.61	0.70	0.47	0.51	0.57	0.64

APPENDIX F STATA DO FILE

Thesis do file March* - Printed on 20/04/2017 2:37:09 PM

```
use "C:\Users\rhassan\Desktop\masters\Spring 2017\Thesis\biobank\Stata\Thesis data March.dta", clear

encode Gender , generate(GenderCode)
label define GenderCode  2 "Male" 1 "Female", modify
label value GenderCode GenderCode
label list GenderCode

generate age=.
replace age = 1 if (Age>=18  & Age<=35)
replace age = 2 if (Age>=35.1  & Age<=55)
replace age = 3 if (Age>=55.1)
label variable age "Age coded"
label define age  1 "18 - 35" 2 "35.1- 55" 3 ">55", modify
label value age age
label list age
tab age

tab LtCIMT
tab RtCIMT
replace RtCIMT=LtCIMT if RtCIMT==0
replace LtCIMT=RtCIMT if LtCIMT==0
gen AverageCIMT= (LtCIMT+ RtCIMT)/2
sum AverageCIMT
histogram AverageCIMT

        gen CataverageCIMT=.
        replace CataverageCIMT = 1 if ( GenderCode==2 & Age<30  & AverageCIMT>=0.485)
        replace CataverageCIMT = 1 if ( GenderCode==2 & Age>=31 & Age <=40 & AverageCIMT>=0.535)
        replace CataverageCIMT = 1 if ( GenderCode==2 & Age>=41 & Age <=50 & AverageCIMT>=0.59)
        replace CataverageCIMT = 1 if ( GenderCode==2 & Age>50 & AverageCIMT>=0.66)
        replace CataverageCIMT = 1 if ( GenderCode==1 & Age<30  & AverageCIMT>=0.45)
        replace CataverageCIMT = 1 if ( GenderCode==1 & Age>=31 & Age <=40 & AverageCIMT>=0.50)
        replace CataverageCIMT = 1 if ( GenderCode==1 & Age>=41 & Age <=50 & AverageCIMT>=0.55)
        replace CataverageCIMT = 1 if ( GenderCode==1 & Age>50 & AverageCIMT>=0.615)
        replace CataverageCIMT = 2 if ( RtCIMT ==0 & LtCIMT ==0)
        replace CataverageCIMT = 0 if (CataverageCIMT ==.)
        label define CataverageCIMT   1 "above 75th percentile" 0 "below 75th percentile" 2 "no CIMT data", modify
        label value CataverageCIMT CataverageCIMT
        tab CataverageCIMT

        gen CatLtCIMT=.
        replace CatLtCIMT = 1 if ( GenderCode==2 & Age<30  & LtCIMT>=0.49)
        replace CatLtCIMT = 1 if ( GenderCode==2 & Age>=31 & Age <=40 & LtCIMT>=0.57)
        replace CatLtCIMT = 1 if ( GenderCode==2 & Age>=41 & Age <=50 & LtCIMT>=0.61)
        replace CatLtCIMT = 1 if ( GenderCode==2 & Age>50 & LtCIMT>=0.70)
        replace CatLtCIMT = 1 if ( GenderCode==1 & Age<30  & LtCIMT>=0.47)
        replace CatLtCIMT = 1 if ( GenderCode==1 & Age>=31 & Age <=40 & LtCIMT>=0.51)
        replace CatLtCIMT = 1 if ( GenderCode==1 & Age>=41 & Age <=50 & LtCIMT>=0.57)
        replace CatLtCIMT = 1 if ( GenderCode==1 & Age>50 & LtCIMT>=0.64)
        replace CatLtCIMT = 2 if ( LtCIMT ==0)
        replace CatLtCIMT = 0 if (CatLtCIMT ==.)
        label define CatLtCIMT   1 "above 75th percentile" 0 "below 75th percentile" 2 "no CIMT data", modify
        label value CatLtCIMT CatLtCIMT
        tab CatLtCIMT

        gen CatRtCIMT=.
        replace CatRtCIMT = 1 if ( GenderCode==2 & Age<30  & RtCIMT>=0.48)
        replace CatRtCIMT = 1 if ( GenderCode==2 & Age>=31 & Age <=40 & RtCIMT>=0.50)
        replace CatRtCIMT = 1 if ( GenderCode==2 & Age>=41 & Age <=50 & RtCIMT>=0.57)
        replace CatRtCIMT = 1 if ( GenderCode==2 & Age>50 & RtCIMT>=0.62)
        replace CatRtCIMT = 1 if ( GenderCode==1 & Age<30  & RtCIMT>=0.43)
        replace CatRtCIMT = 1 if ( GenderCode==1 & Age>=31 & Age <=40 & RtCIMT>=0.49)
        replace CatRtCIMT = 1 if ( GenderCode==1 & Age>=41 & Age <=50 & RtCIMT>=0.53)
        replace CatRtCIMT = 1 if ( GenderCode==1 & Age>50 & RtCIMT>=0.59)
        replace CatRtCIMT = 2 if ( RtCIMT ==0)
```

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```
 66          replace CatRtCIMT = 0 if (CatRtCIMT ==.)
 67          label define CatRtCIMT   1 "above 75th percentile" 0 "below 75th percentile"
      2 "no CIMT data", modify
 68          label value CatRtCIMT CatRtCIMT
 69          tab CatRtCIMT
 70
 71          gen CatCIMT=.
 72          replace CatCIMT = 1 if ( CatLtCIMT==1 & CatRtCIMT==1)
 73          replace CatCIMT = 0 if ( CatLtCIMT==0 & CatRtCIMT==0)
 74          replace CatCIMT = 3 if ( CatLtCIMT==1 & CatRtCIMT==0)
 75          replace CatCIMT = 3 if ( CatLtCIMT==0 & CatRtCIMT==1)
 76          replace CatCIMT = 2 if ( CatCIMT ==.)
 77          label define CatCIMT   1 "above 75th percentile" 0 "below 75th percentile" 3
      "discripancy", modify
 78          label value CatCIMT CatCIMT
 79          tab CatCIMT
 80
 81   label variable levelofeducation "What is the highest level of education that you
      have completed?"
 82   label define levelofeducation  1 "Did not attend or complete primary school" 2
      "Primary school" 3 "Secondary school" 4 "Technical or professional school (but less
      than University)" 5 "University" 6 "Postgraduate degree" 9999 "Prefer not to answer"
       7777"None of the above", modify
 83   label list levelofeducation
 84   label value levelofeducation levelofeducation
 85   sum levelofeducation
 86   tabulate levelofeducation CataverageCIMT
 87
 88   label variable sleep "In a typical week during the last year, approximately how
      many hours of sleep did you get in a 24 hour period?  (Include naps)"
 89   replace sleep =1 if (sleep == 1)
 90   replace sleep =2 if (sleep>=2 & sleep <=3)
 91   replace sleep =3 if (sleep ==4)
 92   replace sleep =5 if (sleep ==9999)
 93   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
 94   label value sleep sleep
 95   tab sleep
 96
 97
 98   gen educationtrend=.
 99   replace educationtrend = 1 if ( levelofeducation >=1 & levelofeducation<=2)
100   replace  educationtrend = 2 if ( levelofeducation >=3 & levelofeducation <=4)
101   replace  educationtrend = 3 if ( levelofeducation >=5 & levelofeducation <=6)
102   replace  educationtrend = 4 if ( levelofeducation >7000)
103   label define educationtrend  1 "Primary or less" 2 "Technical or Secondary" 3
      "University or more" 4 "NOA or PNA", modify
104   label list educationtrend
105   label value educationtrend educationtrend
106   tab educationtrend
107
108
109   label variable employment "During the last 12 months, what has been your employment
      status??"
110   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
111   label list employment
112   label value employment employment
113   tab employment
114
115   gen employmenttrend=.
116   replace employmenttrend = 1 if ( employment >=1 & employment<=3)
117   replace  employmenttrend = 2 if ( employment >=5 & employment <=6)
118   replace  employmenttrend = 3 if ( employment ==4)
119   replace  employmenttrend = 4 if ( employment ==7)
120   replace  employmenttrend = 5 if ( employment >7000)
121   label define employmenttrend  1 "Employed or business owner" 2 "Housewife or
      Unemployed" 3 "Retired" 4 "Student or Trainee" 5 "NOA or PNA" , modify
122   label list employmenttrend
123   label value employmenttrend employmenttrend
124   tab employmenttrend
```

