Development and Validation of a Diagnostic Model – The Hypertension Population Risk Tool (HTNPoRT) – to Predict Hypertension and Describe Risk Profiles: A Population-Based Cross-Sectional Study of Canadians

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Preface

Contributors: The student (RI) conceived the original study and was responsible for devising the methodology, conducting all analyses, and interpretating results in consultation with his supervisor Dr. Douglas G. Manuel (DGM), thesis advisory committee members Tracey Bushnik (TB), Manish M. Sood (MMS), and Monica Taljaard (MT), and collaborator Finlay A. McAlister (FAM). The student (RI) is the primary author who drafted the thesis manuscript, while all co-authors contributed substantially to its revision. All authors approved the final version to be submitted and agreed to be accountable for all aspects of the work. No patients or members of the public were involved in designing this study, nor will they be involved in dissemination.

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Ethics approval: Research ethics approval has been granted by the Ottawa Health Science Network Research Ethics Board on November 22, 2024 (Appendix 1).

Abstract

Background: Hypertension is preventable, and existing models predicting hypertension lack use for individual and population health planning.

Methods: The Hypertension Population Risk Tool (HTNPoRT) was derived from 19,643 adult respondents in the Canadian Health Measures Survey. Sex-specific logistic regression models predicting hypertension presence were developed using 16 predictors: 4 sociodemographics, 3 psychosocial measures, 2 health status indicators, 5 health behaviours, and 2 chronic conditions.

Results: The final HTNPoRT models were discriminating (c-statistic, men: 0.86; women: 0.88), and well-calibrated in the overall population (observed v. predicted relative difference, men: 1.02%; women: 1.41%) and nearly all equity-relevant subgroups (179 out of 181). Age, diabetes, and body mass index were most influential predictors of hypertension seen on SHAP-derived risk profiles, while predictability of adiposity measures differed across sex.

Conclusions: The public and health policymakers can use the models and risk profiles of HTNPoRT to support planning and decision-making on addressing the hypertension burden.

(150/150 words)

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List of Abbreviations

C-statistic – Concordance statistic

CHMS – Canadian Health Measures Survey

CI – Confidence interval

DBP – Diastolic blood pressure

HTNPoRT – Hypertension Population Risk Tool

MEC – Mobile examination centre

mm Hg – Millimeters of mercury

OR – Odds ratio

SBP – Systolic blood pressure

SHAP – SHapley Additive exPlanation

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Chapter 1 - Introduction

1.1. Background

Hypertension affects about 1 in 4 Canadians and is the world's leading risk factor for preventable cardiovascular disease and all-cause mortality (1, 2). In 2019, hypertension accounted for around 10.8 million deaths worldwide and was found to be the leading cause of attributable disability-adjusted life-years in those aged 50 and over (2). Hypertension prevention is considered a major public health concern (3). However, over the past decades, reducing the burden of high blood pressure has focused mainly on screening, treating, and controlling hypertension; less on preventing hypertension or addressing any of its modifiable risk factors. Hypertension has many modifiable risk factors, such as physical inactivity, unhealthy diet, obesity, diabetes, and chronic kidney disease (1). Studies worldwide have shown an association between a range of these modifiable risk factors and an increase in blood pressure or the prevalence of hypertension (4). Managing these risk factors through maintaining healthy lifestyles can help offset genetic predispositions to hypertension, while community-based interventions can lower blood pressure in the population (5, 6). Hypertension awareness, treatment, and control rates are usually lower overall in younger individuals, a population in which preventative strategies could prove most effective (7, 8). The effect of the ageing population and worsening obesity on the burden of hypertension warrants better understanding of risk factors for hypertension, since there are still gaps in knowledge in risk factor dose-responses and risk factor interactions (i.e., if certain risk factor associations attenuate at older ages), both of which can inform hypertension prevention.

Diagnostic models predicting hypertension can guide decision-making on preventing hypertension by supporting the identification of high-risk subpopulations and informing the evaluation and design of preventive interventions tailored to population needs (9). Preferably, diagnostic model output should be transparent and understandable by informing what risk factors or predictors contribute to its calculation. Diagnostic models can better support assessment of preventive interventions when they incorporate information relating to a person or population's risk profile. A risk profile refers to the cumulative assessment of an individual's exposure to multiple risk factors that can be altered through lifestyle changes or medical interventions (10). It encompasses quantifying and characterizing various behavioral, physiological, and biochemical factors that contribute to the probability of a specific health condition or outcome (11, 12). Reporting predictors that influence a risk prediction gives diagnostic calculations transparency on how it was specifically calculated, and which predictors are more important in its calculation. Separately, people who have an unhealthy risk profile (i.e., exposures to risk where there is evidence of reversible risk) can use their profile to estimate the potential benefit of preventive interventions, such as adhering to the Dietary Approaches to Stop Hypertension (DASH) diet known to significantly reduce blood pressure and the risk of hypertension in intervention trials (4). This process, outside the scope of this study, involves combining risk estimates with the relative benefit of interventions, as ascertained from separate intervention studies.

1.2. Rationale

A simple online tool with a diagnostic model predicting the probability of hypertension presence and providing risk profiles can help improve engagement with the public in understanding their risk of hypertension and getting their blood pressure checked to potentially help improve overall health. However, there is a lack of these readily available hypertension prevention tools for individuals and population health planners.

Most existing models predicting hypertension are designed for clinical settings, but neither for the purpose of population health planning nor for the purpose of providing individuals simple lifestyle advice. Models fulfilling these purposes must have predictors which are available to the public, representative of the population, and regularly collected to update estimates if needed. Additionally, these models must also be developed from large representative datasets and have a variety of sociodemographics as predictors to facilitate risk assessment and equity evaluation across important subpopulations such as age, ethnicity, and education. Furthermore, including modifiable risk factors as predictors allows for the evaluation of preventative strategies. Most existing hypertension prediction models include predictors which are not ideal for population health planning and difficult to collect from individuals wanting simple lifestyle advice. These include models which have genetic factors (13–17), biomarkers (18–21), and clinically obtained measures (like blood pressure itself) (15–23) as predictors. Moreover, many existing prediction models are developed from people of only one ethnicity (17, 24–26) and there has been no model developed to predict hypertension which is representative of the Canadian population (8, 27).

Therefore, a diagnostic model with easy-to-collect and modifiable risk factors as predictors (with dose-responses and interactions pre-specified), and derived from multiethnic population-based survey data, can form the basis of tools which can readily predict and understand hypertension risk at individual or population levels, helping reduce the burden of hypertension.

1.3. Objectives

The overall goal of this study was to use national population data and robust statistical models to increase our understanding of hypertension risk factor epidemiology, yield hypertension risk profiles which can support the identification of high-risk individuals, and evaluate the relative importance of risk factors, including individual and population attributions to hypertension. Our specific objectives were to:

1. Describe the association between sociodemographic, behavioral and disease risk factors and the prevalence of hypertension.
2. Develop and validate a diagnostic model - the Hypertension Population Risk Tool (HTNPoRT) - that can be used by members of the public to predict their probability of currently having hypertension, assess their hypertension risk profiles, and identify their most influential risk factors for hypertension.

1.4. Structure of thesis

This thesis manuscript has four chapters and was written using a thesis by articles format following guidelines set by the University of Ottawa. Chapter 1 gives background information on the burden of hypertension and the usefulness of diagnostic prediction models and risk profiles in addressing such burden, while also providing the rationale and objectives for this study. Chapter 2 details the methodology and analysis plan required to fulfill the study's two specific objectives. Chapter 3 presents the key findings surrounding the development and validation of HTNPoRT, as well as the relationships between HTNPoRT predictors and hypertension. Finally, Chapter 4 interprets the study's key findings and discusses the potential of HTNPoRT in addressing the hypertension burden.

Chapter 2 - Methods

2.1. Study design: The planning and implementation of our analyses followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (28) and the TRIPOD-AI (Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis) checklist (29). We used population-based survey data from the Canadian Health Measures Survey (CHMS) to develop and validate the sex-specific models for HTNPoRT. The statistical approach to developing the model followed recommendations by both Steyerberg and Harrell (30, 31).

The protocol for the development and validation of HTNPoRT was registered and published (32). We adhered to the protocol with the following exceptions: the definition of alcohol consumption was changed from never, former, light, or moderate-to-heavy drinkers to never, low-risk (i.e., former or light), moderate, or heavy drinkers to correctly align with Canada's Low-Risk Alcohol Drinking Guideline; the variance inflation factor threshold for significant collinearity was decreased from 10 to 2.5; bivariable analysis and likelihood ratio tests were not performed; knot quantities were validated with partial association χ^2 statistics; sensitivity analyses were performed to assess if model performance was affected by any missing data, other imputed datasets, skewness, possible collinear predictors, linear interactions, unadjusted blood pressures, and potential anti-hypertensive medication misclassification; optimism was quantified for c-statistics; adjusted odds ratio plots for non-linear predictors and interactions were added to convey relationships between predictors and hypertension further; and final model determination was based off both model performance and reducing user burdens.

2.2. Data source: Data for the study included the first (data collected from March 19, 2007 to February 25, 2009), second (August 27, 2009 to November 30, 2011), third (January 5, 2012 to

December 13, 2013), fourth (January 7, 2014 to December 16, 2015), fifth (January 19, 2016 to December 19, 2017) and sixth (January 3, 2018 to December 19, 2019) cycles of the Canadian Health Measures Survey (CHMS) conducted by Statistics Canada.

The CHMS is a cross-sectional survey that collects questionnaire and directly measured health information from community-dwelling individuals aged 3 to 79 living in the 10 provinces. People living in the three territories or on reserves and settlements in the provinces, the institutionalized population, residents of certain remote regions, and full-time Canadian Forces members are excluded (about 4% of the Canadian population). The CHMS involves an in-person household interview and a subsequent visit to a mobile examination centre (MEC), while using a stratified three-stage sample made up of one or two randomly selected respondents from each dwelling selected in a sampled collection site. The household interview gathers general demographic and socioeconomic data and detailed health, nutrition, and lifestyle information. At the MEC, direct physical measurements are taken, including collection of blood and urine samples, as well as blood pressure which was used to derive hypertension. Information about medication use is obtained in the household interview and at the MEC. CHMS participants receive an accelerometer to wear for one week to monitor activity levels (33). This made the CHMS a robust database (with diverse primary data on several risk factors and blood pressure) for developing and validating a hypertension diagnostic model which was representative of the Canadian population.

Authorized investigation team members had access to the deidentified, electronic CHMS data on restricted hard drives at the University of Ottawa's Research Data Centre (RDC) managed by Statistics Canada. Details regarding data access are available in Appendix 2.

2.3. Participants: The population under study was community-dwelling adult Canadians aged between 20 and 79 in the first six cycles of the Canadian Health Measures Survey (CHMS). Respondents were excluded if they were under 20 or over 79, pregnant at the time of the CHMS interview, or had missing values for the outcome.

2.4. Outcome: Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were both measured with the BpTRU™ BPM-300 device (BpTRU Medical Devices Ltd., Coquitlam, British Columbia) at the MEC. The BpTRU™ is an automated electronic monitor that has been validated and recommended for use by Hypertension Canada (34, 35). Although BpTRU™ SBP and DBP readings are slightly lower than conventional manual blood pressure readings, the BpTRU™ readings may estimate blood pressure status more accurately (36). Following a five-minute rest period, six measurements were taken at one-minute intervals for each participant while unattended, and the last five measurements were averaged together to determine the average SBP and DBP levels (37). The average blood pressure readings were then adjusted using the following correction factors to approximate manual sphygmomanometer readings, as is standard for CHMS analyses estimating hypertension prevalence: adjusted SBP = 11.4 + (0.93 * SBP) and adjusted DBP = 15.6 + (0.83 * DBP) (1, 36).

Presence of hypertension was the outcome for this study and was derived from blood pressure readings and antihypertensive medication status. Respondents were considered hypertensive if their mean adjusted SBP was 140 mm Hg or higher or mean adjusted DBP was 90 mm Hg or higher, or if they had been taking a medication to treat hypertension in the month before the measurement being taken. Respondents with diabetes or chronic kidney disease were considered hypertensive if their mean adjusted SBP was 130 mm Hg or higher or mean adjusted DBP was

80 mm Hg or higher, or if they had been taking a medication to treat hypertension in the month before the measurement being taken. Respondents with hypertension were considered controlled if their mean adjusted SBP and DBP were lower than the respective cut-offs while taking a medication to treat hypertension in the month before the measurement being taken.

2.5. Measures: Candidate predictor variables were identified from existing literature on hypertension risk factors and from recommendations from knowledge users in clinical hypertension and public health. A total of 17 risk factors were selected as candidate variables, including four sociodemographic variables (age, marital status, education, and working status), three psychosocial measures (mental health, stress, and community belonging), three health status variables (hypertension family history, body mass index, and waist-to-height ratio), five health behaviours (alcohol consumption, cigarette smoking, physical activity, fruit and vegetable consumption, and sleep duration), and two chronic condition variables (diabetes and chronic kidney disease). Only variables present in at least four out of the six cycles in the CHMS were selected as predictor variables for HTNPoRT, given that hypertension family history and sleep duration are candidate predictor variables not asked in the last two cycles. Variables with small differences in ascertainment or measurement were harmonized across all six cycles. Like the definition of hypertension, the following definitions of the aforementioned risk factors serving as predictor variables followed previously published studies which used the CHMS (1, 38).

2.5.1. Sociodemographic measures. Sex at birth was defined as "male" or "female". Age was defined as years at MEC visit. Highest education level was classified as "less than secondary school graduation", "secondary school graduation", or "post-secondary graduation". Marital status was defined as "married or common-law", "widowed, separated, or divorced", or "single and never married". Working status was based on respondents' answers to the question of whether they were employed as of the previous week.

2.5.2. Psychosocial measures. Psychosocial measures included respondents' self-rated mental health, self-perceived stress, and sense of belonging to the community, each encoded on an ordinal scale.

2.5.3. Health status measures. Family history for hypertension was defined as if respondents ever had an immediate family member with hypertension (excluding during pregnancy). Body mass index was measured in kg/m^2 upon dividing weight by height squared, while waist-to-height ratio was displayed as a percentage upon dividing waist circumference by height.

2.5.4. Health behaviours. Alcohol consumption was defined as whether respondents were either never, low-risk (i.e., former or light), moderate, or heavy drinkers according to Canada's Low-Risk Alcohol Drinking Guideline. Smoking was defined as whether respondents were current smokers, former smokers, or never smokers. Average moderate-to-vigorous physical activity (MVPA) minutes per week were computed from week-long accelerometer data containing at least one day of valid data (see Appendix 2 for further details). Fruit and vegetable consumption was derived as the sum of frequency of daily consumption of select fruit, fruit juices, tomatoes, potatoes, greens, collards, and others (1). Sleep duration was defined as hours of sleep per night.

2.5.5. Chronic conditions. Diabetes was defined as having a positive self-report, having a level of serum glycated hemoglobin A1c of 6.5% or higher, or having taken a glucose-lowering medication in the month before the survey. Chronic kidney disease was defined as having an estimated glomerular filtration rate less than 60 mL/min/1.73 m^3 (1).

2.5.6. Medication use. Current medications were recorded during the household and clinic interviews, and these were assigned to codes from the Anatomical Therapeutic Chemical (ATC) classification system, corresponding to beta blockers, agents acting on the renin-angiotensin system, thiazide diuretics, calcium channel antagonists, other antihypertensive agents, as well as glucose-lowering medications (38).

2.6. Sample size: Statistics Canada recommends calculations for power of observational studies, given that the CHMS is highly clustered. In every cycle, a random sample of individuals of all ages are chosen from 16-18 collection sites which themselves are sampled from 5 regions. With the collection sites serving as the primary sampling units and the regions as the strata, the degrees of freedom for each cycle are computed as the number of primary sampling units minus the number of strata, giving 11 degrees of freedom per each cycle (cycle 2 has 13 degrees of freedom due to 18 collection sites). Therefore, there is a maximum of 68 degrees of freedom available for estimating regression model parameters at the national level when all six cycles of the CHMS are combined. Following Statistics Canada recommendations, we limited our pre-specifications and the number of parameters to the maximum degrees of freedom minus 1 (i.e., 67) as 1 degree of freedom is reserved for estimating the intercept.

To increase the sample size and thus, the likelihood of developing a robust prediction model, the six cycles of the CHMS were combined. The minimum sample size for developing the models was calculated with the approach by Riley et al. which considers factors such as the proportion of the outcome in the study population and the anticipated predictive performance of the model (39, 40). Using this approach, the minimum sample size needed to develop each sex-specific model was 3,139 with 823 events per model, assuming the maximum 67 predictor parameters (arising from 17 candidate predictors and their pre-specified interactions), an outcome proportion of 26.2% in the study population, a shrinkage factor of 0.90, and a minimum c-statistic of 0.77 from a previous hypertension model in Canada (8). Upon deriving the study population, a total sample size of 19,643 respondents (9,633 males and 10,010 females) was obtained, with 5,152 of those respondents (2,681 males and 2,471 females) having hypertension. Therefore, the minimum estimates were surpassed, yielding a sufficient sample size for the proposed analyses.

2.7. Analysis plan: The analytic plan was developed following the guidelines for clinical models by Steyerberg and Harrell (30, 31). This plan was constructed after accessing study data but before evaluation of descriptive statistics and any model fitting. Important considerations that informed the analytic approach included full pre-specification of predictors, implementation of flexible functions for certain continuous variables, and use of survey weights for variance estimation and population inferences. All analyses were stratified by sex and thus sex-specific models for HTNPoRT were developed and validated given sex differences in hypertension risk (1). Including sex interactions with all the predictors would have rendered the model overcomplex and have surpassed the maximum 68 degrees of freedom available for estimating regression model parameters in the sample, which already provided a wealth of data for conducting simpler analyses.

2.7.1. Data imputation and cleaning

All independent variables with missing data were imputed once to create one imputed dataset, using a model derived from the multiple imputation using chained equations (MICE) method (41). The imputation model included the study outcome, all predictor variables in their pre-specified form, and the cycle of the CHMS. Respondents with missing outcome values were excluded from the study. Variables missing from more than two cycles of the CHMS were not included. Only one imputed dataset was generated from one imputation since the sample was large with mostly low missingness and no differences in model performance were expected when deriving the models from other imputed datasets generated with the same imputation model.

Continuous variables with skewed variation were truncated to the 99.5th percentile. Variance inflation factors (VIFs) were used to assess any multicollinearity between predictors prior to any analyses, with waist-to-height ratio to be eliminated if it was significantly collinear with body mass index (VIF > 2.5). Sensitivity analyses were later performed to assess if model performance was affected by either dropping missing data, using four other imputed datasets generated with the same imputation model, leaving skewness, or if necessary, re-including waist-to-height ratio and its pre-specified interactions with age and body mass index. Sensitivity analyses were also performed to assess how both model performance and cumulative predicted probabilities were affected by deriving hypertension with unadjusted blood pressures and by excluding respondents qualifying for hypertension on medications alone (i.e., with controlled hypertension).

2.7.2. Descriptive analyses

Frequency distributions were reported for categorical risk factors, while descriptive statistics (e.g., median and interquartile ranges, as well as density plots) were reported for continuous risk factors before and after the imputation of missing data, but all prior to truncation.

2.7.3. Model estimation

The relationship between the candidate risk factors and hypertension in each sex stratum was examined using multiple logistic regression, which incorporated the two-way interactions between age and clinically relevant variables identified in the literature, as well as, if necessary, an identified interaction between body mass index and waist-to-height ratio. The initial models were fitted using the pre-specified form for each chosen predictor and any specified interactions, presented in Table 1, for a total of 68 degrees of freedom including the intercept.

Continuous measures were modelled using restricted cubic splines if they were known to have a non-linear dose-response relation with hypertension in existing literature. Knots for restricted cubic splines were placed at fixed quantiles of the distribution, specifically the 5^{th}, 35^{th}, 65^{th}, and 95^{th} percentiles for age (with 4 knots and thus the most degrees of freedom allocation as biggest risk factor), and the 10^{th}, 50^{th}, and 90^{th} percentiles for other transformed measures (with 3 knots being adequate to capture their associations). Continuous measures which were not modelled with splines were specified as linear terms instead and were assessed for any departures from linearity. If any such measure demonstrated departure, they were to be log-transformed. Partial association χ^2 statistics were used to validate the degree of freedom allocations of continuous predictors, with the linear predictors having 3 knots in this step and other predictors retaining their initial pre-specification. Interactions between spline terms were allowed, with another sensitivity analysis being performed to assess whether model performance was affected by using linear interactions. All measures were centered on their weighted means before modelling, while combined survey and bootstrap weights for the six cycles were incorporated into the models.