```
125
126
127   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)"
128   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 80,000 per month" 9999 "Prefer not to answer" 8888 "do not know"
      , modify
129   label list income
130   label value income income
131   tab income
132
133   gen incometrend=.
134   replace incometrend = 1 if ( income ==1)
135   replace  incometrend = 2 if ( income >=2 & income <=3)
136   replace  incometrend = 3 if ( income >=4 & income <=5)
137   replace  incometrend = 4 if ( income >7000)
138   label define incometrend  1 "Less than 10,000 per month" 2 "Between 10,000 and
      49,999 per month" 3 "More than 50,000 per month" 4 "DNK or PNA" , modify
139   label list incometrend
140   label value incometrend incometrend
141   tab incometrend
142
143   label variable homeownership "Can you tell us about the ownership status of your
      home?"
144   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"
145   tab homeownership
146   label list homeownership
147   label value homeownership homeownership
148
149   label variable timeyouhavespentsitting  "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)"
150   recode timeyouhavespentsitting 1/4=1 5/12=2 13/25=3
151   label define timeyouhavespentsitting 1 "Short,sitting <5 hours/day" 2
      "Moderate,sitting 5-12 hours per day" 3 "Long,>12 hours/day" , modify
152   tab timeyouhavespentsitting
153   rename timeyouhavespentsitting sitting
154   label define sitting 1 "Short,sitting <5 hours/day" 2 "Moderate,sitting 5-12 hours
      per day" 3 "Long,>12 hours/day" 0 "missing data" , modify
155   label value sitting sitting
156
157   recode lowMETS 1/7000=1 0=0
158   label define lowMETS 1 "lowMETS", modify
159   label value lowMETS lowMETS
160   recode modMETS 1/2000=1 0=0
161   label define modMETS 1 "modMETS", modify
162   label value modMETS modMETS
163   recode vigMETS 1/5500=1 0=0
164   label define vigMETS 1 "vigMETS", modify
165   label value vigMETS vigMETS
166
167   gen Noactivity=.
168   replace Noactivity =1 if ( lowMETS ==0 & modMETS ==0 & vigMETS ==0)
169   replace  Noactivity =0 if (Noactivity ==.)
170   label define Noactivity 1 "No activity" 0 "activity" , modify
171   label value Noactivity Noactivity
172
173   gen PA=.
174   label variable PA "metabolic equivalents for Physcical Activity"
175   replace PA =2 if ( lowMETS ==1)
176   replace PA =3 if ( modMETS ==1)
177   replace PA =4 if ( vigMETS ==1)
178   replace PA =1 if ( Noactivity ==1)
179   label define PA 2 "lowMETS " 3 "modMETS" 4 "vigMETS" 1 "Noactivity" , modify
180   label value PA PA
181
182   recode housemembers 0=0 1/5=1 6/10=2 10/100=3
183   label define housemembers  0 "alone" 1 "1-5 house members" 2 "6-10 house members" 3
```

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       ">10 house members" 9999 "PNA", modify
  184  label value housemembers housemembers
  185  tab housemembers
  186
  187  label define workingnightshifts  1 "No, never worked at night" 2 "Yes, less than 2
       nights per month" 3 "Yes, 3 nights per month or more" 9999 "PNA", modify
  188  label value workingnightshifts workingnightshifts
  189  tab workingnightshifts
  190
  191  recode smoking 1=1 2=4 3 5=3 4=2
  192  label define smoking  1 "Never smoker" 3 "Occasional smoker" 2 "Stopped smoking" 4
       "Current smoker"  9999 "PNA", modify
  193  label value smoking smoking
  194  tab smoking
  195
  196  label define Waterpipe  1 "yes" 0 "No"  9999 "PNA", modify
  197  label value Waterpipe Waterpipe
  198  tab Waterpipe
  199
  200  label variable passivesmoker "Does anyone in your household smoke cigarettes,
       cigars or pipes? "
  201  label define passivesmoker  1 "Yes, 1 household member smokes" 2 "Yes, 2 or more
       household members smoke" 0 "No" 9999 "Prefer not to answer"
  202  label value passivesmoker passivesmoker
  203  label list passivesmoker
  204  tab passivesmoker
  205
  206
  207  label variable HODM "History of Diabetes"
  208  label define HODM  1 "yes" 0 "No"  9999 "PNA", modify
  209  label value HODM HODM
  210  tab HODM
  211
  212  label variable HOC "History of hypercholestemia"
  213  label define HOC  1 "yes" 0 "No"  9999 "PNA" 8888 "DNR", modify
  214  label value HOC HOC
  215  tab HOC
  216
  217  label variable HOBP "History of Hypertension"
  218  label define HOBP  1 "yes" 0 "No"  9999 "PNA" 8888 "DNR", modify
  219  label value HOBP HOBP
  220  tab HOBP
  221
  222  label variable HOHA "History of MI"
  223  label define HOHA  1 "yes" 0 "No"  9999 "PNA" 8888 "DNR", modify
  224  label value HOHA HOHA
  225  tab HOHA
  226
  227  label variable HOS "History of Stroke"
  228  label define HOS  1 "yes" 0 "No"  9999 "PNA" 8888 "DNR", modify
  229  label value HOS HOS
  230  tab HOS
  231
  232  replace PHBP =0 if ( PHBP ==7777)
  233  replace PHBP =0 if ( PHBP ==8888)
  234  replace PHBP =0 if ( PHBP ==9999)
  235  replace PMI =0 if ( PMI ==7777)
  236  replace PMI =0 if ( PMI ==8888)
  237  replace PMI =0 if ( PMI ==9999)
  238  replace PS =0 if ( PS ==7777)
  239  replace PS =0 if ( PS ==9999)
  240  replace PD =0 if ( PD ==9999)
  241  replace PD =0 if ( PD ==7777)
  242  replace PO =0 if ( PO ==7777)
  243  replace PO =0 if ( PO ==9999)
  244  replace MHBP =0 if ( MHBP ==7777)
  245  replace MMI =0 if ( MMI ==7777)
  246  replace MS =0 if ( MS ==7777)
  247  replace MD =0 if ( MD ==7777)
  248  replace MO =0 if ( MO ==7777)
  249
  250
```

```
251
252   gen FHBP=.
253   replace FHBP= 1 if (PHBP==1 & MHBP==.)
254   replace FHBP= 1 if (PHBP==1 & MHBP==0)
255   replace FHBP= 2 if (PHBP==. & MHBP==1)
256   replace FHBP= 2 if (PHBP==0 & MHBP==1)
257   replace FHBP= 3 if (PHBP==1 & MHBP==1)
258   label variable FHBP " family hitory of hypertension"
259   label define FHBP 1 "Paternal HBP" 2 "maternal HBP" 3 "Both"
260   label value FHBP FHBP
261   tab FHBP
262   tab FHBP CataverageCIMT if CataverageCIMT <=1, chi2 col
263
264   gen FHMI=.
265   replace FHMI= 1 if (PMI==1 & MMI==.)
266   replace FHMI= 1 if (PMI==1 & MMI==0)
267   replace FHMI= 2 if (PMI==. & MMI==1)
268   replace FHMI= 2 if (PMI==0 & MMI==1)
269   replace FHMI= 3 if (PMI==1 & MMI==1)
270   label variable FHMI " family hitory of MI"
271   label define FHMI 1 "Paternal MI" 2 "maternal MI" 3 "Both"
272   label value FHMI FHMI
273   tab FHMI
274
275   gen FS=.
276   replace FS= 1 if (PS==1 & MS ==.)
277   replace FS= 1 if (PS==1 & MS==0)
278   replace FS= 2 if (PS==. & MS==1)
279   replace FS= 2 if (PS==0 & MS==1)
280   replace FS= 3 if (PS==1 & MS==1)
281   label variable FS " family hitory of Stroke"
282   label define FS 1 "Paternal History of stroke" 2 "maternal History of stroke" 3
      "Both", modify
283   label value FS FS
284   tab FS
285
286   gen FD=.
287   replace FD= 1 if (PD==1 & MD ==.)
288   replace FD= 1 if (PD==1 & MD==0)
289   replace FD= 2 if (PD==. & MD==1)
290   replace FD= 2 if (PD==0 & MD==1)
291   replace FD= 3 if (PD==1 & MD==1)
292   label variable FD " family hitory of diabetes"
293   label define FD 1 "Paternal History of Diabetes" 2" maternal History of diabetes" 3
      "Both", modify
294   label value FD FD
295   tab FD
296
297   gen FO=.
298   replace FO= 1 if (PO==1 & MO ==.)
299   replace FO= 1 if (PO==1 & MO==0)
300   replace FO= 2 if (PO==. & MO==1)
301   replace FO= 2 if (PO==0 & MO==1)
302   replace FO= 3 if (PO==1 & MO==1)
303   label variable FO " family hitory of Obesity"
304   label define FO 1 "Paternal History of Obesity" 2" maternal History of Obesity" 3
      "Both", modify
305   label value FO FO
306   tab FO
307
308   tab FHBP CataverageCIMT if CataverageCIMT <=1, chi2 col
309   tab FHMI CataverageCIMT if CataverageCIMT <=1, chi2 col
310   tab FS CataverageCIMT if CataverageCIMT <=1, chi2 col
311   tab FD CataverageCIMT if CataverageCIMT <=1, chi2 col
312   tab FO CataverageCIMT if CataverageCIMT <=1, chi2 col
313
314   label variable vegandiet "no meat, fish, eggs, dairy products"
315   label variable Vegetariandiet "allows dairy products"
316
317   replace lowcaloriediet =0 if ( lowcaloriediet ==9999)
318   replace lowsaltdiet =0 if ( lowsaltdiet ==9999)
319   replace lowfatdiet =0 if ( lowfatdiet ==9999)
```

```
320   replace vegandiet =0 if ( vegandiet ==9999)
321   replace Vegetariandiet =0 if ( Vegetariandiet ==9999)
322   replace noredmeateater =0 if ( noredmeateater ==9999)
323   replace anotherspecialdiet =0 if ( anotherspecialdiet ==9999)
324   replace Nospecialdiet =0 if ( Nospecialdiet ==9999)
325
326   gen specialdiet=.
327   replace specialdiet= 1 if (lowcaloriediet==1)
328   replace specialdiet= 2 if (lowsaltdiet==1)
329   replace specialdiet= 3 if (lowfatdiet==1)
330   replace specialdiet= 4 if (vegandiet==1)
331   replace specialdiet= 5 if (Vegetariandiet==1)
332   replace specialdiet= 6 if (noredmeateater==1)
333   replace specialdiet= 7 if (anotherspecialdiet==1)
334   replace specialdiet= 8 if (Nospecialdiet==1)
335   label variable specialdiet "Any special diet"
336   label define specialdiet 1 "lowcaloriediet" 2" lowsaltdiet" 3 "lowfatdiet" 4
      "vegandiet" 5 "Vegetariandiet" 6 "noredmeateater" 7 "anotherspecialdiet" 8
      "Nospecialdiet" , modify
337   label value specialdiet specialdiet
338   tab specialdiet
339
340
341   label variable fastfood "foods from home delivery, take-away, or fast food
      restaurants?"
342   replace fastfood =1 if ( fastfood ==1)
343   replace fastfood =2 if ( fastfood >=2 & fastfood <=3)
344   replace fastfood =3 if ( fastfood >=4 & fastfood <=5)
345   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
346   label value fastfood fastfood
347   tab fastfood
348
349   label variable Dairydiet "Dairy Diet"
350   replace Dairydiet =1 if ( Dairydiet  >=0 & Dairydiet <=5)
351   replace Dairydiet =2 if ( Dairydiet  >=6 & Dairydiet <=20)
352   replace Dairydiet =3 if ( Dairydiet  >=21)
353   replace Dairydiet =9999 if ( Dairydiet >=999)
354   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
355   label value Dairydiet Dairydiet
356   tab Dairydiet
357
358   label variable fatdiet "Fat in iet as evident from type of milk you consumed most
      often during the last year, Whole, Reduced or Fat-free milk"
359   label define fatdiet 1 "Whole fat diet" 2 "Reduced fat diet" 3 "Fat-free diet" 4
      "balanced fat diet" 5 "DNK" 9999 "Prefer not to answer", modify
360   label value fatdiet fatdiet
361   tab fatdiet
362
363
364   label variable SBPCat "Average SBP of 3 readings?"
365   label variable DBPCat "Average DBP of 3 readings?"
366   recode SBPCat 77/119.99999=1 120/139.99999=2 140/159.999999=3 160/250=4
367   label define SBPCat 1 "Normal <120 " 2 "Prehypertension <140" 3 "Stage 1
      hypertension <160" 4 "Stage 2 hypertension >=160"
368   label value SBPCat SBPCat
369   tab SBPCat
370
371   recode DBPCat 30/79.9999=1 80/89.99999=2 90/99.9999=3 100/250=4
372   label define DBPCat 1 "Normal <80 " 2 "Prehypertension <90" 3 "Stage 1 hypertension
      <100" 4 "Stage 2 hypertension >=100"
373   label value DBPCat DBPCat
374   tab DBPCat
375
376   gen CatAveragepulse =.
377   replace CatAveragepulse = 0 if (Age<26  & Averagepulse <=65)
378   replace CatAveragepulse = 0 if (Age>=26 & Age <=35 & Averagepulse<=65)
379   replace CatAveragepulse = 0 if (Age>35 & Age <=45 & Averagepulse<=66)
380   replace CatAveragepulse = 0 if (Age>45 & Age <=55 & Averagepulse<=67)
381   replace CatAveragepulse = 0 if (Age>55 & Age <=65  & Averagepulse<=67)
382   replace CatAveragepulse = 0 if (Age>65 & Averagepulse<=65)
```

```
383   replace CatAveragepulse = 1 if (Age<26  & Averagepulse >65 & Averagepulse <=73)
384   replace CatAveragepulse = 1 if (Age>=26 & Age <=35 & Averagepulse >65 & Averagepulse
       <=74)
385   replace CatAveragepulse = 1 if (Age>35 & Age <=45 & Averagepulse >66 & Averagepulse
      <=75)