2.7.4. Model specification

Flexible modeling of chosen continuous predictors used restricted cubic splines and employed piecewise cubic functions smoothed at aforementioned knot placements at fixed quantiles of the distribution to ensure tail stability (31). Approximating the full model with a reduced model employed the stepdown approach described by Harrell and Ambler (31, 42). Predictors and interactions which contributed the least to each model's R^2 were dropped sequentially from each respective model until removing the next predictor or interaction decreased the R^2 to less than 95% of the initial model's R^2.

2.7.5. Model validation

To compare between the full and reduced models for each sex, the models were validated with the internal bootstrap approach. The models were refitted and evaluated on 1,000 bootstrap samples, each randomly drawn with replacement from the original sample they were derived on. The models were validated within their original derivation sample as well.

2.7.6. Assessment of model performance

Assessment of overall model performance across the derivation and the bootstrap samples was detailed, focusing on measures of predictive accuracy, discrimination, and calibration. Predictive accuracy was gauged by Nagelkerke's R^2 and the Brier score, reflecting the proportion of variance explained by predictive variables and the accuracy of predicted probabilities computed by R language, respectively (43). Discrimination, or the model's ability to distinguish between those who have the outcome and those who do not, was appraised via a concordance statistic (c-statistic) and its 95% confidence interval from a receiver operating characteristic (ROC) curve plotting the sensitivity against the false-positive rate (1 – specificity) for a range of thresholds of the predicted probability (31, 43). Optimism for the c-statistic was quantified using the 1,000 bootstrap samples of internal validation (31). Discrimination was also appraised by comparing the 90:10 and 95:5 predicted probability ratios, which are the predicted probabilities at the 90th and 95th percentiles divided by those at the 10th and 5th percentiles, respectively. The ratios show the spread of predicted risk, with higher ratios indicating more a discriminating model.

Calibration, or the agreement between observed and predicted estimates, was assessed in four ways. First, by comparing overall observed and predicted hypertension probability (calibration-on-the-whole). Second, through calibration slopes, derived by regressing the outcome on predicted probability. A calibration slope of 1 indicates perfect calibration, verified using the Wald test. Third, through visual inspection of a calibration plot that is fitted with Local Estimated Scatterplot Smoothing (LOESS) (44). Fourth, to ensure model fairness, calibration was assessed across different subgroups of importance to clinicians and policy makers (e.g., age group, sociodemographic groups, health behaviours). Such subgroups included most of the predictor variables for the model (Table 1), as well as additional variables and alternate derivations of predictor variables. The clinically relevant standard of calibration was defined as a less than 20% difference between observed and predicted estimates within subgroups having a hypertension prevalence of at least 5%. Centering variables around their means will facilitate recalibration in new populations.

2.7.7. Model presentation

Our planned knowledge translation approach aligns with the Population Health Planning Knowledge-to-Action Model (45), previously devised and assessed by our team (46). Following model validation and performance assessment, all sex-specific logistic models were presented using beta coefficients, as well as odds ratios and their corresponding 95% confidence intervals adjusted with SHapley Additive exPlanation (SHAP) for the full models only. SHAP-adjusted odds ratios quantified the average model-estimated effect of being in a given risk category compared to the respective reference category. These were calculated by exponentiating the difference between the mean SHAP value (coded as log odds in this step) for the risk category and the mean SHAP value for the reference category (47). SHAP values reflect each risk factor variable's contribution to individual predictions in an additive, localized manner and inherently account for complex non-linearities and interactions within the model, providing a more nuanced representation of variable importance (48). SHAP plots were used to show the ranked importance of risk factors increasing and decreasing the value of the predicted probability for a given individual using one of the models. In addition, partial effects plots, as well as model-adjusted odds ratio plots for non-linear predictors and interactions, were employed to help convey the relationships between all predictors and outcomes clearly, enhancing interpretability for the general audience and decision-makers. To enhance accessibility to HTNPoRT models, we will render them executable via an interactive Excel calculator (see here) and later a web application offering a user-friendly, point-and-click approach for wide use.

Sex-specific weighted means will be used to predict current hypertension probability if users do not know information for such risk factors or leave such information incomplete. Users can change their risk factor values to their own reference values to see their difference in predicted hypertension probability. The predicted hypertension probability at present time, the SHAP plot, and the feature modification (once HTNPoRT is rendered executable online) will comprise the hypertension risk profile for users.

Table 1. Predictor variables for the Hypertension Population Risk Tool (HTNPoRT)

Variable	Scale	Initial variable specification	Variable form, full model[1]	Variable form, reduced model[2]
Sociodemographic measures				
Sex	Categorical	Stratified: – Male – Female	N/A	N/A
Age	Continuous	4-knot restricted cubic spline: – 20-79 years	Unchanged	Unchanged
Marital status	Categorical	3 categories: – Married or common-law – Widowed, separated, or divorced – Single and never married	Unchanged	Excluded
Highest education level	Categorical	3 categories: – Less than secondary school graduation – Secondary school graduation – Post-secondary school graduation	Unchanged	Excluded
Working status	Categorical	2 categories: – Has a job – Does not have a job	Unchanged	Excluded
Psychosocial measures				
Self-rated mental health	Categorical	2 categories: – Poor or fair – Good, very good, or excellent	Unchanged	Excluded
Self-perceived stress	Categorical	2 categories: – Not at all to a bit – Quite a bit or extremely	Unchanged	Excluded
Sense of belonging[§]	Categorical	2 categories: – Strong – Weak	Unchanged	Excluded
Health status measures				
Hypertension family history	Categorical	2 categories: – Yes – No	Unchanged	Unchanged
Body mass index[§]	Continuous	3-knot restricted cubic spline: – 13.83-56.77 kg/m^2	3-knot restricted cubic spline: – 13.83-49.00 kg/m^2 (truncated)	Unchanged

Waist-to-height ratio§	Continuous	3-knot restricted cubic spline: – 25.5-108.6%	Excluded (collinear)	N/A[3]
Health behaviours				
Alcohol consumption	Categorical	4 categories: – Never drank – Low-risk drinker – Moderate drinker – Heavy drinker	Unchanged	Excluded
Smoking status§	Categorical	3 categories: – Current smoker – Former smoker – Never smoker	Unchanged	Excluded
Physical activity minutes§	Continuous	3-knot restricted cubic spline: – 0-2,004 minutes per week	3-knot restricted cubic spline: – 0-792 minutes per week (truncated)	Excluded
Daily fruit and vegetable consumption	Continuous	Linear: – 0-19 times per day	Linear: – 0-10 times per day (truncated)	Excluded
Sleep duration§	Continuous	Linear: – 0-18 hours per night	Unchanged	Excluded
Chronic conditions				
Diabetes§	Categorical	2 categories: – Yes – No	Unchanged	Unchanged
Chronic kidney disease§	Categorical	2 categories: – Yes – No	Unchanged	Excluded

[1] 56 degrees of freedom (including intercept)

[2] 17 degrees of freedom (including intercept)

[3] When not excluded due to collinearity, waist-to-height ratio and its age interaction replace body mass index and its age interaction in only the male reduced model after stepdown

§ Age interaction included

3.1. Participants

Upon deriving the study population, a total sample size of 19,643 respondents (9,633 males and 10,010 females) was obtained, with 5,152 of those respondents (2,681 males and 2,471 females) having hypertension and a near even split between respondents with controlled and uncontrolled hypertension. The crude weighted prevalence of hypertension in the population was 25% among men and 22% among women. Median age among men was 46 years (interquartile range (IQR): 33-58) and among women was 47 years (IQR: 34-59). Weighted characteristics of the study populations are presented in Table 2, with raw information about missingness available in Appendix 3. Density plots for continuous variables are available in Appendix 4. Hypertension family history and sleep duration had the most missing data (30-38%) as they were not collected in all six cycles of the CHMS. Meanwhile, most other predictors had less than 2% missing data, while physical activity minutes and diabetes had between 6-11% missing data (Appendix 3).

Table 2. Weighted characteristics of the study populations for HTNPoRT

	Male[1]	**Female[1]**
Overall		
Total	9,633	10,010
Hypertensive	2,681 (25%)	2,471 (22%)
– Uncontrolled	1,300 (12%)	1,238 (11%)
– Controlled	1,381 (13%)	1,233 (11%)
Sociodemographic measures		
Age (years)	46 (33, 58)	47 (34, 59)
Marital status		
– Married or common-law	6,904 (67%)	6,069 (64%)
– Widowed, separated, or divorced	1,083 (8.6%)	2,211 (15%)
– Single and never married	1,646 (25%)	1,730 (21%)
Highest education level		
– Less than secondary school graduation	1,138 (13%)	1,155 (10%)
– Secondary school graduation	1,713 (22%)	1,805 (19%)
– Post-secondary school graduation	6,782 (66%)	7,050 (71%)
Working status		
– Has a job	6,836 (74%)	5,907 (65%)
– Does not have a job	2,797 (26%)	4,103 (35%)
Psychological measures		
Self-rated mental health		
– Poor or fair	570 (6.7%)	794 (8.9%)
– Good, very good, or excellent	9,063 (93%)	9,216 (91%)
Self-perceived stress		
– Not at all to a bit	7,617 (77%)	7,593 (74%)
– Quite a bit or extremely	2,016 (23%)	2,417 (26%)
Sense of belonging		
– Strong	6,395 (65%)	6,940 (66%)

– Weak	3,238 (35%)	3,070 (34%)
Health status measures		
Hypertension family history		
– Yes	4,795 (52%)	5,485 (57%)
– No	4,838 (48%)	4,525 (43%)
Body mass index (kg/m^2)	27.0 (24.2, 30.3)	25.8 (22.5, 30.2)
Health behaviours		
Alcohol consumption		
– Never drank	918 (10%)	1,777 (18%)
– Low-risk drinker	7,638 (78%)	7,557 (75%)
– Moderate drinker	431 (4.6%)	408 (3.9%)
– Heavy drinker	646 (7.2%)	268 (3.2%)
Smoking status		
– Current smoker	1,949 (23%)	1,662 (17%)
– Former smoker	3,326 (31%)	2,881 (27%)
– Never smoker	4,358 (46%)	5,467 (56%)
Physical activity minutes (minutes/week)	106 (41, 216)	86 (28, 182)
Daily fruit and vegetable consumption (times consumed/day)	3.00 (2.09, 4.14)	3.52 (2.51, 4.64)
Sleep duration (hours/night)	7.00 (6.00, 8.00)	7.00 (6.00, 8.00)
Chronic conditions		
Diabetes		
– Yes	1,099 (10%)	831 (7.3%)
– No	8,534 (90%)	9,179 (93%)
Chronic kidney disease		
– Yes	525 (4.5%)	723 (5.8%)
– No	9,108 (96%)	9,287 (94%)

[1] Median (Q1, Q3); n (unweighted counts) (weighted %)

3.2. Model development and specification

Predictor variables for the full and reduced models are shown in Table 1. The male and female full models have 56 degrees of freedom with 16 predictors (5 continuous) and 7 age interactions (Table 1). The final male and female reduced models have 17 degrees of freedom with 4 predictors (2 continuous) and 2 age interactions. Continuous predictors modelled as linear terms do not depart from linearity and as splines, had significantly lower partial association χ^2 statistics than ones originally pre-specified with splines; such statistics (age having the highest) thus justified the initial degree of freedom allocations for continuous predictors. Meanwhile, waist-to-height ratio was excluded due to being significantly collinear with body mass index (VIF > 2.5) (Appendix 5). Beta coefficients for the full and reduced models are available in Appendix 6.

3.3. Model performance

Table 3 presents a summary of indicators of model performance. Both the full male and female models are discriminating, indicating excellent ability to separate those who have hypertension and those who do not (male c-statistic: 0.87, 95% confidence interval (CI): 0.86-0.87; female c-statistic: 0.88, 95% CI: 0.87-0.89 across derivation and bootstrap samples). C-statistics were unchanged upon optimism correction. Also, predicted probabilities of hypertension at present time closely approximate observed proportions of hypertension within the overall population (observed v. predicted relative difference across the derivation sample, 1.94% in men and 1.20% in women; observed v. predicted relative difference across bootstrap samples, 2.09% in men and 1.15% in women). Figure 1 presents the calibration plots of the observed proportions regressed on the full models' predicted probabilities for both men and women. Calibration slopes closely approximate 1 (0.91 in men and 0.93 in women across the derivation sample, and 0.95 in men and 0.97 in women across bootstrap samples).

Among men, the full model was well-calibrated in all 91 predefined equity-relevant subgroups as there was no more than a 20% difference between observed and predicted estimates within all eligible subgroups where at least 5% of individuals were hypertensive. Likewise, among women, the full model was well-calibrated in all 90 predefined equity-relevant subgroups (Appendix 7). Figure 2 shows the calibration assessment of the full models across age in men and women, with the models being well-calibrated across all eligible age subgroups. The calibration assessment of the full models for the rest of the equity-relevant subgroups can be found in Appendix 7.

Table 3. Goodness of fit summary statistics for HTNPoRT in full and reduced models across the derivation and bootstrap samples

	Derivation sample		**Bootstrap samples**	
	Full model	**Reduced model**	**Full model**	**Reduced model**
Male model				
Discrimination				
c-statistic (95% CI)[1]	0.87 (0.86-0.87)	0.86 (0.85-0.87)	0.87 (0.86-0.87)	0.86 (0.85-0.87)
90:10 predicted probability ratio[2]	68.9	45.2	94.2	52.7
95:5 predicted probability ratio[2]	221.3	121.7	445.8	180.8
Calibration				
Observed v. predicted	1.94%	0.90%	2.09%	1.02%
Calibration slope	0.91	0.98	0.95	0.98
Overall performance				
Brier score	0.129	0.131	0.129	0.131
Nagelkerke's R^2	0.458	0.449	0.474	0.452
Female model				
Discrimination				
c-statistic (95% CI) [1]	0.88 (0.87-0.89)	0.88 (0.87-0.88)	0.88 (0.87-0.89)	0.88 (0.87-0.88)
90:10 predicted probability ratio[2]	95.7	81.7	154.3	97.6
95:5 predicted probability ratio[2]	256.8	208.3	714.5	310.6
Calibration				
Observed v. predicted	1.20%	1.52%	1.15%	1.41%
Calibration slope	0.93	0.95	0.97	0.99
Overall performance				
Brier score	0.114	0.116	0.114	0.116
Nagelkerke's R^2	0.485	0.474	0.500	0.480

[1] c-statistics unchanged upon optimism correction

[2] The 90:10 and 95:5 predicted probability ratios show the spread of the predicted risk, with higher ratios indicating a more discriminating model. A 95:5 predicted probability ratio of 20 indicates that the predicted probability of hypertension is 20 times higher for a person in the 95th percentile of risk than for a person in the 5th percentile of risk.

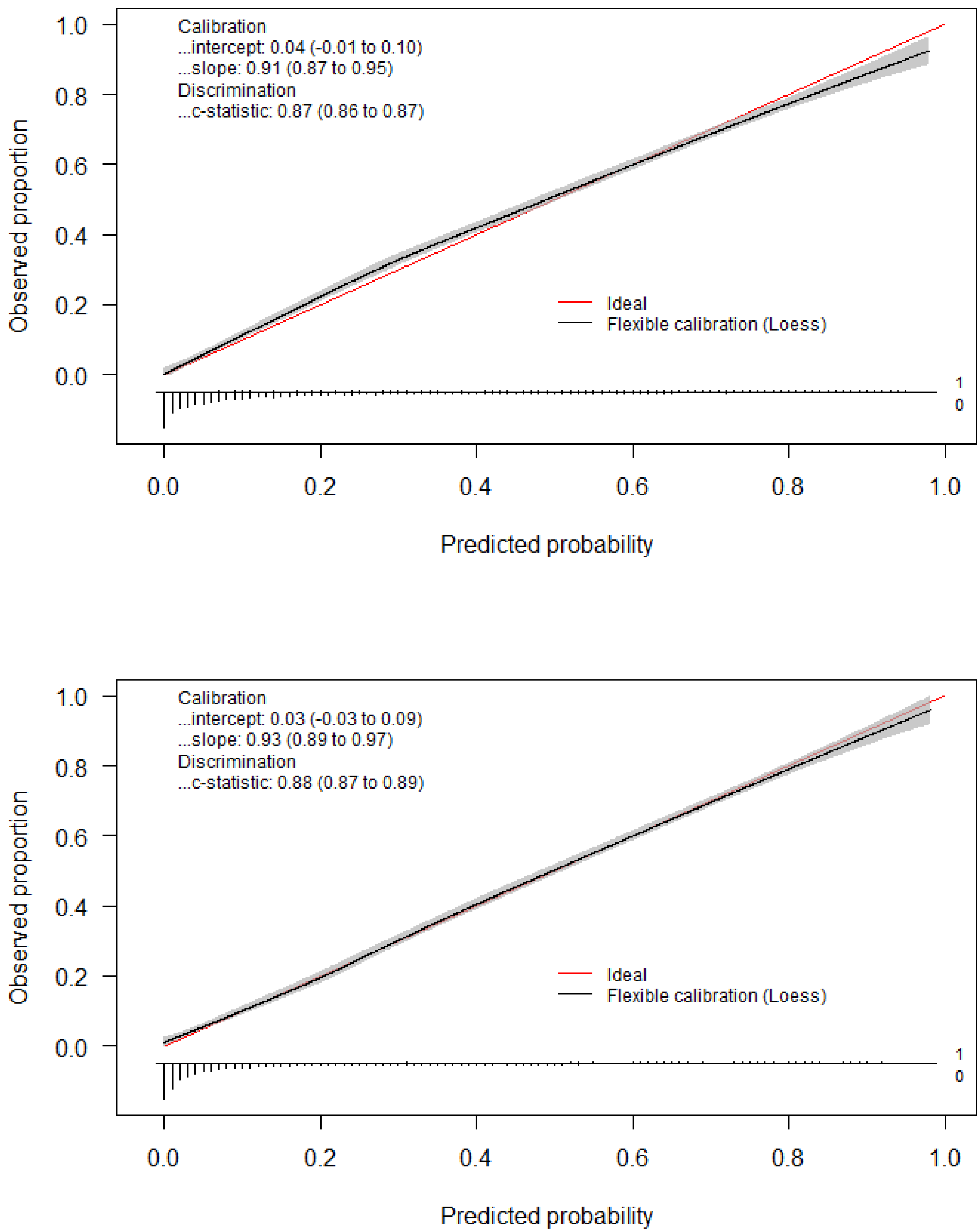


Figure 1. Calibration plots for full models; predicted hypertension probability versus observed hypertension proportion in men (top) and women (bottom)