386   replace CatAveragepulse = 1 if (Age>45 & Age <=55 & Averagepulse >67 & Averagepulse
      <=76)
387   replace CatAveragepulse = 1 if (Age>55 & Age <=65  & Averagepulse >67 & Averagepulse
       <=75)
388   replace CatAveragepulse = 1 if (Age>65 & Averagepulse >65 & Averagepulse <=73)
389   replace CatAveragepulse = 2 if (Age<26  &  Averagepulse >73)
390   replace CatAveragepulse = 2 if (Age>=26 & Age <=35 & Averagepulse >74)
391   replace CatAveragepulse = 2 if (Age>35 & Age <=45 & Averagepulse >75)
392   replace CatAveragepulse = 2 if (Age>45 & Age <=55 & Averagepulse >76)
393   replace CatAveragepulse = 2 if (Age>55 & Age <=65  & Averagepulse >75)
394   replace CatAveragepulse = 2 if (Age> 65 &  Averagepulse >73)
395   label define CatAveragepulse 0 "Excellent pulse for age & rate" 1 "Average pulse
      for age & rate" 2 "Poor pulse for age & rate", modify
396   label value  CatAveragepulse CatAveragepulse
397   tab CatAveragepulse
398
399   gen BMICat=.
400   replace BMICat=1 if (BMI<18.5)
401   replace BMICat=2 if (BMI>=18.5 & BMI<25)
402   replace BMICat=3 if (BMI>=25 & BMI<30)
403   replace BMICat=4 if (BMI>=30)
404   label define BMICat 1 "Underweight <18.5" 2 "Normal >=18.5 - <25" 3 "Overweight
      >=25 - <30" 4 "Obese >=30"
405   label value BMICat BMICat
406   tab BMICat
407
408   gen CRPcode=.
409   replace  CRPcode= 1 if (CRP <=3)
410   replace CRPcode = 2 if (CRP >4)
411   label define CRPcode  1 "low to average risk <=3" 2 "high risk >4" , modify
412   label value CRPcode CRPcode
413   tab CRPcode
414
415   gen Cholesterolcode=.
416   replace  Cholesterolcode= 0 if (Cholesterol <=5.29999)
417   replace  Cholesterolcode= 1 if (Cholesterol >=5.3) & (Cholesterol <=6.299999)
418   replace Cholesterolcode = 2 if (Cholesterol >=6.3)
419   label define Cholesterolcode  0 "optimal <5.3" 1 "intermediate"  2 "high >6.3",
      modify
420   label value Cholesterolcode Cholesterolcode
421   tab Cholesterolcode
422
423   gen Fibrinogencode=.
424   replace  Fibrinogencode= 0 if (Fibrinogen <=234.9999)
425   replace  Fibrinogencode= 1 if (Fibrinogen >=235) & (Fibrinogen <=349.99999)
426   replace Fibrinogencode = 2 if (Fibrinogen >=350)
427   label define Fibrinogencode  0 "optimal <235" 1 "intermediate risk"  2 "high risk
      >350"
428   label value Fibrinogencode Fibrinogencode
429   tab Fibrinogencode
430
431   gen Glucosecode=.
432   replace  Glucosecode= 0 if (FBS <=4.8284)
433   replace  Glucosecode= 1 if (FBS >=4.8285) & (FBS <=6.1049)
434   replace Glucosecode = 2 if (FBS >=6.105)
435   label define Glucosecode  0 "optimal <4.8" 1 "intermediate risk"  2 "high risk >6.1"
      , modify
436   label value Glucosecode Glucosecode
437   tab Glucosecode
438
439   gen HBA1Ccode=.
440   replace  HBA1Ccode= 0 if (HBA1C <=6.49999)
441   replace  HBA1Ccode= 1 if (HBA1C >=6.5) & (HBA1C <=9.59999)
442   replace HBA1Ccode = 2 if (HBA1C >=9.6)
443   label define HBA1Ccode  0 "optimal <6.5" 1 "intermediate risk"  2 "high risk >9.6"
444   label value HBA1Ccode HBA1Ccode
445   tab HBA1Ccode
```

```
446
447   gen HDLcode=.
448   replace  HDLcode= 0 if (HDL >=1.6835)
449   replace  HDLcode= 1 if (HDL <=1.6834) & (HDL >=1.1655)
450   replace HDLcode = 2 if (HDL <=1.1654)
451   label define HDLcode  0 "optimal > 1.6" 1 "intermediate risk"  2 "high risk <1.1"
452   label value HDLcode HDLcode
453   tab HDLcode
454
455   gen LDLcode=.
456   replace  LDLcode= 0 if (LDL <=0.777)
457   replace LDLcode = 1 if (LDL >=0.778)
458   label define LDLcode  0 "optimal/intermediate risk <0.77"  1 "high risk >0.77"
459   label value LDLcode LDLcode
460   tab LDLcode
461
462   gen TGcode=.
463   replace  TGcode= 0 if (TG <=1.129)
464   replace  TGcode= 1 if (TG >=1.13) & (TG <=1.6899)
465   replace TGcode = 2 if (TG >=1.6999)
466   label define TGcode   0 "optimal <1.13" 1 "intermediate risk"  2 "high risk >1.69"
467   label value TGcode TGcode
468   tab TGcode
469
470   replace comorbidties =1 if ( comorbidties >0 & comorbidties <3)
471   replace comorbidties =2 if ( comorbidties >=3)
472   label define comorbidties   0 "no comorbidties" 1 "1-2 comorbidties" 2 ">3
      comorbidties"
473   label value comorbidties comorbidties
474   label list comorbidties
475
476   replace Fcomorbidties =1 if ( Fcomorbidties >0 & Fcomorbidties <5)
477   replace Fcomorbidties =2 if ( Fcomorbidties >=5)
478   label define Fcomorbidties   0 "no Fcomorbidties" 1 "1-4 Fcomorbidties" 2 ">=5
      Fcomorbidties"
479   label value Fcomorbidties Fcomorbidties
480   label list Fcomorbidties
481
482   keep if CataveragecIMT!=2
483
484   **Table 1
485   by age, sort : summarize AverageCIMT if GenderCode==1, detail
486   by age, sort : summarize AverageCIMT if GenderCode==2, detail
487
488   **Table 2
489   tab age CataveragecIMT, chi2 row
490   tab GenderCode CataveragecIMT, chi2 row
491
492   **Table 3
493   tab incometrend CataveragecIMT, chi2 row
494   tabodds CataveragecIMT incometrend if incometrend<4
495
496   tab homeownership CataveragecIMT if homeownership <=4 , chi2 row
497
498   tabodds CataveragecIMT housemembers
499   tab housemembers, nol
500   tabodds CataveragecIMT housemembers if housemembers<3
501
502   tab educationtrend
503   tab educationtrend, nol
504   tab educationtrend CataveragecIMT if educationtrend <4 , chi2 row
505   tabodds CataveragecIMT educationtrend if educationtrend <4
506
507   tab employmenttrend
508   tab employmenttrend CataveragecIMT if employmenttrend <=4 , chi2 row
509
510
511   **Table 4
512   tab PA
513   tabodds CataveragecIMT PA
514   tab PA CataveragecIMT, chi2 row
515
```

```
516   tab sitting, nol
517   tab sitting CataverageCIMT if sitting > 0, chi2 row
518   tabodds CataverageCIMT sitting if sitting > 0
519
520   tabodds CataverageCIMT lowMETS
521   tabodds CataverageCIMT modMETS
522   tabodds CataverageCIMT vigMETS
523
524   tab sleep
525   tab  sleep CataverageCIMT if sleep <5, chi2 row
526   tabodds CataverageCIMT sleep if sleep <5