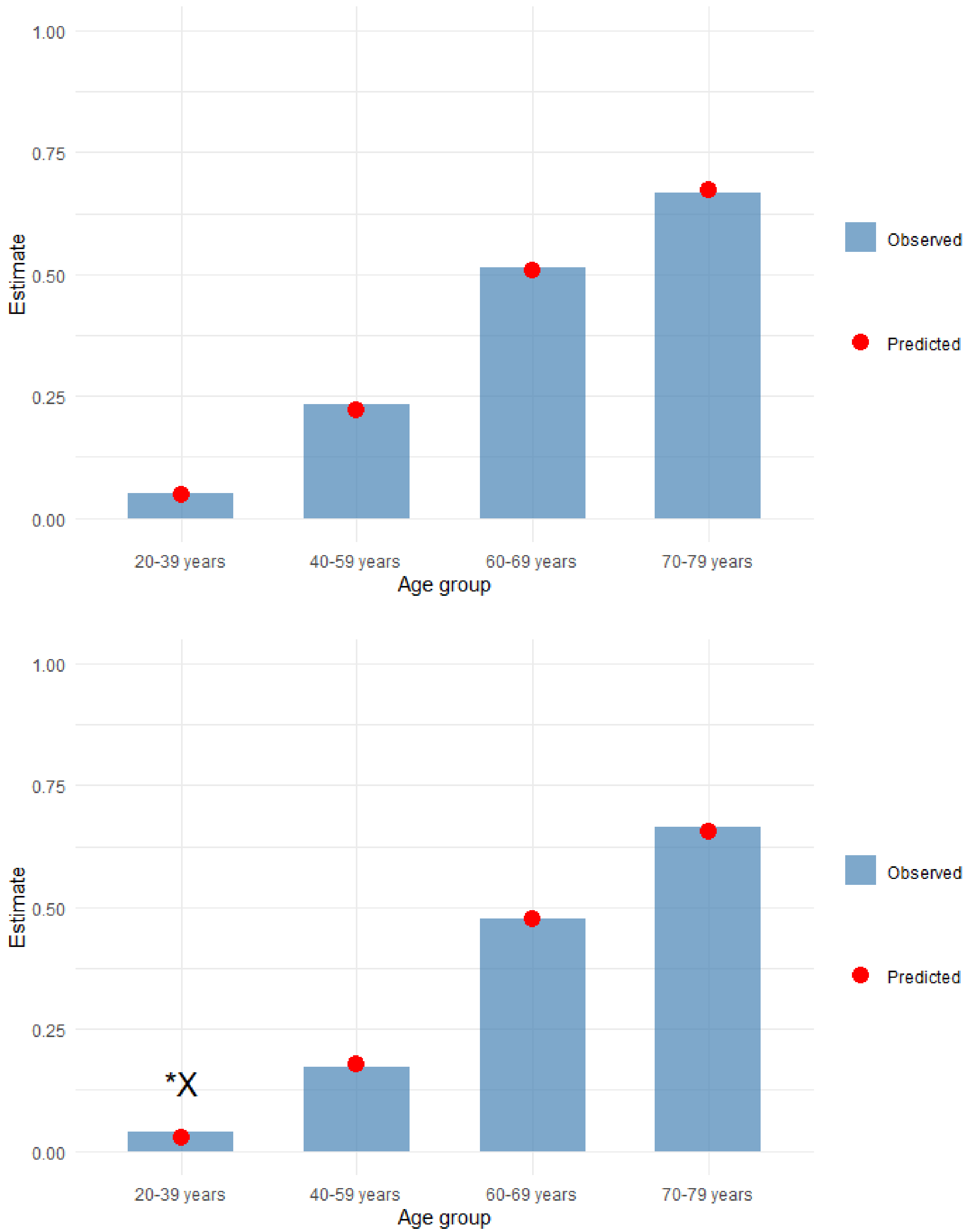
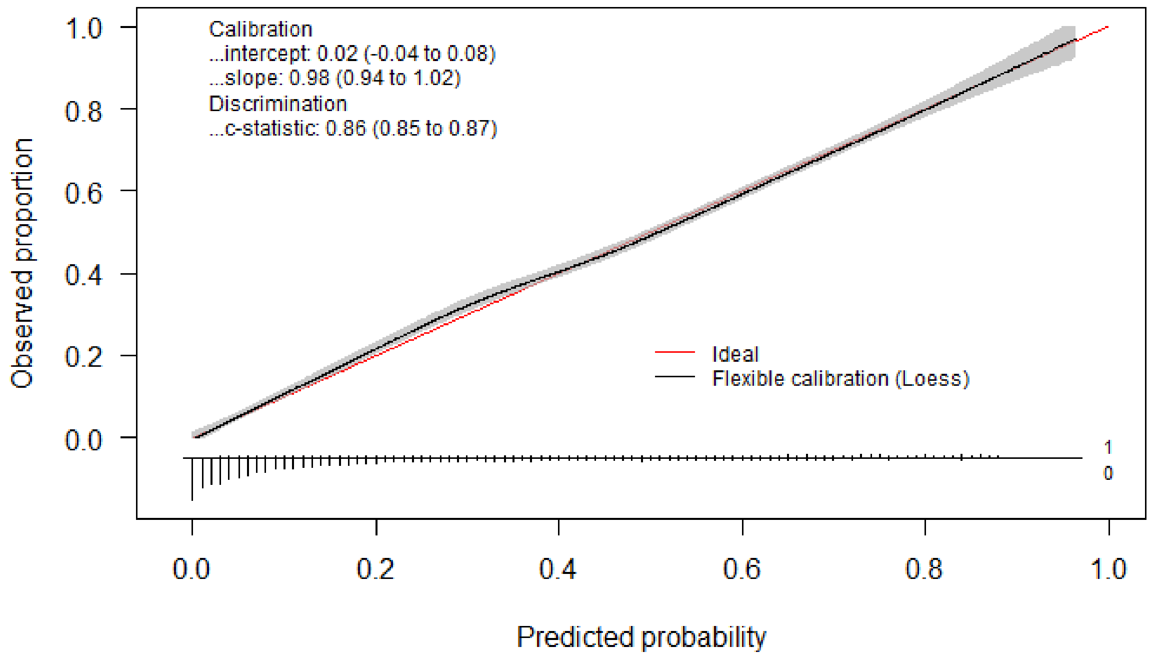


Figure 2. Calibration assessment of full models across age in men (top) and women (bottom); X is excluded subgroup with observed estimate less than 5% while * is subgroup with difference between observed and predicted estimates over 20%

In the reduced models, overall discriminative performance was similar in men (c-statistic: 0.86, 95% CI: 0.85-0.87) and women (c-statistic: 0.88, 95% CI: 0.87-0.88) across the derivation and bootstrap samples, with c-statistics remaining unchanged after optimism correction. As expected, the 90:10 and 95:5 predicted probability ratios degraded from full to reduced models in both men and women, demonstrating that the difference between individuals in the highest risk percentiles and those in the lowest risk percentiles shrunk slightly with the reduced models. As also seen commonly with model reduction, calibration slopes improved in both men (0.98 across derivation and bootstrap samples) and women (0.95 across the derivation sample and 0.99 across bootstrap samples). Meanwhile, predicted probabilities more closely approximated observed proportions in men yet less so in women (observed v. predicted relative difference across the derivation sample, 0.90% in men and 1.52% in women; observed v. predicted relative difference across bootstrap samples, 1.02% in men and 1.41% in women) (Table 3). Figure 3 presents the calibration plots of the observed proportions regressed on the reduced models' predicted probabilities for both men and women.

Calibration across equity-relevant subgroups degraded in men only. The difference between observed proportions and predicted probabilities for the reduced models was greater than the predefined difference of 20% for men with chronic kidney disease and men who are heavy alcohol drinkers (Appendix 8). Figure 4 shows the calibration assessment of the reduced models across chronic kidney disease in men and women, with the models being well-calibrated in all but one chronic kidney disease subgroups. The calibration assessment of the reduced models for the rest of the equity-relevant subgroups can be found in Appendix 8.



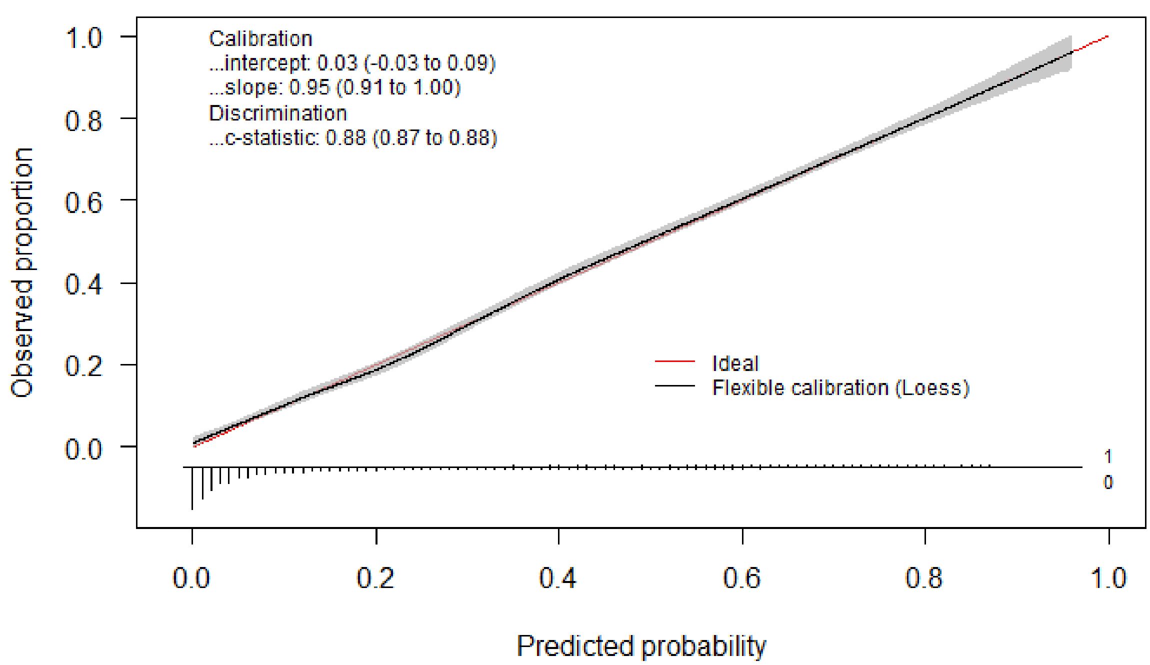


Figure 3. Calibration plots for reduced models; predicted hypertension probability versus observed hypertension proportion in men (top) and women (bottom)

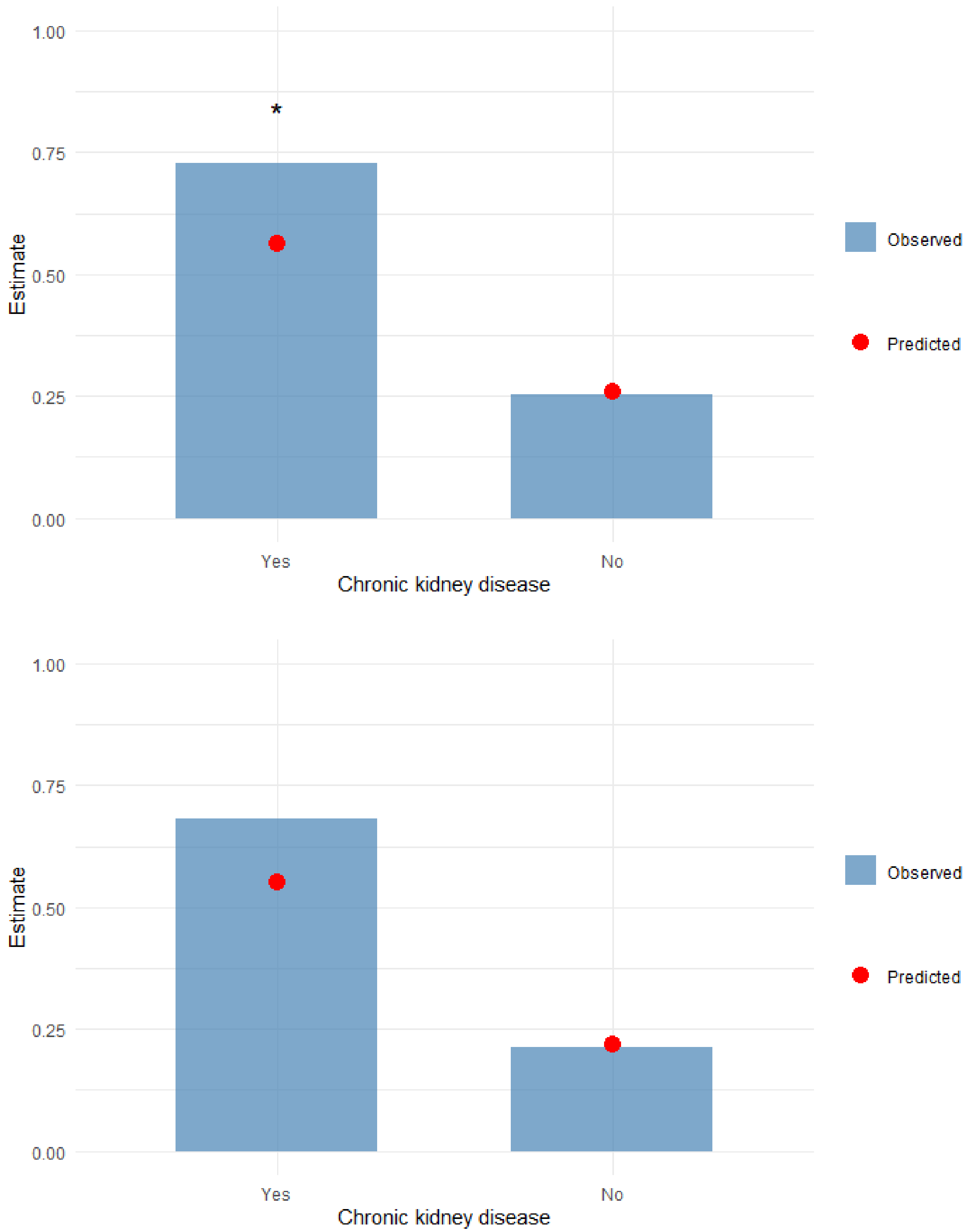


Figure 4. Calibration assessment of reduced models across chronic kidney disease in men (top) and women (bottom); * is subgroup with difference between observed and predicted estimates over 20%

In full models removing respondents with missing data, discriminative performance decreased slightly in men (c-statistic: 0.85, 95% CI: 0.83-0.86) and remained consistent in women (c-statistic: 0.88, 95% CI: 0.87-0.89) when compared to the primary full models, while the calibration slope improved in men (0.92) and degraded in women (0.88). In reduced models removing respondents with missing data, discriminative performance was identical in both men (c-statistic: 0.86, 95% CI: 0.85-0.87) and women (c-statistic: 0.88, 95% CI: 0.87-0.89) when compared to the primary reduced models, but the calibration slope degraded slightly in men (0.96) and remained consistent in women (0.95). Full and reduced models derived from four other imputed datasets, which were generated using the same imputation model, demonstrated identical overall discriminative performance and calibration slopes as the primary full and reduced models derived from the original imputed dataset.

In full models with skewed variables remaining untruncated, discriminative performance was identical to the primary full models in both men (c-statistic: 0.87, 95% CI: 0.86-0.87) and women (c-statistic: 0.88, 95% CI: 0.87-0.89), as were the calibration slopes. In reduced models with skewed variables remaining untruncated, discriminative performance was also identical to the primary reduced models in both men (c-statistic: 0.86, 95% CI: 0.85-0.87) and women (c-statistic: 0.88, 95% CI: 0.88-0.89), as were the calibration slopes. This was nearly the case for full and reduced models with linear interactions instead of interactions between spline terms, but the full model's calibration slope improved in men (0.93). Meanwhile, in full models with waist-to-height ratio and both its interactions with age and body mass index re-included, discriminative performance was identical to the primary full models without waist-to-height ratio in both men (c-statistic: 0.87, 95% CI: 0.86-0.87) and women (c-statistic: 0.88, 95% CI: 0.87-0.89), but the calibration slope degraded slightly in both men (0.90) and women (0.92).

Upon using unadjusted blood pressures to determine hypertension, 5,033 respondents (2,616 males and 2,417 females) had hypertension. In full models predicting hypertension presence ascertained with unadjusted blood pressures, discriminative performance was similar to the primary full models in both men (c-statistic: 0.86, 95% CI: 0.85-0.87) and women (c-statistic: 0.88, 95% CI: 0.87-0.89), while the calibration slope improved in men (0.92) and remained consistent in women (0.93). In reduced models predicting hypertension presence ascertained with unadjusted blood pressures, discriminative performance was identical to the primary reduced models in both men (c-statistic: 0.86, 95% CI: 0.85-0.87) and women (c-statistic: 0.88, 95% CI: 0.87-0.88), as were the calibration slopes. Cumulative predicted probability curves for models predicting hypertension presence ascertained with both adjusted and unadjusted blood pressures were virtually identical and overlapping.

In full models excluding respondents with controlled hypertension, discriminative performance was similar to the primary full models in both men (c-statistic: 0.86, 95% CI: 0.85-0.87) and women (c-statistic: 0.89, 95% CI: 0.88-0.90), but the calibration slope degraded slightly in both men (0.90) and women (0.91). In reduced models excluding respondents with controlled hypertension, discriminative performance decreased slightly in men (c-statistic: 0.85, 95% CI: 0.84-0.86) and remained consistent in women (c-statistic: 0.88, 95% CI: 0.87-0.89) when compared to the primary reduced models, while the calibration slope improved in both men (1.01) and women (0.97). As expected, restricting the outcome definition to only uncontrolled hypertension reduced the predicted risk distribution, producing a leftward shift in the cumulative predicted probability curves as more respondents received lower predicted probabilities from the models (Appendix 9).

3.4. Associations of model predictors with hypertension

SHAP-adjusted odds ratios (ORs) obtained from the full models, along with 95% confidence intervals (CIs), are available in Table 4 and describe the overall association between model predictors and hypertension in the study population while accounting for non-linearities and interactions in the model.

Table 4. SHAP-adjusted odds ratios and 95% confidence intervals obtained from full models; association between model predictors and hypertension accounting for non-linear effects and interactions

	Male	**Female**
	OR (95% CI)	OR (95% CI)
Sociodemographic measures		
Age		
– 20-39 years	Reference	Reference
– 40-59 years	6.86 (6.28-7.49)	7.95 (7.27-8.69)
– 60-69 years	23.5 (21.3-25.9)	30.5 (27.6-33.7)
– 70-79 years	44.7 (39.4-50.8)	57.3 (50.8-64.6)
Marital status		
– Married or common-law	Reference	Reference
– Widowed, separated, or divorced	1.01 (1.01-1.01)	1.02 (1.02-1.02)
– Single and never married	1.04 (1.04-1.04)	1.11 (1.11-1.11)
Highest education level		
– Post-secondary school graduation	Reference	Reference
– Secondary school graduation	1.04 (1.03-1.04)	1.15 (1.15-1.16)
– Less than secondary school graduation	1.41 (1.40-1.42)	1.11 (1.11-1.12)
Working status		
– Has a job	Reference	Reference
– Does not have a job	0.87 (0.87-0.88)	1.11 (1.10-1.11)
Psychological measures		
Self-rated mental health		
– Good, very good, or excellent	Reference	Reference
– Poor or fair	0.93 (0.92-0.93)	0.85 (0.84-0.85)
Self-perceived stress		
– Not at all to a bit	Reference	Reference
– Quite a bit or extremely	0.93 (0.93-0.94)	0.98 (0.98-0.98)
Sense of belonging		
– Strong	Reference	Reference
– Weak	1.51 (1.49-1.53)	1.25 (1.25-1.26)
Health status measures		

Hypertension family history		
– No	Reference	Reference
– Yes	2.25 (2.22-2.29)	2.45 (2.40-2.49)
Body mass index		
– Neither overweight nor obese (< 25.0 kg/m^2)	Reference	Reference
– Overweight (25.0 - < 30.0 kg/m^2)	1.87 (1.81-1.93)	1.68 (1.64-1.73)
– Obese (>= 30.0 kg/m^2)	3.32 (3.20-3.44)	2.98 (2.89-3.06)
Health behaviours		
Alcohol consumption		
– Never drank	Reference	Reference
– Low-risk drinker	1.20 (1.18-1.23)	0.79 (0.79-0.80)
– Moderate drinker	1.83 (1.77-1.89)	1.36 (1.34-1.38)
– Heavy drinker	3.51 (3.40-3.61)	1.44 (1.41-1.47)
Smoking status		
– Never smoker	Reference	Reference
– Former smoker	1.05 (1.04-1.06)	1.10 (1.09-1.11)
– Current smoker	0.84 (0.83-0.85)	0.86 (0.85-0.87)
Physical activity minutes		
– 150 minutes/week or more	Reference	Reference
– Less than 150 minutes/week	1.24 (1.22-1.26)	1.36 (1.33-1.38)
Daily fruit and vegetable consumption		
– Consumed 5 times/day or more	Reference	Reference
– Consumed less than 5 times/day	1.00 (1.00-1.00)	1.08 (1.08-1.09)
Sleep duration		
– 7 hours/night or more	Reference	Reference
– Less than 7 hours/night	0.92 (0.91-0.93)	0.88 (0.87-0.89)
Chronic conditions		
Diabetes		
– No	Reference	Reference
– Yes	6.15 (5.78-6.55)	4.19 (4.02-4.37)
Chronic kidney disease		
– No	Reference	Reference
– Yes	3.64 (3.46-3.84)	3.44 (3.27-3.62)

It is important to note that with waist-to-height ratio and its interactions still in the model, the SHAP-adjusted odds ratios (with the reference being neither overweight nor obese) were 0.95 (95% CI: 0.93-0.96) for overweight men, 0.88 (95% CI: 0.86-0.90) for obese men, 1.23 (95% CI: 1.21-1.24) for overweight women, and 2.50 (95% CI: 2.45-2.55) for obese women. Meanwhile, the SHAP-adjusted odds ratios (with the reference having a healthy waist circumference below

50%) were 3.16 (95% CI: 3.09-3.23) for men with a waist-to-height ratio of at least 50% but below 60%, 6.24 (95% CI; 6.04-6.44) for men with a waist-to-height ratio of at least 60%, 1.92 (95% CI; 1.88-1.97) for women with a waist-to-height ratio of at least 50% but below 60%, and 1.76 (95% CI: 1.72-1.81) for women with a waist-to-height ratio of at least 60%.

Relationships between predictors and hypertension have been visualized on partial effects plots available in Appendix 10, as well as on model-adjusted odds ratio plots of non-linear predictors and interactions available in Appendix 11. Figure 5 specifically is the first two plots of Appendix 11, in which the odds of hypertension from being a given age (compared to being 20 years old) steeply increase with age to almost 1,000 by age 79. The next four plots of Appendix 11 show the odds ratios curving upward with increasing body mass index and downward with increasing physical activity minutes.

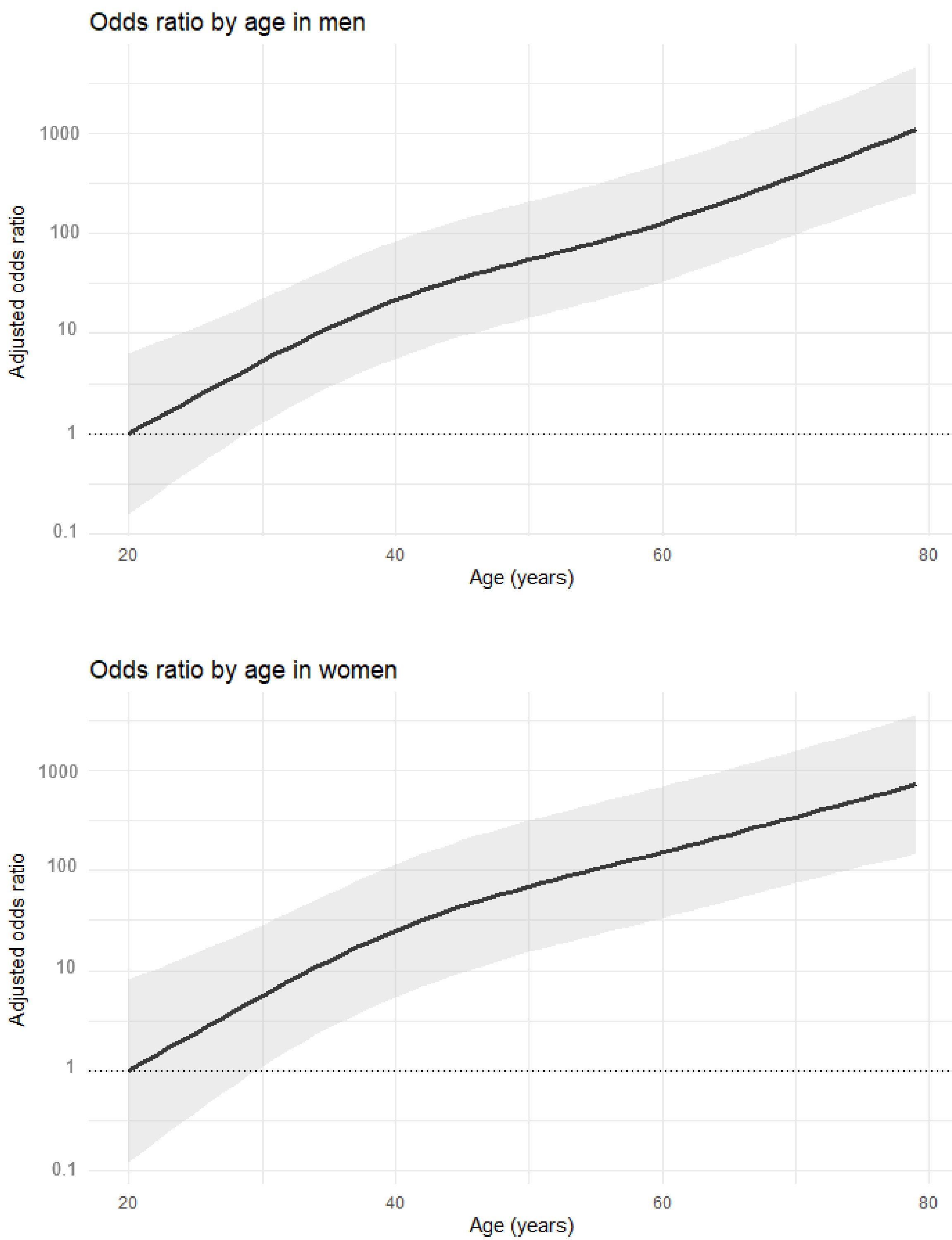
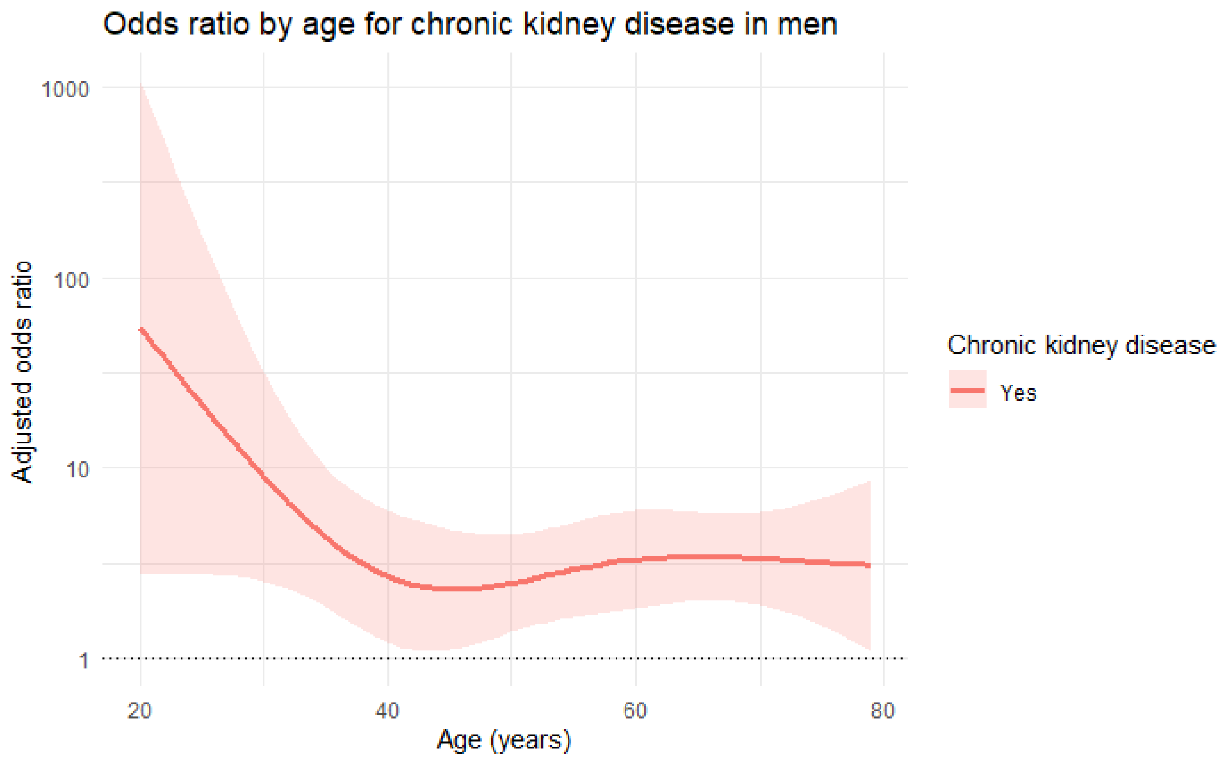


Figure 5. Model-adjusted odds ratios by age in men (top) and women (bottom); reference is being 20 years old

Meanwhile, in the age interaction plots (i.e., the last fourteen plots in Appendix 11), the odds ratios for interacting risk factors mostly decrease and/or approach 1 with older age, while differences in odds ratios tend to become lower between most predictor categories and quantiles at older ages. There is an exception for current smoking as its odds ratios increase past 1 in older men and decrease past 1 in older women, while diverging from the odds ratios of former smoking at older ages as well. However, the confidence interval bands for current and former smoking odds ratios (with never smoking being the reference category) include 1 across all ages. Taken directly from Appendix 11, Figure 6 presents an age interaction plot with a categorical risk factor, particularly showing how odds ratios of chronic kidney disease decrease across age in both men and women. Likewise, Figure 7 presents an age interaction plot with a continuous risk factor, particularly showing how odds ratios of certain body mass indexes also decrease across age in both men and women.

The odds ratios were notably at least 10 times higher at the youngest ages than at the oldest ages for both men and women with chronic kidney disease compared to men and women without it (Figure 6). Similarly, the odds ratios were notably at least 10 times higher at the youngest ages than at the oldest ages for men with body mass indexes of 25 kg/m^2 and 30 kg/m^2 compared to men with a body mass index of 18.5 kg/m^2 (Figure 7), as well as for men with diabetes compared to men without it (Appendix 11).



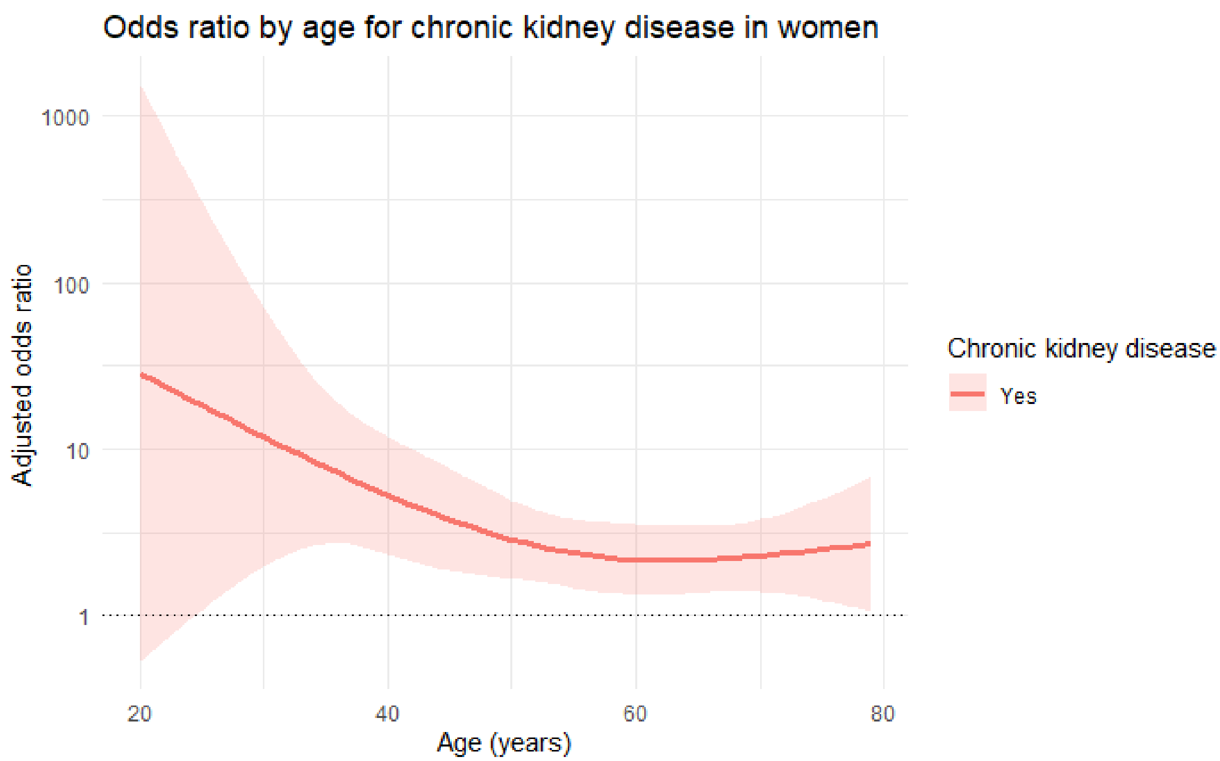


Figure 6. Model-adjusted odds ratios by age for chronic kidney disease in men (top) and women (bottom); reference is not having chronic kidney disease

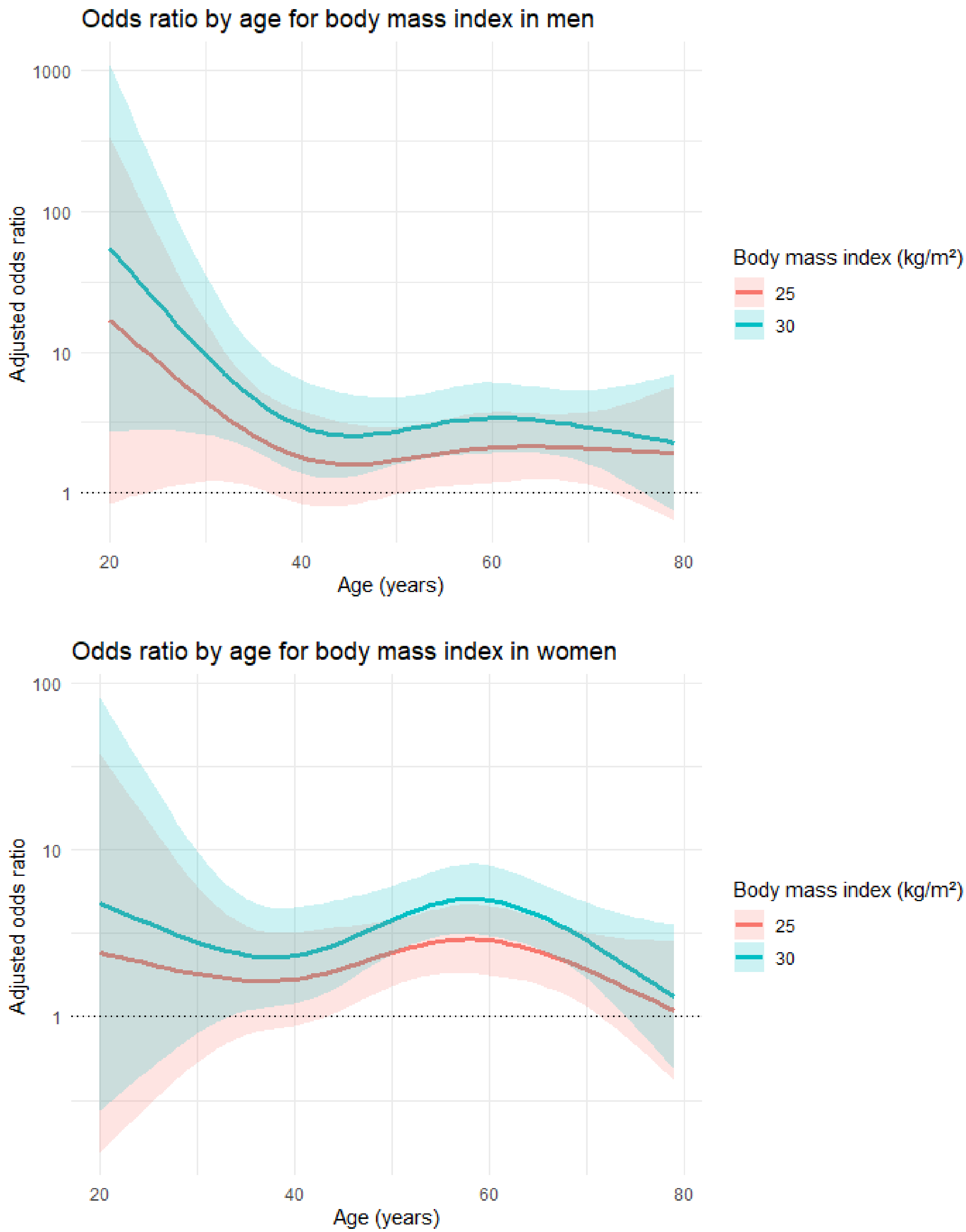


Figure 7. Model-adjusted odds-ratios by age for body mass index in men (top) and women (bottom); reference is having body mass index of 18.5 kg/m^2

3.5. Examples of hypertension risk profiles

Figure 8 demonstrates the basis of a hypertension risk profile for a 24-year-old male using HTNPoRT. For this given individual, the risk profile showcases their predicted probability of hypertension outputted from the male reduced model, the average predicted probability of hypertension among men used to derive the same model, and a SHAP plot showing the ranked importance of their features to their predicted probability value. SHAP values for a given individual are relative to the model's average prediction and sum to the difference between the individual and average predictions (48). Positive SHAP values on the plot represent features shifting the numerical value of the individual's predicted probability higher, while negative SHAP values represent features shifting it lower. This individual's predicted probability of currently having hypertension is 0.20% and the average predicted probability among Canadian men is 27.58%. This individual's presence of a family history of hypertension increases their probability of hypertension relative to the average by around 3.14%, while their age of 24, body mass index of 19.6 kg/m^2, and non-diabetic status decrease their probability of hypertension relative to the average by about 17.19%, 7.89%, and 3.70%, respectively. Therefore, the individual in question could consider not replicating any of their family's concerning lifestyle habits while maintaining their healthy weight and blood sugar to prevent hypertension and improve their profile. Note that family history is associated with hypertension risk through not only genetic factors, but also environmental factors as there are significant differences in body weight control, physical activity, and diet between those with and without a positive family history for hypertension (49).

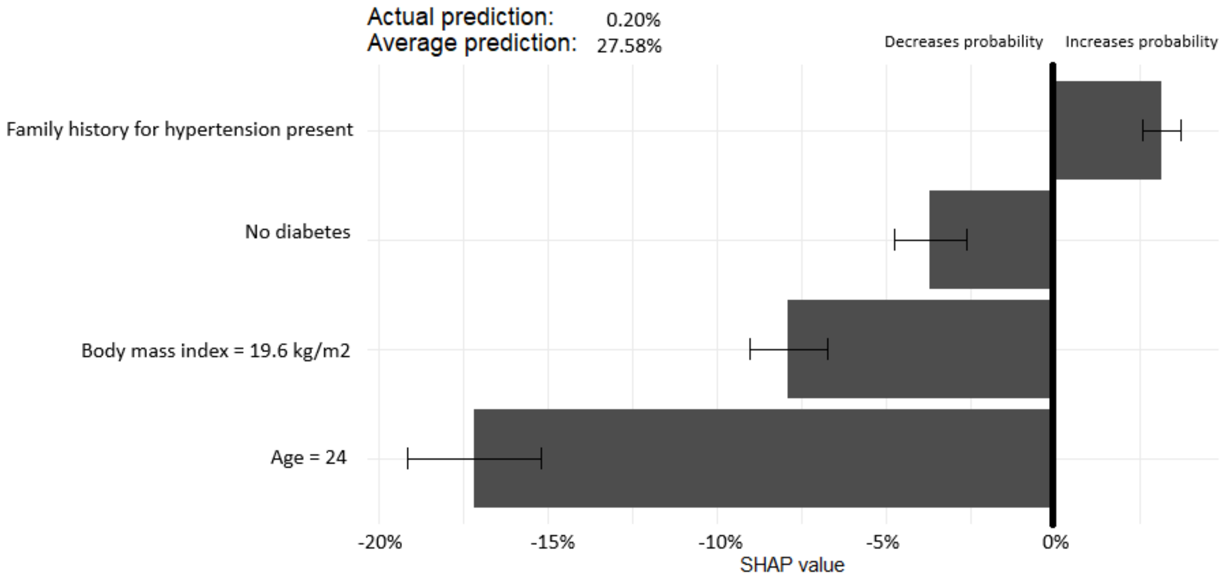


Figure 8. Hypertension risk profile of a 24-year-old male with a predicted hypertension probability of 0.20%; SHAP plot shows importance (i.e., SHAP value) of individual's features (written on left) increasing and decreasing their predicted probability relative to the average predicted probability of 27.58% among Canadian men, with error bars representing standard errors of individual-level SHAP values

Figure 9 demonstrates the basis of a hypertension risk profile for a 74-year-old male also using HTNPoRT. This individual's predicted probability of currently having hypertension is 75.25% and once again, the average predicted probability among Canadian men is 27.58%. Their most influential risk factor on their predicted probability is their age of 74, which increases their probability of hypertension relative to the average by around 27.95%. Next, this individual's diabetes and body mass index of 35.3 kg/m^2 increase their probability of hypertension relative to the average by about 20.17% and 6.90%, respectively. Finally, their absence of a family history of hypertension decreases their probability of hypertension relative to the average by about 5.61%. Therefore, the individual in question could consider specific interventions to effectively lower their weight and control their blood sugar and assess any benefits to their profile and overall health while also considering to get their blood pressure checked.