527
528   **Table 5
529   tab smoking
530   tab smoking, nol
531   tabodds CataverageCIMT smoking if smoking <5
532   tab smoking CataverageCIMT  if smoking <5, chi2 row
533
534   tab Waterpipe
535   tab Waterpipe , nol
536   tabodds CataverageCIMT Waterpipe if Waterpipe <5
537   tab Waterpipe CataverageCIMT  if Waterpipe <5, chi2 row
538
539   tab passivesmoker
540   tab passivesmoker , nol
541   tab passivesmoker CataverageCIMT, chi2 row
542   tabodds CataverageCIMT passivesmoker
543
544   **Table 6
545   tab HODM
546   tab HOC
547   tab HOBP
548   tab HOHA
549   tab HOS
550   tab HODM CataverageCIMT if HODM <5, chi2 col
551   tab HOC CataverageCIMT if HOC <5, chi2 col
552   tab HOBP CataverageCIMT if HOBP <5, chi2 col
553   tab HOHA CataverageCIMT if HOHA <5, chi2 col
554   tab HOS CataverageCIMT if HOS <5, chi2 col
555
556   tab FHBP CataverageCIMT, chi2 row
557   tab FHMI CataverageCIMT, chi2 row
558   tab FS CataverageCIMT, chi2 row
559   tab FD CataverageCIMT, chi2 row
560   tab FO CataverageCIMT, chi2 row
561
562   **Table 7:
563   tab specialdiet
564   tab specialdiet CataverageCIMT, chi2 row
565
566   tab fastfood, nol
567   tabodds CataverageCIMT fastfood if fastfood<=3
568   tab fastfood CataverageCIMT if fastfood <=3, chi2 row
569
570   tab Dairydiet
571   tabodds CataverageCIMT Dairydiet
572   tab  Dairydiet CataverageCIMT, chi2 row
573
574   tab fatdiet
575   tab fatdiet, nol
576   tab  fatdiet CataverageCIMT, chi2 row
577   tab  fatdiet CataverageCIMT if fatdiet <=4, chi2 row
578   recode fatdiet 4 2 = 2
579   label define fatdiet 1 "Whole fat diet" 2 "Reduced/balanced fat diet" 3 "Fat-free
      diet" 5 "DNK" 9999 "Prefer not to answer", modify
580   label value fatdiet fatdiet
581   tab fatdiet
582   label list fatdiet
583   tab  fatdiet CataverageCIMT if fatdiet <=4, chi2 row
584   tabodds CataverageCIMT fatdiet if fatdiet <=4
585
586   **Table 8
```

```
587   sum Height, detail
588   sum Height if CataverageCIMT==0 , detail
589   sum Height if CataverageCIMT==1 , detail
590
591   sum weight if CataverageCIMT==0 , detail
592   sum weight if CataverageCIMT==1 , detail
593
594   sum BMI if CataverageCIMT==0 , detail
595   sum BMI if CataverageCIMT==1 , detail
596
597   sum Waist if CataverageCIMT==0 , detail
598   sum Waist if CataverageCIMT==1 , detail
599
600   sum Waisthipratio if CataverageCIMT==0 , detail
601   sum Waisthipratio if CataverageCIMT==1 , detail
602
603   sum Fatpercent if CataverageCIMT==0 , detail
604   sum Fatpercent if CataverageCIMT==1 , detail
605
606   tab BMICat
607   tab  BMICat CataverageCIMT, chi2 row
608   tabodds  CataverageCIMT BMICat
609
610   tabodds  CataverageCIMT SBPCat
611   tab  SBPCat CataverageCIMT, chi2 row
612
613   tabodds  CataverageCIMT DBPCat
614   tab  DBPCat CataverageCIMT, exact row
615
616   tab CatAveragepulse
617   tab CataverageCIMT CatAveragepulse
618   tabodds  CataverageCIMT CatAveragepulse
619
620   **table 9
621   sum APTT if CataverageCIMT==0 , detail
622   sum APTT if CataverageCIMT==1 , detail
623   sum CRP if CataverageCIMT==0 , detail
624   sum CRP if CataverageCIMT==1 , detail
625   sum Cholesterol if CataverageCIMT==0 , detail
626   sum Cholesterol if CataverageCIMT==1 , detail
627   sum Fibrinogen if CataverageCIMT==0 , detail
628   sum Fibrinogen if CataverageCIMT==1 , detail
629   sum FBS if CataverageCIMT==0 , detail
630   sum FBS if CataverageCIMT==1 , detail
631   sum HBA1C if CataverageCIMT==0 , detail
632   sum HBA1C if CataverageCIMT==1 , detail
633   sum HDL if CataverageCIMT==0 , detail
634   sum HDL if CataverageCIMT==1 , detail
635   sum LDL if CataverageCIMT==0 , detail
636   sum LDL if CataverageCIMT==1, detail
637   sum TG if CataverageCIMT==0 , detail
638   sum TG if CataverageCIMT==1 , detail
639   sum Homocysteine if CataverageCIMT==0 , detail
640   sum Homocysteine if CataverageCIMT==1 , detail
641
642
643   tab  CRPcode CataverageCIMT, exact row
644
645   tab Cholesterolcode
646   tabodds CataverageCIMT Cholesterolcode
647   tab  Cholesterolcode CataverageCIMT, chi2 row
648
649   tab Fibrinogencode
650   tab  Fibrinogencode CataverageCIMT, exact row
651
652   tab Glucosecode
653   tabodds CataverageCIMT Glucosecode
654   tab  Glucosecode CataverageCIMT, chi2 row
655
656   tab HBA1Ccode
657   tabodds CataverageCIMT HBA1Ccode
658   label list HBA1Ccode
```

```
659   tab  HBA1Ccode CataverageCIMT, chi2 row
660
661   tab HDLcode
662   tab  HDLcode CataverageCIMT, chi2 row
663
664   tab LDLcode
665   tab  LDLcode CataverageCIMT, exact row
666
667   tab TGcode
668   tab  TGcode CataverageCIMT, chi2 row
669   tabodds CataverageCIMT TGcode
670   label list TGcode
671
672   **appendix:
673   tab age homeownership if homeownership< 7777, chi2 row
674   tab age homeownership if homeownership< 7777, chi2 col
675   tab age sitting if sitting > 0, chi2 col
676   tab PA sitting if sitting > 0, chi2 col
677   tab PA sitting if sitting > 0, chi2 row
678   tab age Waterpipe, chi2 col
679   by GenderCode , sort : summarize Waisthipratio
680
681
682   **coding to missing
683   replace educationtrend = .a if educationtrend ==4
684   tab educationtrend
685   codebook educationtrend
686   replace employmenttrend = .a if employmenttrend ==5
687   replace incometrend = .a if incometrend ==4
688   replace fatdiet = .a if fatdiet ==5
689   replace sitting = .a if sitting ==0
690
691
692   mvdecode employment levelofeducation income homeownership fatdiet housemembers
      workingnightshifts smoking Waterpipe passivesmoker HODM HOHA HOBP HOS HOC, mv(9999=
      .a  8888= .b 7777= .c)
693
694   **Table 10
695   tab age
696   tab age, nol
697   logistic  CataverageCIMT i.age
698   test 2.age 3.age
699   **0.0000
700
701   tab GenderCode
702   tab GenderCode, nol
703   logistic  CataverageCIMT i.GenderCode
704   **0.0000
705
706   tab incometrend
707   tab incometrend, nol
708   logistic  CataverageCIMT i.incometrend if incometrend<4