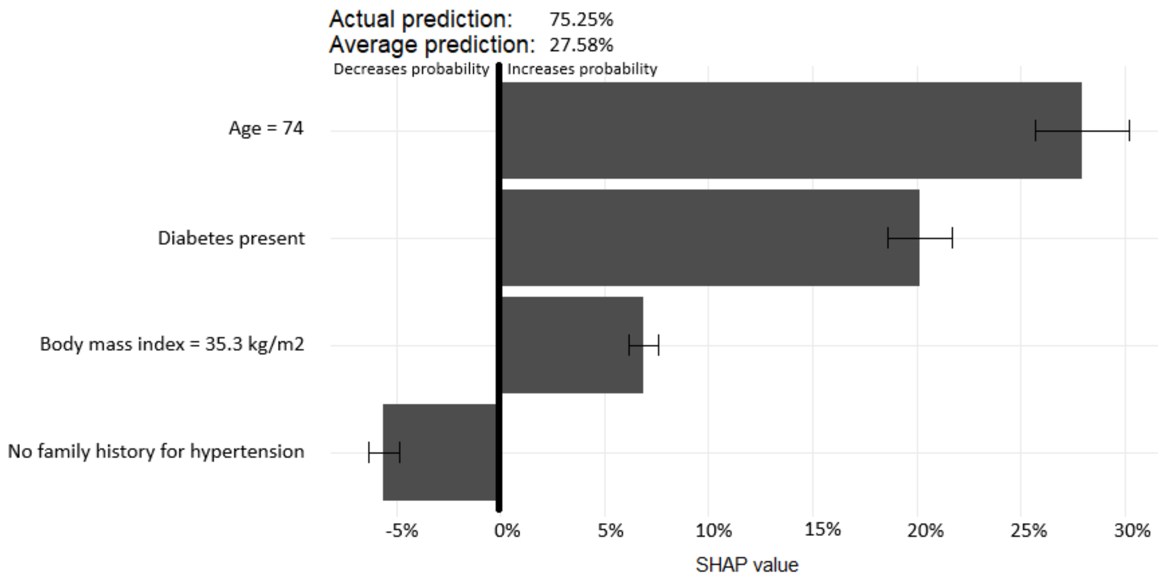


Figure 9. Hypertension risk profile of a 74-year-old male with a predicted hypertension probability of 75.25%; SHAP plot shows importance (i.e., SHAP value) of individual's features (written on left) increasing and decreasing their predicted probability relative to the average predicted probability of 27.58% among Canadian men, with error bars representing standard errors of individual-level SHAP values

Although the risk profiles of Figures 8 and 9 can inform its user of features increasing and decreasing the value of their predicted probability of hypertension, standard error bars have been placed on the SHAP values to show the uncertainty associated with these values and have been computed for a single individual rather than the whole study population. With the individual-level standard error bars being added and the model data being cross-sectional with no causal inferences allowed, individuals should therefore be cautious while making any lifestyle-related decisions and perhaps facilitate a discussion on their risk profiles with their health provider, all upon identifying and characterizing their most influential risk factors for hypertension.

Chapter 4 - Discussion

The Hypertension Population Risk Tool (HTNPoRT) is a diagnostic predictive model for hypertension. It can be used to inform and educate the public in understanding their risk of hypertension. The sex-specific diagnostic models of HTNPoRT are discriminating and well-calibrated models predicting hypertension probability at present time in community-dwelling Canadian adults, developed and validated using nationally representative, multiethnic, and routinely collected population-based survey data from the CHMS. The models incorporate easy-to-collect and modifiable predictors available to the public, making HTNPoRT suited for individual and population health planning. The models also yield SHAP-derived risk profiles designed to show which predictors are most important in the computation of predicted hypertension probabilities and highlight people who would benefit from targeted interventions. Given that HTNPoRT is well-calibrated across a wide range of equity-relevant subgroups, Canadian individuals, whether they have been formally diagnosed with hypertension or not, can use its models and their risk profiles to make informed decisions upon identifying and characterizing their most influential risk factors for hypertension. Healthcare decision-makers can use the models and risk profiles to identify populations at risk of hypertension who need closer follow-up and earlier preventative interventions. Model predictors are centered on their weighted means, allowing for recalibration in populations with different risk factor distributions, and risk assessment in those giving incomplete responses by predicting with population means.

Prediction models like HTNPoRT can support identifying high-risk hypertension subpopulations and informing the evaluation and design of preventive interventions tailored to population needs (9). This is particularly important for younger adults aged 20-39, included in our sample as preventive interventions are more likely to be effective in them (7, 8). HTNPoRT can also support identifying individuals with undiagnosed hypertension and encouraging them to get their blood pressure checked, as undiagnosed and untreated hypertension can lead to complications such as cardiovascular disease and premature death (4). The use of the population-based CHMS to develop and validate HTNPoRT improves on generalizability issues of existing hypertension models typically designed in clinical settings. Not only does the CHMS represent 96% of the Canadian population, but it also has diverse primary data on blood pressure and a comprehensive list of risk factors measured using a standardized survey, thus allowing for robust public-health focused applications outside clinical settings. Despite possible misclassifications arising from respondents misunderstanding medication use or using multi-purpose medications, the inclusion of antihypertensive medications in the hypertension definition captures those with both controlled and uncontrolled hypertension without adversely affecting model performance. Meanwhile, the standardized measurement of blood pressure with the automated electronic BpTRU™ allows for more accuracy in ascertaining the outcome regardless of correction factors. While also helping to reduce model overfitting and increase prediction precision, the large sample size from the survey provides us with statistical power to develop and validate HTNPoRT with more risk factors and greater specification. HTNPoRT's favourable performance can be attributed to greater model specification, including more variables, interaction terms, and flexible modelling of continuous variables with restricted cubic splines. Increased model complexity may be often associated with overfitting, but our pre-specification of predictors limited this risk for the well-performing HTNPoRT, as well as the risk of type I errors as predictors were included in the models regardless of strength of association. The high discriminative ability of our models means that multiple different risk factors together (e.g., sociodemographics and health behaviours) are important in predicting hypertension.

Compared to HTNPoRT, existing models predicting hypertension in Canada (c-statistic: 0.77) did not consider dose-response relationships of its continuous predictors and excluded interaction terms, all while being derived from data only from Alberta (8, 27). A recent review identified 75 regression-based diagnostic and prognostic models predicting hypertension in various settings elsewhere across the world (50). The overall pooled c-statistic for these models was 0.75 (95% CI: 0.73-0.77), with 18 of the models having a c-statistic of at least 0.80 and thus demonstrating excellent calibration. Only one model demonstrated exceptional discrimination with a c-statistic of at least 0.90 (c-statistic: 0.97) (13). However, these well-performing models include genetic, biomarker, and clinically obtained predictors (like blood pressure itself) which are insufficient for individual and population-level applications. The only model in the review using all easy-to-collect risk factors as predictors was a diagnostic model which predicted hypertension among individuals aged 18 and older using telephone-based health survey data from the American Centers for Disease Control and Prevention (c-statistic: 0.74) (51). Its predictors included age, sex, marital status, highest education level, income level, weight, height, exercise, smoking frequency, alcohol drinking frequency, diabetes, and hyperlipemia. Although this model is appropriate for population health planning and individuals wanting simple lifestyle advice, it did not specify dose-response relationships for its continuous risk factors, rendering its performance weaker than HTNPoRT. A diagnostic model outside of the recent review, which also used only easy-to-collect risk factors as predictors, predicted hypertension among 353 patients in two Burundi hospitals, rivaling HTNPoRT with excellent discrimination (c-statistic: 0.89) (52). Its predictors included age group, highest education level, hypertension family history, body mass index group, current smoking status, and chronic kidney disease. However, its low sample size, development from a clinical population, and categorization of continuous risk factors limits its generalizability and usefulness in evaluating hypertension prevention strategies. Nonetheless, none of the models were known to have included for their users, a risk profile showcasing the influence of their predictors on their predicted hypertension outcome.

Diagnostic prediction models are not used to inform causal inferences, but regardless, the SHAP-adjusted odds ratios presented in Table 4 are mostly in line with associations between risk factors and hypertension seen in causal literature, with a few exceptions: current smoking, insufficient sleep, poor or fair mental health, and high stress. Although relationships between these few risk factors and cardiovascular disease are well-established, relationships between these same risk factors and hypertension are rather more weak and inconclusive (4). First, current smoking is seen to have a protective effect against hypertension classification as compared to never smoking in both men (OR: 0.84, 95% CI: 0.83-0.85) and women (OR: 0.86, 95% CI: 0.85-0.87). Despite smoking being one of the leading avoidable risks for overall morality, the association between smoking and hypertension appears to be weak in magnitude and not well-established across published literature, with some studies reporting insignificant yet inverse relationships (4, 53). One study postulated that the association between smoking and the development of hypertension is diverse in different urban settings (54). Moreover, the inverse associations can be attributed to current smokers having lower body mass indexes compared to former and never smokers (55).

Second, there is also an inverse association between insufficient sleep and hypertension in both men (OR: 0.92, 95% CI: 0.91-0.93) and women (OR: 0.88, 95% CI: 0.87-0.89). Additionally, inverse associations were even seen between having poor or fair mental health and hypertension in both men (OR: 0.93, 95% CI: 0.92-0.93) and women (OR: 0.85, 95% CI: 0.84-0.85), as well as between high stress and hypertension in both men (OR: 0.93, 95% CI: 0.93-0.94) and women (OR: 0.98, 95% CI: 0.98-0.98). Observational studies have reported weak associations between the three aforementioned risk factors and hypertension (4). Furthermore, regarding a potential reason for the inverse associations, men and women with shorter sleep durations, poorer mental health, and higher perceived stress levels tend to be younger in age (56–58).

Meanwhile, being a low-risk drinker has a protective effect as compared to never drinking in women only (OR: 0.79, 95% CI: 0.79-0.80), though this has been observed in a few studies which stated that light alcohol consumption may reduce hypertension risk in women through favourable changes in high-density lipoprotein cholesterol (59, 60). On the other hand, compared to eating a healthy diet (i.e., eating fruits and vegetables at least 5 times daily), eating a poor diet has no association in men (OR: 1.00, 95% CI: 1.00-1.00) and a very weak positive association in women (OR: 1.08, 95% CI: 1.08-1.09). Poor diet is clearly associated with hypertension risk as the DASH and Mediterranean diets are interventions which are known to significantly reduce blood pressure and hypertension risk (4), but this effect is not represented by the only diet measure available for and used in HTNPoRT. Relationships observed between diet and health can be attenuated when diet is ascertained through self-reporting as it is difficult to ascertain diet accurately through such means (61).

When waist-to-height ratio and its interactions are included in the model, increasing waist-to-height ratio becomes highly associated with increased odds of hypertension in only men, while increasing body mass index becomes highly associated with increased odds of hypertension in only women (see paragraph immediately following Table 4). These associations are so strong that increasing body mass index becomes slightly protective in men and increasing waist-to-height ratio becomes less associated with hypertension in women at the population level. The average SHAP values for the male index categories and the female ratio categories thus have been depleted a bit beyond and to almost of those of their reference categories, respectively, by the male ratio and female index. Moreover, body mass index is removed from the male model in the stepdown procedure, as waist-to-height ratio is from the female model (Table 1). One cohort study showed that men with higher body mass indexes had no increased hypertension risk when their waist-to-height ratios were low (62). Waist-to-height ratio being a stronger predictor of hypertension in men and body mass index being a stronger predictor of hypertension in women can likely be due to men tending to accumulate more visceral abdominal fat (better reflected by the ratio) and women tending to accumulate more subcutaneous lower body fat (better reflected by the index); both such accumulations can lead to hypertension (63). With waist-to-height ratio being considered less easy-to-collect than body mass index, body mass index can be considered the more practical measure of adiposity for predicting hypertension in HTNPoRT.

Our specifications of age, body mass index, and physical activity minutes with restricted cubic splines are in line with literature reporting their non-linear dose-responses with hypertension. Increased blood pressure is often seen as a consequence of ageing in industrialized settings, while blood pressure and hypertension risk are health outcomes known to rise non-linearly with increasing age (64, 65). As for body mass index and physical activity minutes, restricted cubic spline analyses demonstrated that hypertension risk increased non-linearly as the former increased and the latter decreased (66, 67). Meanwhile, our specifications of sleep duration and daily fruit and vegetable consumption without any flexible functions align with their linear dose-responses in meta-analyses (68, 69). Regarding our specified two-way interactions between age and clinically relevant variables, with increased blood pressure being inevitable with age, older age can attenuate the magnitude of association of any risk factors interacting with it (64, 70). Obesity, diabetes, and chronic kidney disease are particularly known to be much greater risk factors of hypertension at younger ages than at older ages (1).

Returning to the inverse associations seen with current smoking, insufficient sleep, poor or fair mental health, and high stress, individuals in these risk categories are likely to have highly protective features from stronger predictors. In the sample, current smokers had lower body mass indexes than former and never smokers, while those with poorer mental health and higher stress were younger than those in their respective reference categories (Appendix 12). Furthermore, the odds ratios for those sleeping 7 hours/night (reference category: 2 hours/night) were higher than the odds ratios for those sleeping 4.5 hours/night at younger ages (Appendix 11). This causes the average SHAP value for these risk categories to dip below the average SHAP value for their respective reference categories and thus cause the mean difference (i.e., log(OR)) to become negative across the study populations. Again, SHAP values for a given individual are relative to the model's average prediction and sum to the difference between the individual and average predictions (48). A risk factor like current smoking could thus have a negative SHAP value (or a protective factor like never smoking could thus have a positive SHAP value) at the individual and/or population levels if the model primarily predicts hypertension through heavily stronger predictors like age, diabetes, and body mass index.

For these reasons, as well as to reduce user input burden, the reduced models will serve as the final models at the basis of online tools users can use to ascertain their predicted probability of hypertension and their hypertension risk profile without any counterintuitive information and noise from weaker predictors. The reduced models perform as well as the full models in the overall population and across the most important subpopulations. However, the full models could be considered for subpopulations in which the reduced models do not perform as well (i.e., men with chronic kidney disease and men who are heavy drinkers of alcohol), or for investigating individual or population-level attributions of predictors not in the reduced models. With any use of the full models, caution should be exercised when explaining counterintuitive information on risk profiles; standard error bars were placed on individual-level SHAP values in the reduced model risk profiles (Figures 8-9) and should also be placed in any full model risk profiles.

4.1. Limitations

There are a few key limitations to this study. First, the list of predictors is limited to variables available in the cycles of the CHMS when in fact, there are potential factors outside the CHMS which contribute to hypertension (such as salt intake level and neighbourhood deprivation) and if included, may improve model performance. Ethnicity was not included in the models given that some of its categories had low counts in the CHMS, and merging such categories would have inappropriately combined heterogeneous groups, potentially obscuring important distinctions. Ethnicity is associated with hypertension risk through both genetic and cultural factors. While cultural factors such as diet and lifestyle are accounted for by other sociodemographic or behavioural measures, the genetic contribution remains unmeasured. However, evidence suggests that the genetic component of hypertension risk may be relatively small and less well-defined, making it difficult to quantify precisely (4, 71, 72). Regardless, we assessed 17 variables while not surpassing the allotted 68 degrees of freedom for the survey but still having sufficient statistical power to develop highly specified and complex models.

Second, despite HTNPoRT representing the Canadian adult population aged 20 to 79 years, some groups are not captured by the CHMS, including on-reserve Indigenous individuals. Third, given the cross-sectional nature of the CHMS, we were unable to determine the temporality of the associations between various risk factors and hypertension and thus cannot derive any causal inferences. Fourth, measurement or data encoding errors in the CHMS, as well as use of self-reported predictors, can cause misclassification. This is notable with diet which is difficult to ascertain accurately through self-reporting (61). However, HTNPoRT already has high discrimination and favourable calibration, while other studies found that chronic conditions can be properly assessed using self-reported measures (73, 74). Fifth, logistic regression might be viewed as an inferior approach compared to more sophisticated machine learning approaches, but HTNPoRT is highly specified, so machine learning models would not be expected to perform any better without access to more complex data outside of the CHMS. Nevertheless, HTNPoRT will allow members of the public to explore their hypertension risk profiles in relation to their lifestyle behaviours and facilitate a discussion with a health provider if needed.

4.2. Future directions

Future research could involve externally validating HTNPoRT with a survey which is similar to the CHMS (e.g., National Health and Nutrition Examination Survey), examining associations between risk factors and hypertension in populations excluded from the CHMS, investigating predictabilities of more adiposity measures towards hypertension, and conducting a study to assess whether individuals can adhere to lifestyle advice from HTNPoRT's risk profiles and whether there are benefits to their predicted hypertension probability at follow-up.

4.3. Conclusions

To our knowledge, the models of HTNPoRT are the first regression diagnostic models to predict hypertension in and provide risk profiles for adults aged between 20-79 residing in the 10 provinces. The models are discriminating and well-calibrated. The models and risk profiles can be used by members of the public and health policymakers to support planning and decision-making on addressing hypertension burden.

References

1. Leung AA, Bushnik T, Hennessy D, McAlister FA, Manuel DG. Risk Factors for Hypertension in Canada. Health Rep. 2019 Feb;30(82):3–13.

2. Murray CJL, Aravkin AY, Zheng P, Abbafati C, Abbas KM, Abbasi-Kangevari M, et al. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020;396(10258):1223–49.

3. Nerenberg KA, Zarnke KB, Leung AA, Dasgupta K, Butalia S, McBrien K, et al. Hypertension Canada’s 2018 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children. Can J Cardiol. 2018 May 1;34(5):506–25.

4. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020 Apr;16(4):223.

5. Pazoki R, Dehghan A, Evangelou E, Warren H, Gao H, Caulfield M, et al. Genetic Predisposition to High Blood Pressure and Lifestyle Factors: Associations With Midlife Blood Pressure Levels and Cardiovascular Events. Circulation. 2018 Feb 13;137(7):653–61.

6. Jousilahti P, Laatikainen T, Peltonen M, Borodulin K, Männistö S, Jula A, et al. Primary prevention and risk factor reduction in coronary heart disease mortality among working aged men and women in eastern Finland over 40 years: population based observational study. BMJ. 2016 Mar 1;352:i721.

7. DeGuire J, Clarke J, Rouleau K, Roy J, Bushnik T. Blood pressure and hypertension. Health Rep. 2019 Feb;30(2):14–21.

8. Chowdhury MZI, Leung AA, Sikdar KC, O’Beirne M, Quan H, Turin TC. Development and validation of a hypertension risk prediction model and construction of a risk score in a Canadian population. Sci Rep. 2022 July 27;12(1):12780.

9. Manuel DG, Rosella LC, Hennessy D, Sanmartin C, Wilson K. Predictive risk algorithms in a population setting: an overview. J Epidemiol Community Health. 2012;66:859–65.

10. Jahangiry L, Farhangi MA, Rezaei F. Framingham risk score for estimation of 10-years of cardiovascular diseases risk in patients with metabolic syndrome. J Health Popul Nutr. 2017 Nov 13;36(1):36.

11. 2016 European Guidelines on cardiovascular disease prevention in clinical practice | European Heart Journal | Oxford Academic [Internet]. Available from: https://academic.oup.com/eurheartj/article/37/29/2315/1748952

12. D’Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General Cardiovascular Risk Profile for Use in Primary Care. Circulation. 2008 Feb 12;117(6):743–53.

13. Choi YH, Chowdhury R, Swaminathan B. Prediction of hypertension based on the genetic analysis of longitudinal phenotypes: a comparison of different modeling approaches for the binary trait of hypertension. BMC Proc. 2014 June 17;8(1):S78.

14. Niiranen TJ, Havulinna AS, Langén VL, Salomaa V, Jula AM. Prediction of Blood Pressure and Blood Pressure Change With a Genetic Risk Score. J Clin Hypertens. 2016;18(3):181–6.

15. Lim NK, Lee JY, Lee JY, Park HY, Cho MC. The Role of Genetic Risk Score in Predicting the Risk of Hypertension in the Korean population: Korean Genome and Epidemiology Study. PLOS ONE. 2015 June 25;10(6):e0131603.

16. Lu X, Huang J, Wang L, Chen S, Yang X, Li J, et al. Genetic Predisposition to Higher Blood Pressure Increases Risk of Incident Hypertension and Cardiovascular Diseases in Chinese. Hypertension. 2015 Oct;66(4):786–92.

17. Fava C, Sjögren M, Montagnana M, Danese E, Almgren P, Engström G, et al. Prediction of Blood Pressure Changes Over Time and Incidence of Hypertension by a Genetic Risk Score in Swedes. Hypertension. 2013 Feb;61(2):319–26.

18. Asgari S, Khalili ,Davood, Mehrabi ,Yadollah, Kazempour-Ardebili ,Sara, Azizi ,Fereidoun, and Hadaegh F. Incidence and risk factors of isolated systolic and diastolic hypertension: a 10 year follow-up of the Tehran Lipids and Glucose Study. Blood Press. 2016 May 3;25(3):177–83.