709   **0.02
710
711   tab homeownership
712   tab homeownership, nol
713   logistic  CataverageCIMT i.homeownership if homeownership <=4
714   test 2.homeownership 3.homeownership 4.homeownership
715   **0.04
716
717   tab educationtrend
718   tab educationtrend, nol
719   logistic  CataverageCIMT i.educationtrend if educationtrend <4
720   logistic  CataverageCIMT i.educationtrend
721   test 2.educationtrend 3.educationtrend
722   **0.0015
723
724   tab employmenttrend
725   tab employmenttrend, nol
726   logistic  CataverageCIMT i.employmenttrend if employmenttrend <=4
727   test 2.employmenttrend 3.employmenttrend 4.employmenttrend
728   **  0.0015
```

```
729
730   tab PA
731   tab PA, nol
732   logistic  CataverageCIMT i.PA
733   logistic  CataverageCIMT i.PA
734   test 2.PA 3.PA 4.PA
735   ** 0.34
736
737   tab sitting
738   tab sitting, nol
739   logistic  CataverageCIMT i.sitting if sitting>=1
740   logistic  CataverageCIMT ib3.i.sitting
741   test 2.sitting 3.sitting
742   **0.81
743
744   tab sleep
745   tab sleep, nol
746   logistic  CataverageCIMT i.sleep if sleep <4
747   test 2.sleep 3.sleep
748   **0.494
749
750   tab smoking
751   tab smoking, nol
752   logistic  CataverageCIMT i.smoking if smoking <5
753   logistic  CataverageCIMT i.smoking
754   test 2.smoking 3.smoking 4.smoking
755   **0.44
756
757   logistic  CataverageCIMT ib1.i.Waterpipe if Waterpipe <=1
758   logistic  CataverageCIMT i.Waterpipe
759   **<0.001
760
761   tab passivesmoker
762   tab passivesmoker, nol
763   logistic  CataverageCIMT ib1.i.passivesmoker if passivesmoker <=1
764   logistic  CataverageCIMT i.passivesmoker
765   **0.9
766
767
768
769   logistic  CataverageCIMT i.HODM if HODM <=1
770   logistic  CataverageCIMT i.HOC if HOC <=1
771   logistic  CataverageCIMT i.HOBP if HOBP <=1
772   logistic  CataverageCIMT i.HOHA if HOHA <=1
773   logistic  CataverageCIMT i.HOS if HOS <=1
774
775
776   logistic  CataverageCIMT i.FHBP
777   **0.007
778   logistic  CataverageCIMT i.FHMI if FHMI<4
779   test 2.FHMI 3.FHMI
780   **0.39
781   logistic  CataverageCIMT i.FS if FS<4
782   logistic  CataverageCIMT i.FD if FD<4
783   logistic  CataverageCIMT i.FO if FO <4
784
785
786   logistic  CataverageCIMT ib8.i.specialdiet
787   logistic  CataverageCIMT i.fastfood if fastfood <=3
788   logistic  CataverageCIMT i.Dairydiet
789   logistic  CataverageCIMT i.fatdiet if fatdiet<4
790
791   logistic  CataverageCIMT i.SBPCat
792   logistic  CataverageCIMT i.DBPCat
793   logistic  CataverageCIMT i.BMICat
794   logistic  CataverageCIMT i.CatAveragepulse
795
796   logistic  CataverageCIMT ib2.i.CRPcode
797   logistic  CataverageCIMT i.Cholesterolcode
798   logistic  CataverageCIMT ib2.i.Fibrinogencode
799   logistic  CataverageCIMT i.Glucosecode
800   logistic  CataverageCIMT i.HBA1Ccode
```

```
801   logistic  CataverageCIMT i.HDLcode
802   logistic  CataverageCIMT i.TGcode
803
804   logistic  CataverageCIMT Fatpercent
805   logistic CataverageCIMT BMI
806   logistic CataverageCIMT weight
807   logistic  CataverageCIMT Waist
808   logistic  CataverageCIMT CRP
809   logistic  CataverageCIMT FBS
810   logistic  CataverageCIMT Cholesterol
811   logistic  CataverageCIMT Fibrinogen
812   logistic  CataverageCIMT HBA1C
813   logistic  CataverageCIMT TG
814
815
816   xi: stepwise, pe(.1) pr(.2): logistic CataverageCIMT (i.age) (i.GenderCode) (i.
      incometrend)(i.educationtrend) (i.employmenttrend) (i.FO) (i.FHBP) (i.FS) (i.HODM) (
      i.HOC) (i.HOBP) (i.fastfood)(i.SBPCat) (i.DBPCat) (i.CatAveragepulse) (i.BMICat) (
      Fatpercent) (weight) (Waist) (i.Glucosecode) (i.HBA1Ccode) (i.HDLcode) (FBS) (TG) (
      HBA1C) (i.TGcode) (CRP) (Cholesterol) (Fibrinogen) (BMI) (i.sitting) (i.PA) (APTT) (
      i.sleep)
817   xi: stepwise, pr(.2): logistic CataverageCIMT (i.age) (i.GenderCode) (i.incometrend
      )(i.educationtrend) (i.employmenttrend) (i.FO) (i.FHBP) (i.FS) (i.HODM) (i.HOC) (i.
      HOBP) (i.fastfood)(i.SBPCat) (i.DBPCat) (i.CatAveragepulse) (i.BMICat) (Fatpercent)
      (weight) (Waist) (i.Glucosecode) (i.HBA1Ccode) (i.HDLcode) (FBS) (TG) (HBA1C) (i.
      TGcode) (CRP) (Cholesterol) (Fibrinogen) (BMI) (i.sitting) (i.PA) (APTT) (i.sleep)
818   xi: stepwise,forward  pe(.1) pr(.2): logistic CataverageCIMT (i.age) (i.GenderCode)
      (i.incometrend)(i.educationtrend) (i.employmenttrend) (i.FO) (i.FHBP) (i.FS) (i.HODM
      ) (i.HOC) (i.HOBP) (i.fastfood)(i.SBPCat) (i.DBPCat) (i.CatAveragepulse) (i.BMICat)
      (Fatpercent) (weight) (Waist) (i.Glucosecode) (i.HBA1Ccode) (i.HDLcode) (FBS) (TG) (
      HBA1C) (i.TGcode) (CRP) (Cholesterol) (Fibrinogen) (BMI) (i.sitting) (i.PA) (APTT) (
      i.sleep)
819
820
821   **full model ( based on univariate P value <0.2)
822   logistic  CataverageCIMT i.age i.incometrend i.homeownership i.GenderCode i.
      educationtrend i.employmenttrend i.FHBP i.FS i.FO i.HOBP i.HODM i.HOC i.fastfood i.
      SBPCat i.DBPCat i.CatAveragepulse i.BMICat i.Glucosecode i.HBA1Ccode i.HDLcode
      weight BMI CRP Fibrinogen FBS HBA1C TG i.sitting i.PA i.sleep Waist Fatpercent APTT
      Cholesterol i.TGcode
823   estimates store full
824   test 2.fastfood 3.fastfood
825   logistic  CataverageCIMT age incometrend homeownership  GenderCode  educationtrend
      employmenttrend  FHBP  FS  FO  HOBP  HODM  HOC  fastfood  SBPCat  DBPCat
      CatAveragepulse  BMICat  Glucosecode  HBA1Ccode  HDLcode weight BMI CRP Fibrinogen
      FBS HBA1C TG  sitting  PA  sleep Waist Fatpercent APTT Cholesterol  TGcode
826
827   **shorter model ( based on Wald test P value <0.05)
828   gen sample=e(sample)
829   logistic  CataverageCIMT  i.GenderCode i.SBPCat CRP   if sample==1
830   lrtest full .
831   **0.1368
832
833   logit  CataverageCIMT i.age i.incometrend i.homeownership i.GenderCode i.
      educationtrend i.employmenttrend i.FHBP i.FS i.FO i.HOBP i.HODM i.HOC i.fastfood i.
      SBPCat i.DBPCat i.CatAveragepulse i.BMICat i.Glucosecode i.HBA1Ccode i.HDLcode
      weight BMI CRP Fibrinogen FBS HBA1C TG i.sitting i.PA i.sleep Waist Fatpercent APTT
      Cholesterol i.TGcode
834   logit  CataverageCIMT i.GenderCode i.SBPCat CRP
835   logit  CataverageCIMT i.GenderCode i.SBPCat CRP   if sample==1
836   **coffcients have changed >20 % (?confounders)
837   logit  CataverageCIMT i.GenderCode i.SBPCat CRP   i.age  if sample==1
838   logit  CataverageCIMT i.GenderCode i.SBPCat CRP   i.incometrend  if sample==1
839   logit  CataverageCIMT i.GenderCode i.SBPCat CRP   i.homeownership  if sample==1
840   logit  CataverageCIMT i.GenderCode i.SBPCat CRP   i.educationtrend  if sample==1
841   logit  CataverageCIMT i.GenderCode i.SBPCat CRP   i.employmenttrend  if sample==1
842   logit  CataverageCIMT i.GenderCode i.SBPCat CRP   i.FHBP  if sample==1
843   logit  CataverageCIMT i.GenderCode i.SBPCat CRP   i.FS  if sample==1
844   logit  CataverageCIMT i.GenderCode i.SBPCat CRP   i.FO  if sample==1
845   logit  CataverageCIMT i.GenderCode i.SBPCat CRP   i.HOBP  if sample==1
846   logit  CataverageCIMT i.GenderCode i.SBPCat CRP   i.HODM  if sample==1
847   logit  CataverageCIMT i.GenderCode i.SBPCat CRP   i.HOC  if sample==1
```

```
848   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   i.DBPCat  if sample==1
849   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   i.CatAveragepulse  if sample==1
850   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   i.BMICat  if sample==1
851   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   i.Glucosecode  if sample==1
852   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   i.HBA1Ccode  if sample==1

853   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   i.HDLcode  if sample==1
854   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   weight  if sample==1
855   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   BMI  if sample==1
856   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   FBS  if sample==1
857   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   HBA1C  if sample==1
858   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   TG  if sample==1
859   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   i.sitting  if sample==1
860   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   i.PA  if sample==1
861   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   i.sleep  if sample==1
862   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   Waist  if sample==1
863   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   Fatpercent  if sample==1
864   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   APTT  if sample==1
865   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   Cholesterol  if sample==1
866   logit  CataveragecIMT i.GenderCode i.SBPCat CRP   i.TGcode  if sample==1
867
868   **waist confunded gender
869   logit  CataveragecIMT i.GenderCode i.SBPCat CRP Waist if sample==1
870
871   **significant individual covariates excluded in univariate analysis
872    ** add each variable in at a time and now assess significance by it's P value)
873   logistic  CataveragecIMT i.GenderCode i.SBPCat CRP  Waist smoking if sample==1
874   logistic  CataveragecIMT i.GenderCode i.SBPCat CRP  Waist  passivesmoker if sample==
      1
875   logistic  CataveragecIMT i.GenderCode i.SBPCat CRP  Waist Dairydiet if sample==1
876   logistic  CataveragecIMT i.GenderCode i.SBPCat CRP  Waist fatdiet if sample==1
877   logistic  CataveragecIMT i.GenderCode i.SBPCat CRP  Waist LDL if sample==1
878   logistic  CataveragecIMT i.GenderCode i.SBPCat CRP  Waist HDL if sample==1
879   ** HDL P Value 0.01
880   logistic  CataveragecIMT i.GenderCode i.SBPCat CRP Waist HDL
881
882   **main effects model
883   logistic  CataveragecIMT i.GenderCode i.SBPCat CRP Waist HDL
884
885   **interactions:
886   logistic  CataveragecIMT i.GenderCode i.SBPCat CRP Waist HDL
887   estimates store main
888   logistic  CataveragecIMT i.GenderCode##i.SBPCat CRP Waist HDL
889   lrtest main .
890   **0.41
891   logistic  CataveragecIMT i.GenderCode##c.CRP Waist HDL  i.SBPCat
892   lrtest main .
893   **0.73
894   logistic  CataveragecIMT i.GenderCode##c.Waist HDL i.SBPCat CRP
895   lrtest main .
896   **0.32
897   logistic  CataveragecIMT i.GenderCode##c.HDL i.SBPCat CRP Waist
898   lrtest main .
899   **0.39
900   logistic  CataveragecIMT i.GenderCode i.SBPCat##c.CRP Waist HDL
901   lrtest main .
902   **0.09
903   logistic  CataveragecIMT i.GenderCode i.SBPCat##c.Waist HDL CRP
904   lrtest main .
905   **0.97
906   logistic  CataveragecIMT i.GenderCode i.SBPCat##c.HDL CRP Waist
907   lrtest main .
908   **0.002**
909   logistic  CataveragecIMT i.GenderCode i.SBPCat c.CRP##c.Waist HDL
910   lrtest main .
911   **0.49
912   logistic  CataveragecIMT i.GenderCode i.SBPCat c.CRP##c.HDL Waist
913   lrtest main .
914   **0..87
915   logistic  CataveragecIMT i.GenderCode i.SBPCat CRP c.Waist##c.HDL
916   lrtest main .
917   **0.004**
```

```
918
919   logistic  CataverageCIMT i.GenderCode CRP i.SBPCat##c.HDL c.Waist##c.HDL
920   lrtest main .
921   **0.001**
922
923   **Logistic model for CataverageCIMT, goodness-of-fit test
924   logit CataverageCIMT i.GenderCode CRP i.SBPCat##c.HDL c.Waist##c.HDL if sample ==1
925   estat gof, group(5)
926   lfit, group(5) table
927   **P Value 0.6107, good fit
928
929   ** specification error (hatsq is  0.379, not sig, we don't reject null, and there
      is no specification error)
930   linktest, nolog
931
932   *Classification table, Correctly classified 71.35%
933   lstat
934   *ROC ( AUC 0.66)
935   lroc
936
937   logit CataverageCIMT GenderCode CRP SBPCat##c.HDL c.Waist##c.HDL
938
939   collin CataverageCIMT i.GenderCode CRP i.SBPCat##c.HDL c.Waist##c.HDL if sample ==1
940
941
942
943   nomolog, title(Nomogram of the logistic model ) vli1(CRP,2,55,30,0)  k1(HDL,0.58,
      1.335,1.6)
944
945
946
947
```