19. Kanegae H, Oikawa T, Suzuki K, Okawara Y, Kario K. Developing and validating a new precise risk-prediction model for new-onset hypertension: The Jichi Genki hypertension prediction model (JG model). J Clin Hypertens. 2018;20(5):880–90.

20. Chen Y, Wang C, Liu Y, Yuan Z, Zhang W, Li X, et al. Incident hypertension and its prediction model in a prospective northern urban Han Chinese cohort study. J Hum Hypertens. 2016 Dec;30(12):794–800.

21. Zhang W, Wang L, Chen Y, Tang F, Xue F, Zhang C. Identification of Hypertension Predictors and Application to Hypertension Prediction in an Urban Han Chinese Population: A Longitudinal Study, 2005-2010. Prev Chronic Dis. 2015 Oct 29;12:E184.

22. Syllos DH, Calsavara VF, Bensenor IM, Lotufo PA. Validating the Framingham Hypertension Risk Score: A 4-year follow-up from the Brazilian Longitudinal Study of the Adult Health (ELSA-Brasil). J Clin Hypertens. 2020;22(5):850–6.

23. Lee BJ, Kim JY. A Comparison of the Predictive Power of Anthropometric Indices for Hypertension and Hypotension Risk. PLOS ONE. 2014 Jan 23;9(1):e84897.

24. Parikh NI, Pencina MJ, Wang TJ, Benjamin EJ, Lanier KJ, Levy D, et al. A risk score for predicting near-term incidence of hypertension: the Framingham Heart Study. Ann Intern Med. 2008 Jan 15;148(2):102–10.

25. Paynter NP, Cook NR, Everett BM, Sesso HD, Buring JE, Ridker PM. Prediction of Incident Hypertension Risk in Women with Currently Normal Blood Pressure. Am J Med. 2009 May;122(5):464–71.

26. Kivimäki M, Tabak AG, Batty GD, Ferrie JE, Nabi H, Marmot MG, et al. Incremental predictive value of adding past blood pressure measurements to the Framingham hypertension risk equation: the Whitehall II Study. Hypertens Dallas Tex 1979. 2010 Apr;55(4):1058–62.

27. Chowdhury MZI, Leung AA, Walker RL, Sikdar KC, O'Beirne M, Quan H, et al. A comparison of machine learning algorithms and traditional regression-based statistical modeling for predicting hypertension incidence in a Canadian population. Sci Rep. 2023 Jan 2;13(1):13.

28. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. The Lancet. 2007;370(9596):1453–7.

29. Collins GS, Moons KGM, Dhiman P, Riley RD, Beam AL, Calster BV, et al. TRIPOD+AI statement: updated guidance for reporting clinical prediction models that use regression or machine learning methods. BMJ. 2024 Apr 16;385:e078378.

30. Steyerberg EW. Clinical Prediction Models: A Practical Approach to Development, Validation, and Updating [Internet]. New York, NY: Springer New York; 2009. (Statistics for Biology and Health). Available from: http://link.springer.com/10.1007/978-0-387-77244-8

31. Harrell Jr FE. Regression modeling strategies: With Applications, to Linear Models, Logistic and Ordinal Regression, and Survival Analysis. Springer; 2016.

32. Islam R, Bushnik T, Sood M, Taljaard M, McAlister F, Manuel DG. A Protocol for Development and Validation of a Diagnostic Model – The Hypertension Population Risk Tool (HTNPoRT) – to Predict Hypertension and Describe Risk Profiles: A Population-Based Cross-Sectional Study of Canadians. 2024 Oct 24; Available from: https://osf.io/v27mw

33. Government of Canada SC. Canadian Health Measures Survey (CHMS) [Internet]. 2018. Available from: https://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&Id=1195092

34. Wright JM, Mattu GS, Perry TL, Gelferc ME, Strange KD, Zorn A, et al. Validation of a new algorithm for the BPM-100 electronic oscillometric office blood pressure monitor. Blood Press Monit. 2001;6(3):161–5.

35. Mattu GS, Perry TL, Wright JM. Comparison of the oscillometric blood pressure monitor (BPM-100(Beta)) with the auscultatory mercury sphygmomanometer. Blood Press Monit. 2001;6(3):153–9.

36. Myers MG, McInnis NH, Fodor GJ, Leenen FHH. Comparison between an automated and manual sphygmomanometer in a population survey. Am J Hypertens. 2008;21(3):280–3.

37. Bryan S, Saint-Pierre Larose M, Campbell N, Clarke J, Tremblay MS. Resting blood pressure and heart rate measurement in the Canadian Health Measures Survey, cycle 1. Health Rep. 2010 Mar;21(1):71–8.

38. Bushnik T. Factors associated with hypertension control among older Canadians. Health Rep. 2018 June;29(82).

39. Riley RD, Ensor J, Snell KIE, Harrell FE, Martin GP, Reitsma JB, et al. Calculating the sample size required for developing a clinical prediction model. BMJ. 2020 Mar 18;368:m441.

40. Riley RD, Snell KI, Ensor J, Burke DL, Harrell FE, Moons KG, et al. Minimum sample size for developing a multivariable prediction model: PART II - binary and time-to-event outcomes. Stat Med. 2019 Mar 30;38(7):1276–96.

41. Buuren S van, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. J Stat Softw. 2011;45(3):1–67.

42. Ambler G, Brady AR, Royston P. Simplifying a prognostic model: a simulation study based on clinical data. Stat Med. 2002 Dec 30;21(24):3803–22.

43. Steyerberg EW, Vickers AJ, Cook NR, Gerds T, Gonen M, Obuchowski N, et al. Assessing the performance of prediction models: a framework for traditional and novel measures. Epidemiol Camb Mass. 2010 Jan;21(1):128–38.

44. Vergouwe Y, Steyerberg EW, Eijkemans MJC, Habbema JDF. Substantial effective sample sizes were required for external validation studies of predictive logistic regression models. J Clin Epidemiol. 2005 May;58(5):475–83.

45. Peirson L, Rosella L. Navigating knowledge to action: a conceptual map for facilitating translation of population health risk planning tools into practice. J Contin Educ Health Prof. 2015;35(2):139–47.

46. Rosella LC, Bornbaum C, Kornas K, Lebenbaum M, Peirson L, Fransoo R, et al. Evaluating the Process and Outcomes of a Knowledge Translation Approach to Supporting Use of the Diabetes Population Risk Tool (DPoRT) in Public Health Practice. Can J Program Eval. 2018 Mar;33(1):21–48.

47. Orsini N, Moore A, Wolk A. Interaction Analysis Based on Shapley Values and Extreme Gradient Boosting: A Realistic Simulation and Application to a Large Epidemiological Prospective Study. Front Nutr [Internet]. 2022 July 18 [cited 2025 July 20];9. Available from: https://www.frontiersin.org/journals/nutrition/articles/10.3389/fnut.2022.871768/full

48. Ariza-Garzón MJ, Arroyo J, Caparrini A, Segovia-Vargas MJ. Explainability of a Machine Learning Granting Scoring Model in Peer-to-Peer Lending. IEEE Access. 2020;8:64873–90.

49. Krtalic B, Knezevic T, Zeljkovic-Vrkic T, Kos J, Pecin I, Gellineo L, et al. Family History, Blood Pressure And Life Style. Results From EHUH Study. J Hypertens. 2019 July;37:e230.

50. Chowdhury MZI, Naeem I, Quan H, Leung AA, Sikdar KC, O'Beirne M, et al. Prediction of hypertension using traditional regression and machine learning models: A systematic review and meta-analysis. PLoS ONE. 2022 Apr 7;17(4):e0266334.

51. Wang A, An N, Chen G, Li L, Alterovitz G. Predicting hypertension without measurement: A non-invasive, questionnaire-based approach. Expert Syst Appl. 2015 Nov 30;42(21):7601–9.

52. Iradukunda A, Odjidja EN, Ndayishima SK, Ngendakumana E, Ndayishimiye GP, Sinarinzi D, et al. Prevalence and predictive risk factors of hypertension in patients hospitalized in Kamenge Military hospital and Kamenge University teaching hospital in 2019: A fixed effect modelling study in Burundi. PLOS ONE. 2021 Dec 13;16(12):e0260225.

53. Jareebi MA. The Association Between Smoking Behavior and the Risk of Hypertension: Review of the Observational and Genetic Evidence. J Multidiscip Healthc. 2024 July 10;17:3265–81.

54. Mohammed Nawi A, Mohammad Z, Jetly K, Abd Razak MA, Ramli NS, Wan Ibadullah WAH, et al. The Prevalence and Risk Factors of Hypertension among the Urban Population in Southeast Asian Countries: A Systematic Review and Meta-Analysis. Int J Hypertens. 2021 Feb 10;2021:6657003.

55. Kaufman A, Augustson EM, Patrick H. Unraveling the Relationship between Smoking and Weight: The Role of Sedentary Behavior. J Obes. 2012;2012:735465.

56. Bruce ES, Lunt L, McDonagh JE. Sleep in adolescents and young adults. Clin Med. 2017 Oct;17(5):424–8.

57. Jurewicz I. Mental health in young adults and adolescents – supporting general physicians to provide holistic care. Clin Med. 2015 Apr;15(2):151–4.

58. Johnson MD, Krahn HJ, Galambos NL. Perceived stress trajectories from age 25 to 50 years. Int J Behav Dev. 2023 May 1;47(3):233–42.

59. Okojie OM, Javed F, Chiwome L, Hamid P. Hypertension and Alcohol: A Mechanistic Approach. Cureus. 12(8):e10086.

60. Sesso HD, Cook NR, Buring JE, Manson JE, Gaziano JM. Alcohol Consumption and the Risk of Hypertension in Women and Men. Hypertension. 2008 Apr;51(4):1080–7.

61. Bailey RL. Overview of Dietary Assessment Methods for Measuring Intakes of Foods, Beverages, and Dietary Supplements in Research Studies. Curr Opin Biotechnol. 2021 Aug;70:91–6.

62. Salim AA, Kawasoe S, Kubozono T, Ojima S, Kawabata T, Ikeda Y, et al. Assessment of Future Hypertension Risk by Sex Using Combined Body Mass Index and Waist-to-Height Ratio. Circ Rep. 4(1):9–16.

63. Chang E, Varghese M, Singer K. Gender and Sex Differences in Adipose Tissue. Curr Diab Rep. 2018 July 30;18(9):69.

64. Pinto E. Blood pressure and ageing. Postgrad Med J. 2007 Feb;83(976):109–14.

65. Monaghan C, de Andrade Moral R, Power JM. Modelling the Non-linear Associations between Age and Health: Implications for Care. Age Ageing. 2024 Sept 1;53(Supplement_4):afae178.084.

66. Zhang W, He K, Zhao H, Hu X, Yin C, Zhao X, et al. Association of body mass index and waist circumference with high blood pressure in older adults. BMC Geriatr. 2021 Apr 19;21(1):260.

67. Zhou L, Feng W, Xiang N, Cheng Y, Ya X, Wang M, et al. Association between physical activity dimensions and the risk of hypertension among middle and older adults: A cross-sectional study in China. Front Public Health. 2022 Sept 24;10:995755.

68. Li H, Ren Y, Wu Y, Zhao X. Correlation between sleep duration and hypertension: a dose-response meta-analysis. J Hum Hypertens. 2019 Mar;33(3):218–28.

69. Wu L, Sun D, He Y. Fruit and vegetables consumption and incident hypertension: dose–response meta-analysis of prospective cohort studies. J Hum Hypertens. 2016 Oct;30(10):573–80.

70. Cohen L, Curhan GC, Forman JP. Influence of Age on the Association between Lifestyle Factors and Risk of Hypertension. J Am Soc Hypertens JASH. 2012;6(4):284–90.

71. Takase M, Hirata T, Nakaya N, Nakamura T, Kogure M, Hatanaka R, et al. Associations of combined genetic and lifestyle risks with hypertension and home hypertension. Hypertens Res. 2024 Aug;47(8):2064–74.

72. Basu A. Use of race in clinical algorithms. Sci Adv [Internet]. 2023 May;9(21). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10219586/

73. Ning F, Zhang L, Dekker JM, Onat A, Stehouwer CD, Yudkin JS, et al. Development of coronary heart disease and ischemic stroke in relation to fasting and 2-hour plasma glucose levels in the normal range. Cardiovasc Diabetol. 2012 June 25;11:76.

74. Manuel DG, Tuna M, Bennett C, Hennessy D, Rosella L, Sanmartin C, et al. Development and validation of a cardiovascular disease risk-prediction model using population health surveys: the Cardiovascular Disease Population Risk Tool (CVDPoRT). Can Med Assoc J. 2018 July 23;190(29):E871–82.

Appendices

Appendix 1 – Approval letter from Ottawa Health Science Network Research Ethics Board

The Ottawa Hospital Research Institute | L'Hôpital d'Ottawa Institut de recherche

November 22, 2024

Dr. Douglas Manuel

Ottawa Hospital Research Institute
Admin Services Building
Room 2-012, Box 693
1053 Carling Avenue
Ottawa, ON K1Y 4E9

Re: OHRI Institutional Approval for Ottawa Health Science Network Research Ethics Board (OHSN-REB) Submission

Protocol ID#: 20240693-01H;

Development and Validation of a Diagnostic Model to Predict Hypertension and Describe Risk Profiles: A Population-Based Cross-Sectional Study of Canadians

Dear Dr. Douglas Manuel,

This letter serves as **Ottawa Hospital Research Institute (OHRI)** Institutional Approval for the above-referenced study. Please maintain this documentation in your investigator study file.

Based on the information you provided about this study through the Clinical Research Registration Form, you have satisfied the requirements for institutional (OHRI) approval. This includes initial research ethics approval by OHSN-REB, appropriate departmental/service area notifications and execution (fully signed versions) of all agreement(s) required to begin the study locally. Please note there may be additional agreement(s) pending execution that are required to send funds, samples, or data to external sites, but are not required for you to begin your study locally.

Changes and/or additions to your study that may require additional agreement(s) or revisions to existing agreement(s) must be communicated to the OHRI Contracts Office. This should be undertaken simultaneously with any related OHSN-REB amendment submission.

Changes and/or additions to your study that affect various hospital/institution departments (e.g., pharmacy, Department of Medical Imaging, EORLA, EEG, etc.) must be communicated to the relevant departments.

As mentioned in the 'Response' tab of the Ethics application, you have 3 months from the date of initial OHSN-REB approval to submit French documents including the translation certificate to OHSN-REB through the Translated Documents section of the ethics application (if applicable).

Should you have any questions, please contact REBadministration@ohri.ca or 613-798-5555 extension 16719.

Penny Phillips
Director, Clinical Research Administration
Ottawa Hospital Research Institute | Institut de recherche de l'Hôpital d'Ottawa

Letter generated by Renee Todd (userid:rtodd) on 11/22/2024 7:46:34 AM

Civic Campus, Box 675, 725 Parkdale Avenue, Ottawa, Ontario, K1Y 4E9
613-798-5555 extension 16719 Fax : 613-761-4311 http://www.ohri.ca/ohsn-reb

Appendix 2 – Data access details

Authorized investigation team members were only allowed to have access if they were a deemed employee of Statistics Canada with a keycard to the Research Data Centre (RDC) and a login to their assigned hard drive. A keycard and login were granted after obtaining a "Reality Status" security clearance from Statistics Canada, signing a Microdata Research Contract, and affirming an Oath of Office and Secrecy to Statistics Canada. Such members were only allowed to access the study data for the proposed analyses only and were not allowed to alter or share the original data whatsoever. Any information identifying respondents in the CHMS was kept separate from the data files and can only be accessed by Statistics Canada employees involved in the collection and generation of data (i.e., no one in the investigation team). The CHMS data files available for use to derive average moderate-to-vigorous physical activity (MVPA) minutes per week contain respondents with only 4 or more valid days of accelerometer data. From the complete CHMS accelerometer files stored at Statistics Canada, an approved Statistics Canada employee therefore identified respondents in all cycles who had 1 to 3 valid days of accelerometer data, derived their average MVPA minutes per week, and provided these values in a data file which was placed in the investigation team's assigned hard drive and then merged to the rest of the study data for a more complete analysis.

Only analyses output (not any study data) was transferred by employees at the RDC after being vetted for small cell sizes prior to release. Such output was transferred to a folder which can only by accessed on Statistics Canada's secure network by members of the investigation team at the Health Analysis and Modelling Division. All study records will be retained securely for 10 years upon the completion of this study and then destroyed as per the requirements of the Ottawa Hospital Research Institute.

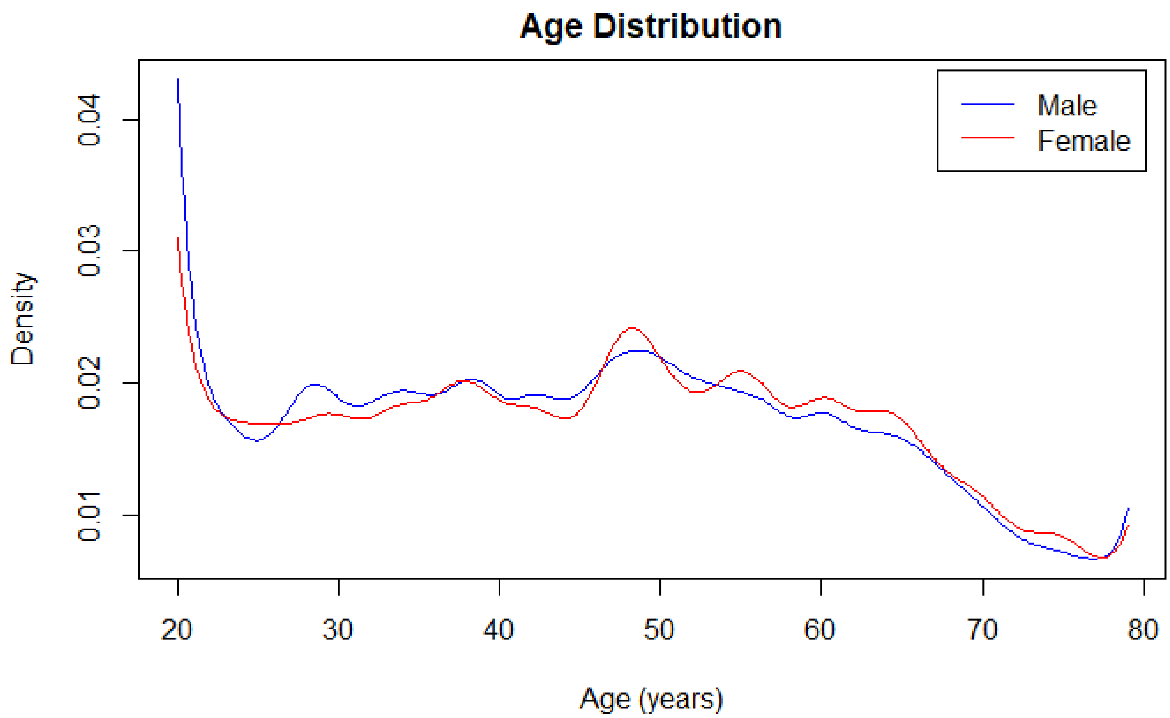
Appendix 3 – Unimputed and unweighted characteristics of the study populations for HTNPoRT

	Male[1]	Female[1]
Overall		
Total	9,633	10,010
Hypertensive	2,681 (27.8%)	2,471 (24.7%)
– Uncontrolled	1,300 (13.5%)	1,238 (12.4%)
– Controlled	1,381 (14.3%)	1,233 (12.3%)
Sociodemographic measures		
Age (years)	47 (36, 62)	47 (36, 63)
Marital status		
– Married or common-law	6,900 (71.6%)	6,064 (60.6%)
– Widowed, separated, or divorced	1,083 (11.2%)	2,211 (22.1%)
– Single and never married	1,646 (17.1%)	1,728 (17.3%)
– Missing	4 (0.04%)	7 (0.07%)
Highest education level		
– Less than secondary school graduation	1,122 (11.7%)	1,140 (11.4%)
– Secondary school graduation	1,691 (17.6%)	1,794 (17.9%)
– Post-secondary school graduation	6,714 (69.7%)	6,996 (69.9%)
– Missing	106 (1.1%)	80 (0.8%)
Working status		
– Has a job	6,816 (70.8%)	5,892 (58.9%)
– Does not have a job	2,772 (28.8%)	4,082 (40.8%)
– Missing	45 (0.5%)	36 (0.4%)
Psychological measures		
Self-rated mental health		
– Poor or fair	566 (5.9%)	785 (7.8%)
– Good, very good, or excellent	9,036 (93.8%)	9,190 (91.8%)
– Missing	31 (0.3%)	35 (0.4%)
Self-perceived stress		
– Not at all to a bit	7,614 (79%)	7,592 (75.8%)
– Quite a bit or extremely	2,015 (20.9%)	2,415 (24.1%)
– Missing	4 (0.04%)	3 (0.03%)
Sense of belonging		
– Strong	6,358 (66%)	6,910 (69%)
– Weak	3,226 (33.5%)	3,048 (30.5%)
– Missing	49 (0.5%)	52 (0.5%)
Health status measures		
Hypertension family history		
– Yes	2,839 (29.5%)	3,432 (34.3%)
– No	3,155 (32.8%)	3,090 (30.9%)
– Missing	486 (5%)	400 (4%)
– Not asked	3,153 (32.7%)	3,088 (30.9%)
Body mass index (kg/m^2)	27.2 (24.6, 30.4)	26.2 (22.8, 30.8)

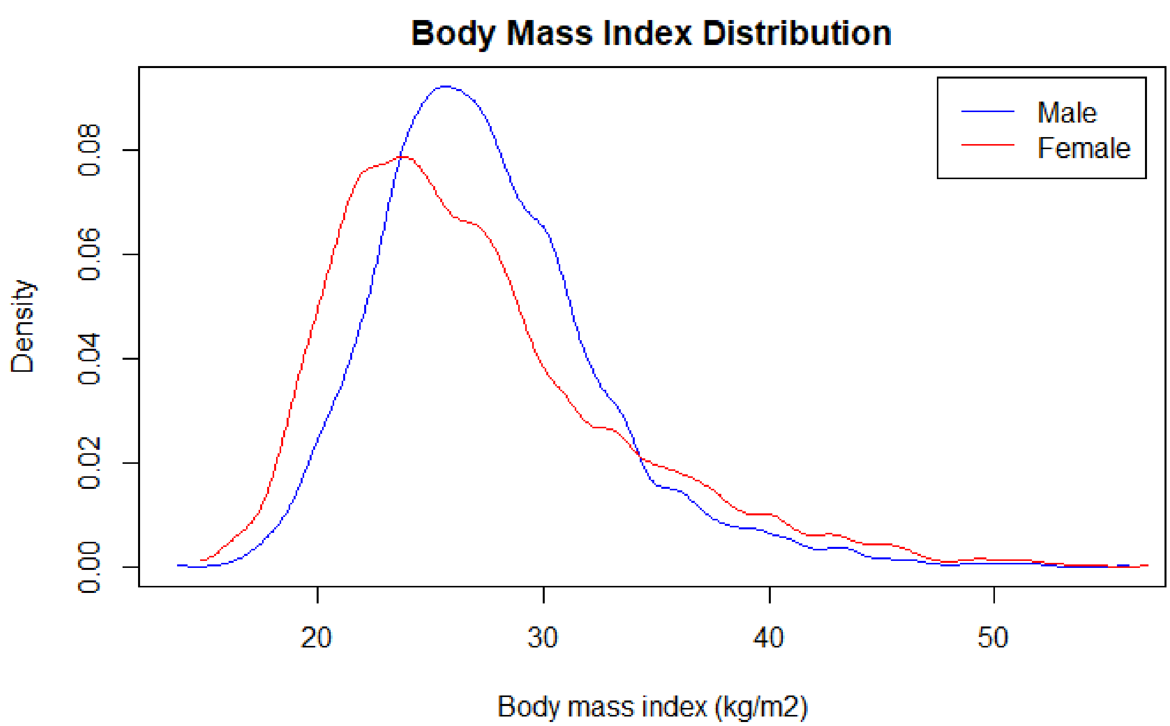
– Not applicable	N/A	3 (0.03%)
– Missing	53 (0.6%)	65 (0.7%)
Health behaviours		
Alcohol consumption		
– Never drank	913 (9.5%)	1,776 (17.7%)
– Low-risk drinker	7,547 (78.4%)	7,506 (75%)
– Moderate drinker	426 (4.4%)	406 (4.1%)
– Heavy drinker	645 (6.7%)	265 (2.6%)
– Missing	102 (1.1%)	57 (0.6%)
Smoking status		
– Current smoker	1,943 (20.2%)	1,656 (16.5%)
– Former smoker	3,314 (34.4%)	2,872 (28.7%)
– Never smoker	4,340 (45.1%)	5,459 (54.5%)
– Missing	36 (0.4%)	23 (0.2%)
Physical activity minutes (minutes/week)	103 (39, 207)	79 (24, 166)
– Missing	977 (10.1%)	959 (9.6%)
Daily fruit and vegetable consumption (times consumed/day)	3.03 (2.14, 4.19)	3.63 (2.61, 4.86)
Sleep duration (hours/night)	7.00 (6.00, 8.00)	7.00 (6.50, 8.00)
– Missing	4 (0.04%)	4 (0.04%)
– Not asked	3,153 (32.7%)	3,088 (30.9%)
Chronic conditions		
Diabetes		
– Yes	1,021 (10.6%)	790 (7.9%)
– No	7,658 (79.5%)	8,549 (85.4%)
– Missing	954 (9.9%)	671 (6.7%)
Chronic kidney disease		
– Yes	511 (5.3%)	710 (7.1%)
– No	8,982 (93.2%)	9,107 (91%)
– Missing	140 (1.5%)	193 (1.9%)

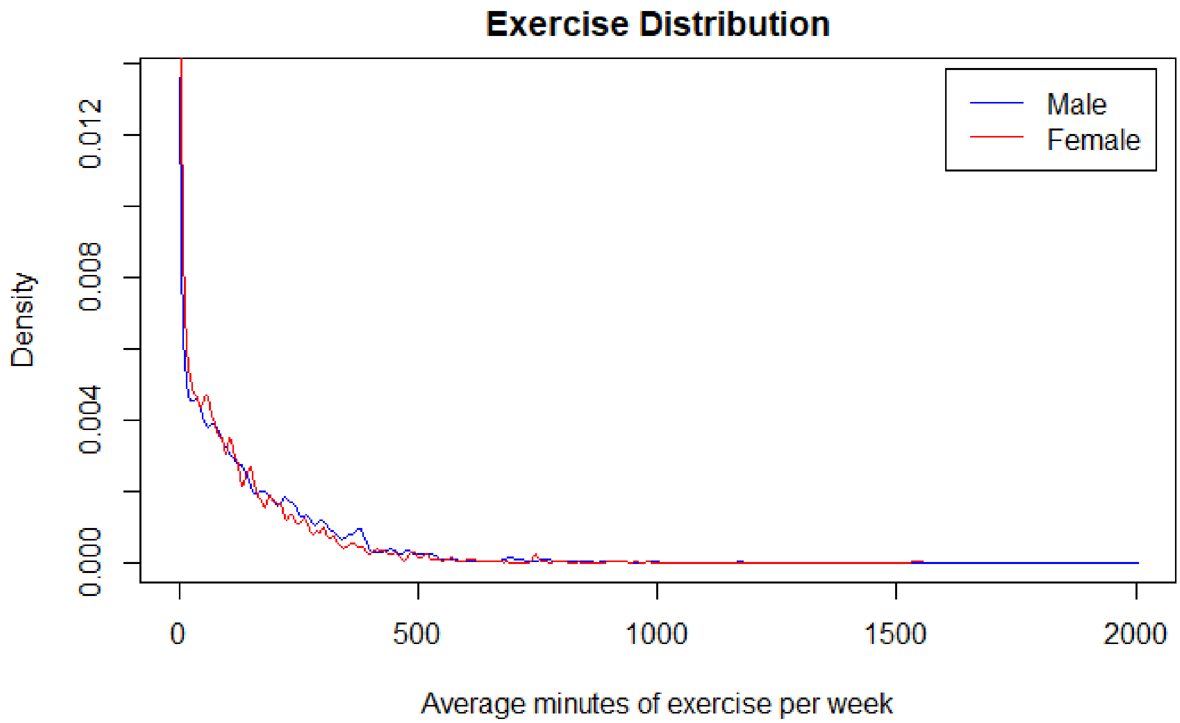
[1] Median (Q1, Q3); n (unweighted counts) (unweighted %)

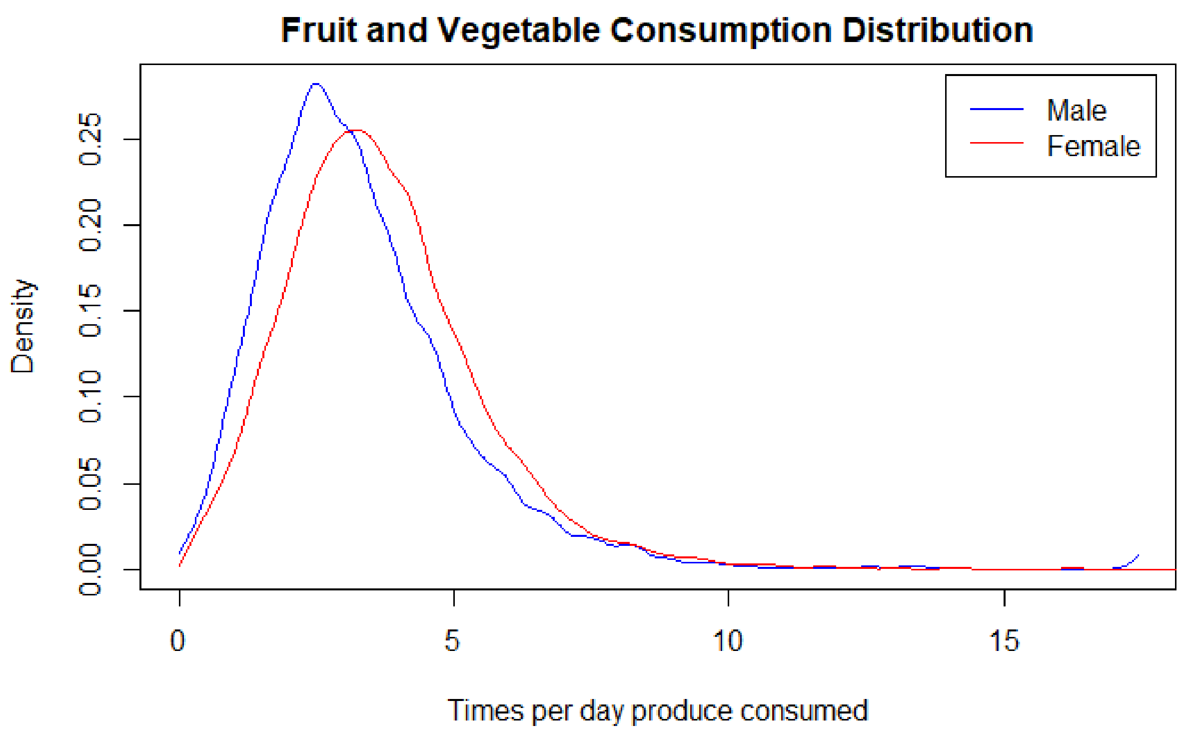
Appendix 4 – Density plots for continuous variables

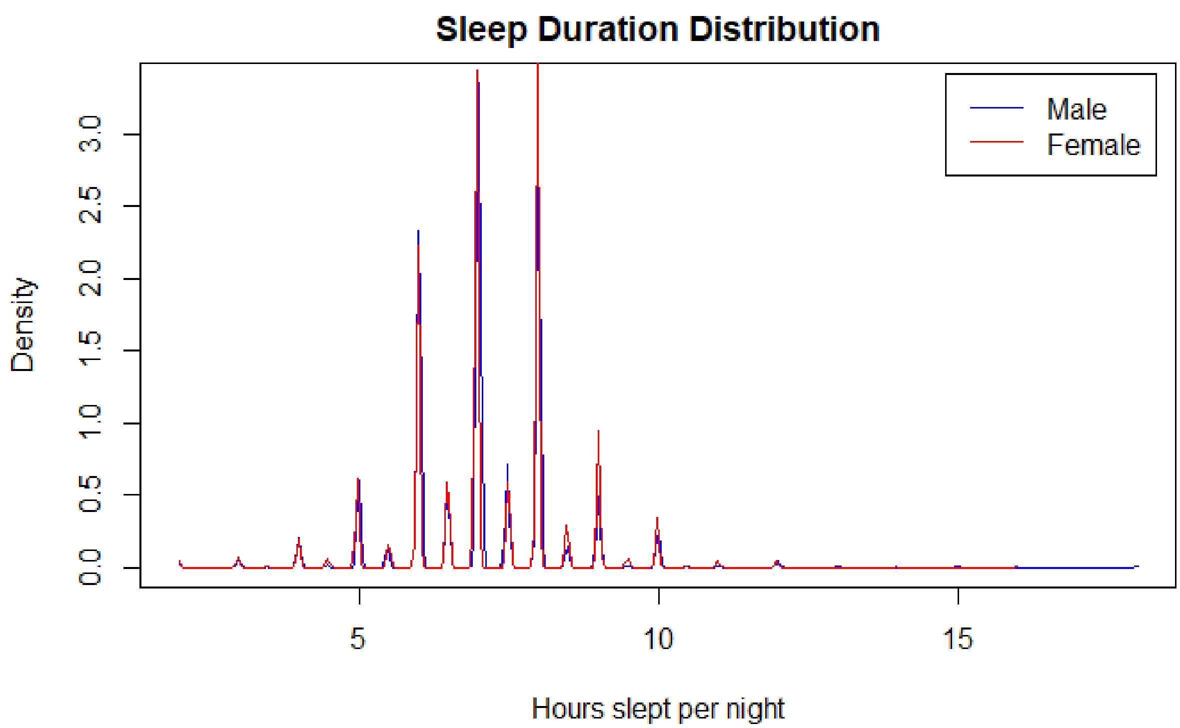


Unimputed:

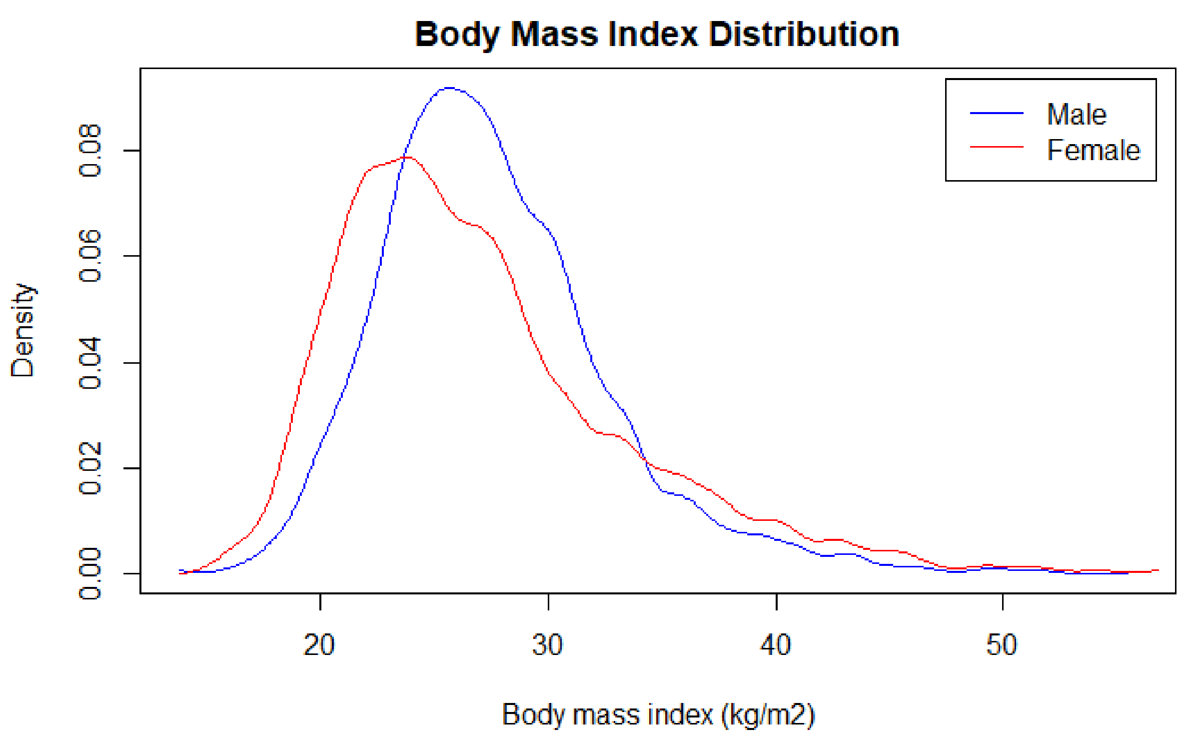


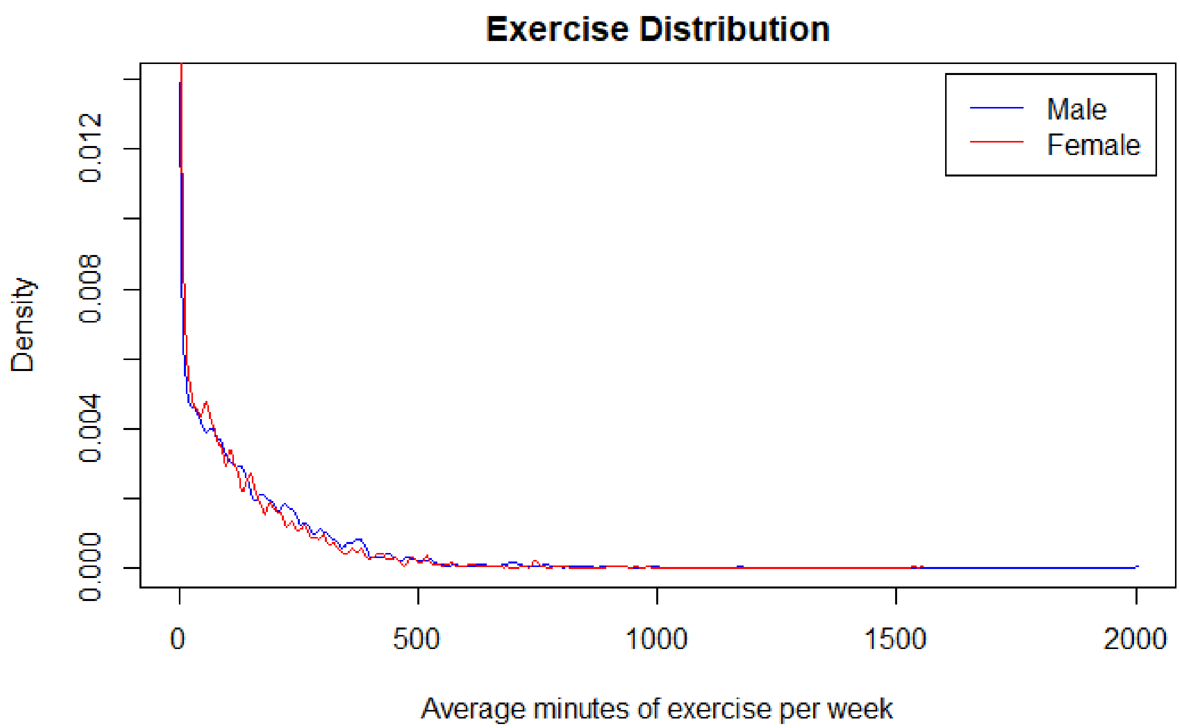

Exercise Distribution
Male
Female
Density
0.000
0.004
0.008
0.012
0
500
1000
1500
2000
Average minutes of exercise per week