APPENDIX G QBB DATA AND BIOLOGICAL SAMPLE RECEIPT FORM

QATAR BIOBANK RESEARCH
DATA AND BIOLOGICAL SAMPLE RECEIPT FORM
(APPENDIX G)

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

1. PROJECT DETAILS	
Project Title	Qatar Biobank data analysis: Lifestyle, biological factors and clinical biomarkers as risk factors of cardiovascular diseases burden in Qatar
Project Duration	8 months
Proposed Start Date	01/10/2016
Grant Source	
Grant Number	

2. PRINICIPAL INVESTIGATOR'S DETAILS	
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QATAR BIOBANK RESEARCH
DATA AND BIOLOGICAL SAMPLE RECEIPT FORM
(APPENDIX G)

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

5. DATA AND BIOLOGICAL SAMPLE PROVIDED
To be filled by IT Manager

NO.	MAIN QUESTIONNAIRE	NO.	NURSE INTERVIEW
1. ☑	Socio-economic status	1. ☑	Ethnicity
2. ☐	Occupational exposure	2. ☑	Occupation
3. ☑	Physical activity	3. ☐	Health screening
4. ☐	Mobile phone usage	4. ☑	Cancer
5. ☑	Sleeping patterns	5. ☑	Other medical conditions
6. ☑	Smoking	6. ☐	Surgery
7. ☐	Childhood conditions / illnesses / family history	7. ☐	Family medical history
8. ☐	Mental health	8. ☐	Medications
9. ☑	General health	9. ☐	Pregnancy and contraception
10. ☑	Respiratory		
11. ☑	Chronic Symptoms		
12. ☐	Women's health		
13. ☑	Chronic diseases		
14. ☐	Antibiotics usage		
15. ☐	Supplement usage		

NO.	DIET QUESTIONNAIRE	NO.	COGNITION TEST
1. ☑	Diet	1. ☐	Memory test
2. ☑	Coffee and tea	2. ☐	Speed of reaction test
3. ☑	Dairy products		
4. ☐	Other type of food consumed		
5. ☑	Fast food		
6. ☑	Drinks		

Mode of data provision:

USB Number: QU-21-Dr Reham

Any other comments:

QATAR BIOBANK ACCESS RECEIPT FORM
(APPENDIX G)

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

Laboratory Data	
1. ☑ **Blood Count, including:** **Haemaglobin, Haematocrit, Red Cell Count, White Cell Count (total), Differential white cell count, Platelet count, Mean corpuscular volume (MCV), Mean Corpuscular Haemaglobin (MCH), Mean Corpuscular Haemaglobin 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, HDL 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 Naturetic Peptide**
7. ☐ **Trace Elements, including:** **Copper, Zinc**	8. ☑ **Others such as HbAc1, Homocysteine**

Medical tests and anthropometrics	
☐	**Test**
☑	**Systolic and diastolic blood pressure**
☑	**Respiratory test**
☑	**Body fat content**
☑	**height**
☑	**weight**
☑	**Waist**
☐	**Hip measurement**
☑	**Waist to Hip Ratio**
☑	**Heart activity**
☐	**Blood flow?**

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☑	Body fat content
☐	Carotid artery scan
☐	Fitness test
☐	Retina test

Mode of data provision:
USB Number:
Any other comments:

PI Signature and Date	IT Manager Signature and Date

5. BIOLOGICAL SAMPLE PROVIDED
Please mention the type and quantity of samples provided
To be filled by Laboratory Supervisor

	No of samples provided on	No of samples provided on
☐ Plasma	_____ X _____ µl	_____ X _____ µl
☐ Serum	_____ X _____ µl	_____ X _____ µl
☐ DNA from Buffy coats	_____ X _____ µl	_____ X _____ µl
☐ Urine	_____ X _____ µl	_____ X _____ µl
☐ Saliva	_____ X _____ µl	_____ X _____ µl

	No of samples provided on	No of samples provided on
☐ Plasma	_____ X _____ µl	_____ X _____ µl
☐ Serum	_____ X _____ µl	_____ X _____ µl
☐ DNA from Buffy coats	_____ X _____ µl	_____ X _____ µl

QATAR BIOBANK RESEARCH
DATA AND BIOLOGICAL SAMPLE RECEIPT FORM
(APPENDIX G)

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

PI Signature and Date	IT Manager Signature and Date Nabila Afridi 26/12/2016

APPENDIX H AGE- AND GENDER-WISE DISTRIBUTION OF AVERAGE CIMT IN THE SCORE INDIAN STUDY AND OUR STUDY POPULATIONS

	Age group	N- Indian	Mean - I	SD- I	N- Qatari	mean - Q	SD-Q	P- Value
Males	30–39 years	186	0.53	0.06	165	0.5	0.06	**<0.001**
	40–49 years	170	0.58	0.08	162	0.55	0.09	**0.001**
	50–59 years	149	0.64	0.13	79	0.62	0.12	0.26
	≥60 years	119	0.73	0.14	36	0.67	0.12	**0.021**
Females	30–39 years	153	0.51	0.06	201	0.48	0.05	**<0.001**
	40–49 years	138	0.58	0.11	196	0.53	0.07	**<0.001**
	50–59 years	129	0.61	0.09	175	0.59	0.08	**0.042**
	≥60 years	113	0.64	0.11	45	0.67	0.09	0.12