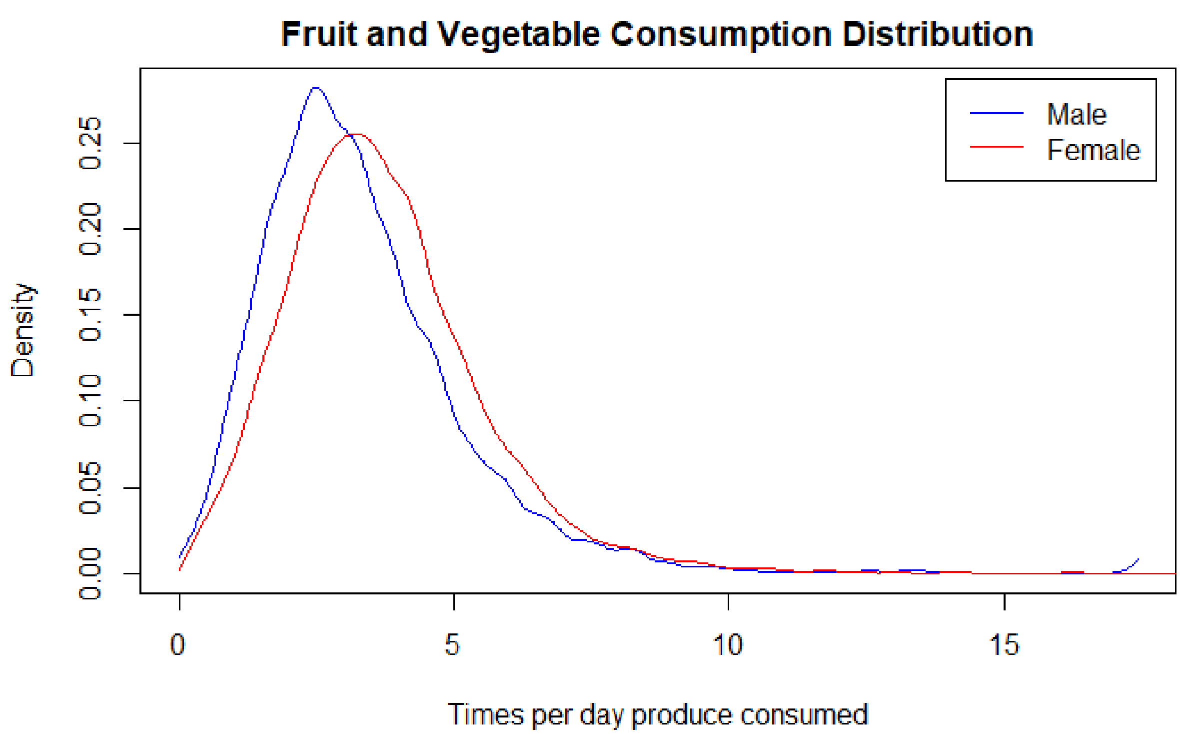

Fruit and Vegetable Consumption Distribution
Male
Female
Density
0.00
0.05
0.10
0.15
0.20
0.25
0
5
10
15
Times per day produce consumed

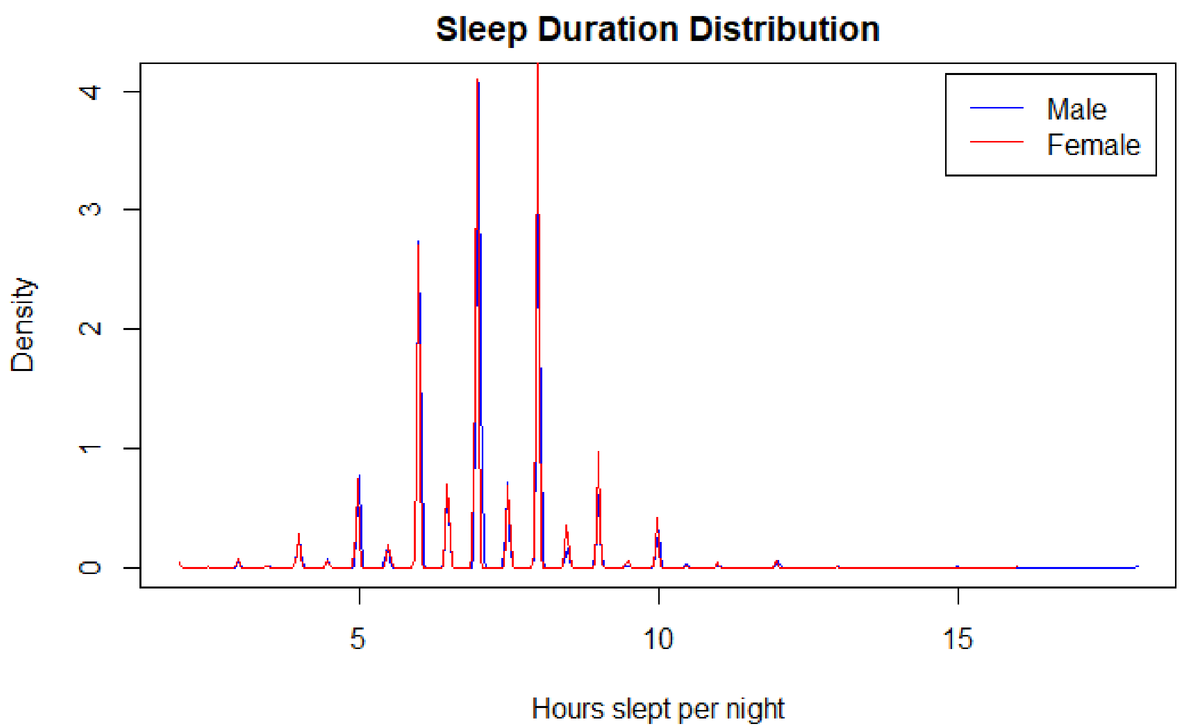

Sleep Duration Distribution
Male
Female
Density
0.0
0.5
1.0
1.5
2.0
2.5
3.0
5
10
15
Hours slept per night

Imputed:


Body Mass Index Distribution
Male
Female
Density
0.00
0.02
0.04
0.06
0.08
20
30
40
50
Body mass index (kg/m2)


Exercise Distribution
Male
Female
Density
0.000
0.004
0.008
0.012
0
500
1000
1500
2000
Average minutes of exercise per week


Fruit and Vegetable Consumption Distribution
Male
Female
Density
0.00
0.05
0.10
0.15
0.20
0.25
0
5
10
15
Times per day produce consumed


Sleep Duration Distribution
Male
Female
Density
0
1
2
3
4
5
10
15
Hours slept per night

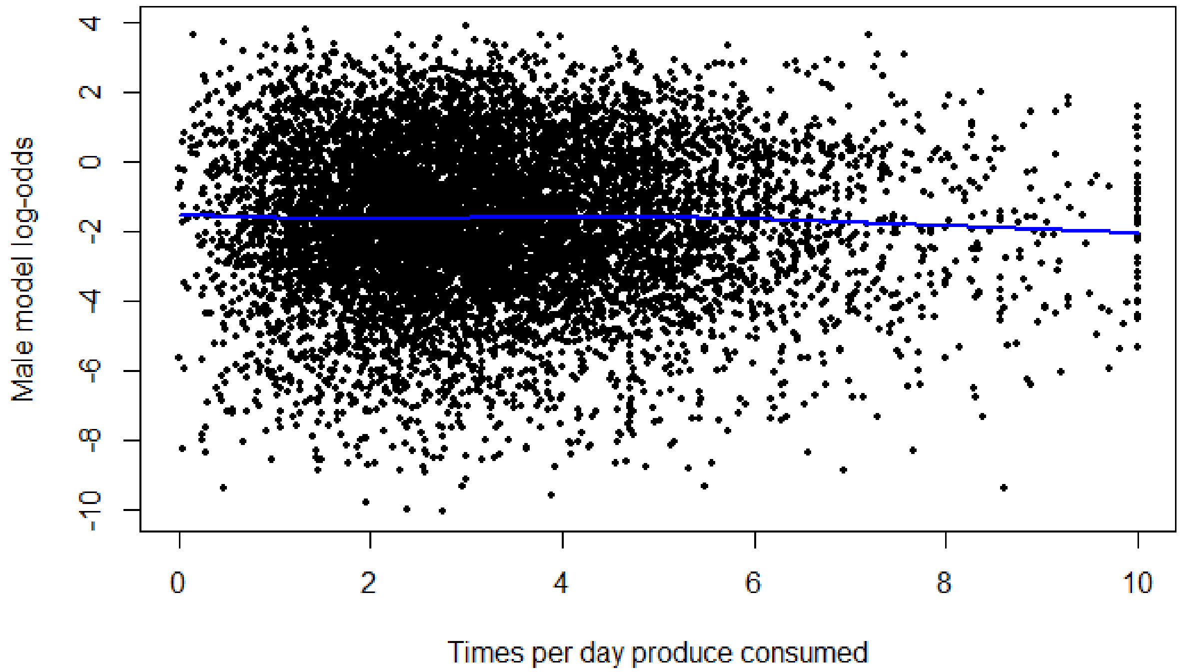
Appendix 5 – Multicollinearity and linearity assessments

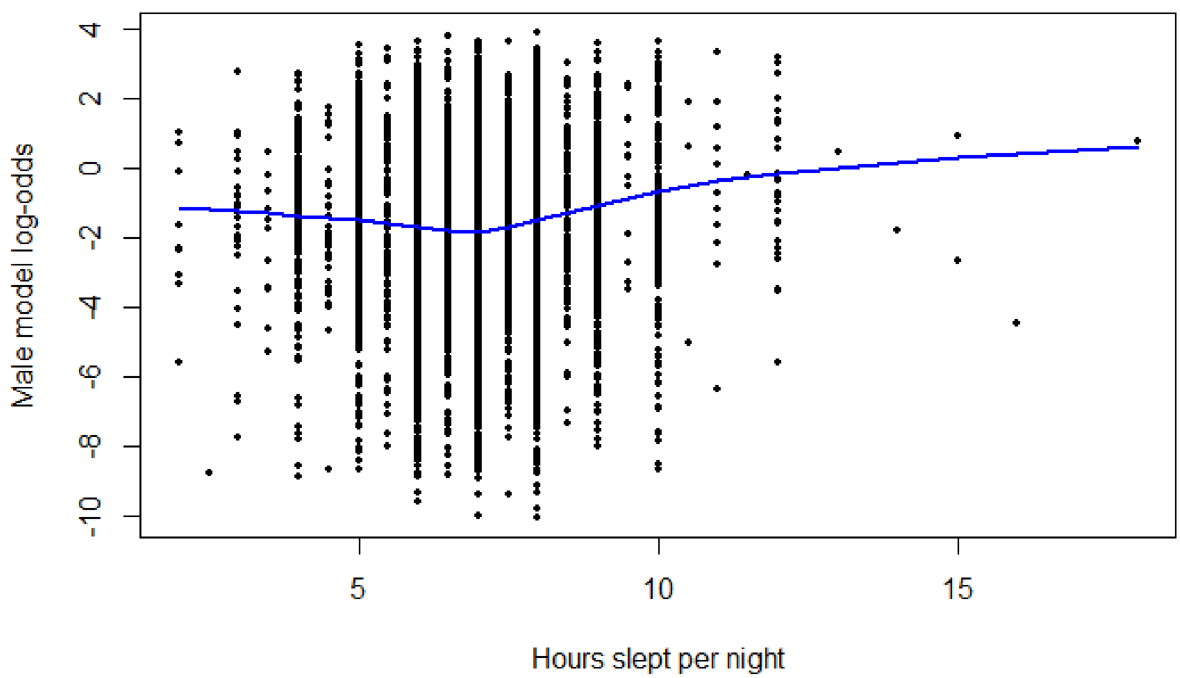
Multicollinearity assessment - variance inflation factors (VIFs) for HTNPoRT candidate predictors

	Male	**Female**
Sociodemographic measures		
Age	2.006	1.898
Marital status		
– Widowed, separated, or divorced	1.286	1.187
– Single and never married	1.282	1.238
Highest education level		
– Secondary school graduation	1.219	1.186
– Less than secondary school graduation	1.230	1.301
Working status	1.393	1.441
Psychological measures		
Self-rated mental health	1.249	1.321
Self-perceived stress	1.282	1.362
Sense of belonging	1.214	1.224
Health status measures		
Hypertension family history	1.116	1.147
Body mass index	5.446*	6.199*
~~Waist-to-height ratio~~	5.342*	5.932*
Health behaviours		
Alcohol consumption		
– Low-risk drinker	1.941	1.401
– Moderate drinker	1.414	1.510
– Heavy drinker	1.688	1.262
Smoking status		
– Former smoker	1.558	1.200
– Current smoker	1.648	1.508
Physical activity minutes	1.171	1.208
Daily fruit and vegetable consumption	1.101	1.141
Sleep duration	1.084	1.095
Chronic conditions		
Diabetes	1.049	1.142
Chronic kidney disease	1.077	1.045

* Significantly collinear (VIF > 2.5) → Waist-to-height ratio removed

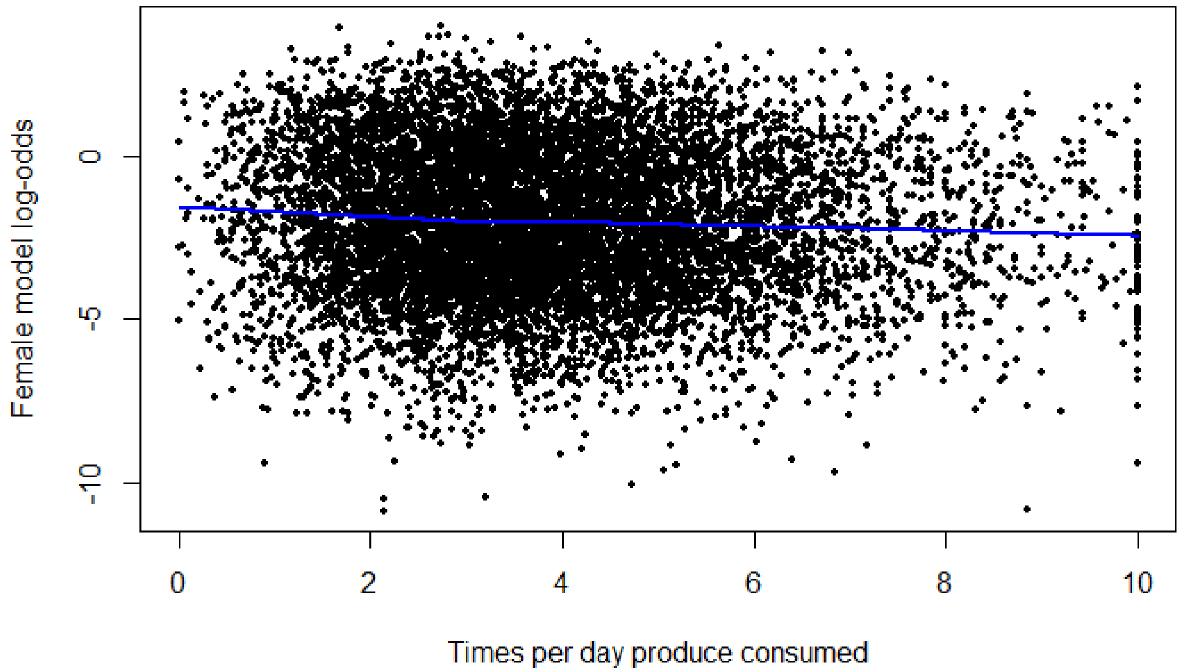
Linearity assessments for daily fruit and vegetable consumption and sleep duration in male model:

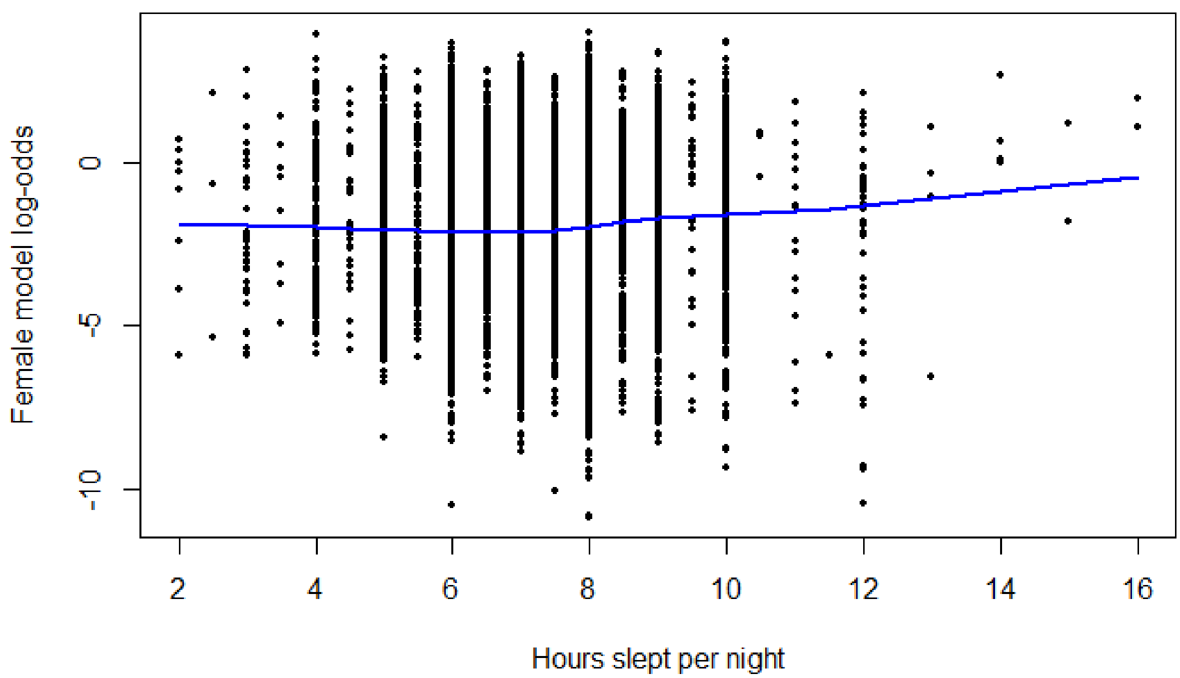




* Sleep duration does not violate assumption based on central trend without outliers

Linearity assessments for daily fruit and vegetable consumption and sleep duration in female model:





* Sleep duration does not violate assumption based on central trend without outliers

Partial association χ^2 statistics for HTNPoRT predictors

	df[1]	Male	Female
Sociodemographic measures			
Age	3	1,021.83	1,070.82
Marital status	2	-1.99	-0.56
Highest education level	2	12.60	1.20
Working status	1	2.93	1.17
Psychological measures			
Self-rated mental health	1	-0.59	-0.43
Self-perceived stress	1	-0.18	-0.68
Sense of belonging	1	19.49	3.20
Health status measures			
Hypertension family history	1	172.21	186.63
Body mass index	2	212.14	224.97
Health behaviours			
Alcohol consumption	3	81.60	23.49
Smoking status	2	2.85	1.59
Physical activity minutes	2	45.19	24.82
Daily fruit and vegetable consumption	2*	8.81	4.25
Sleep duration	2*	-0.20	0.70
Chronic conditions			
Diabetes	1	344.74	235.76
Chronic kidney disease	1	77.43	60.37

[1] df = degrees of freedom

* Modelled as 3-knot restricted cubic spline in this step instead of as pre-specified linear term

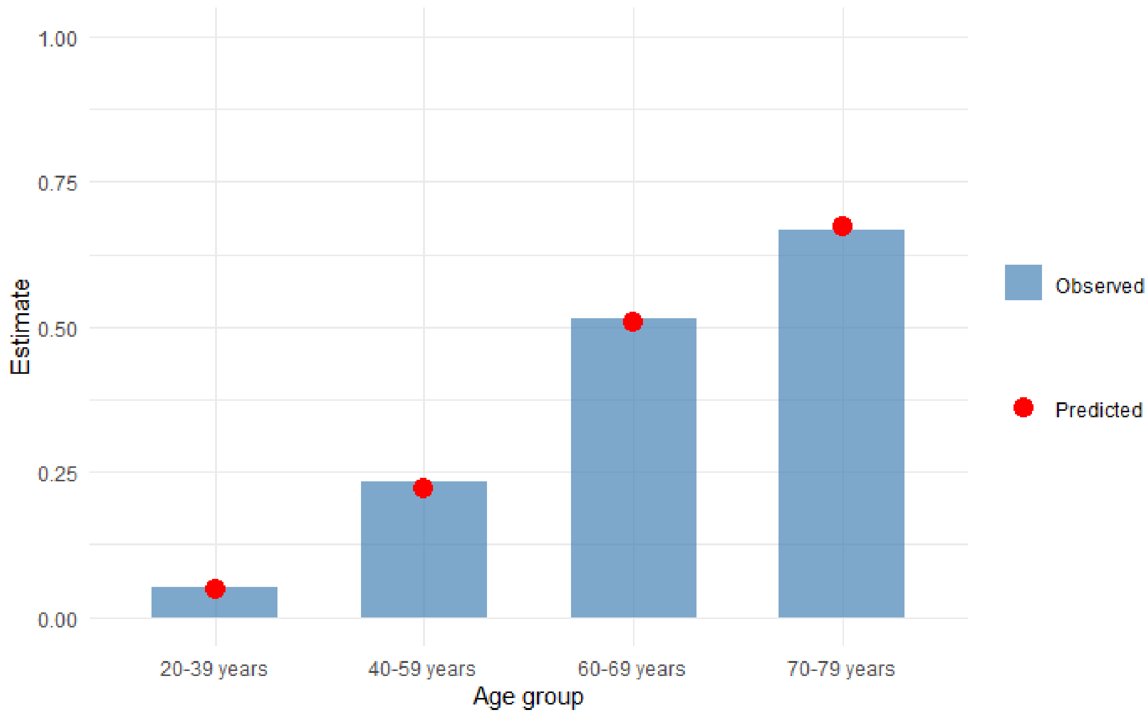
Appendix 6 – Beta coefficients of full and reduced models

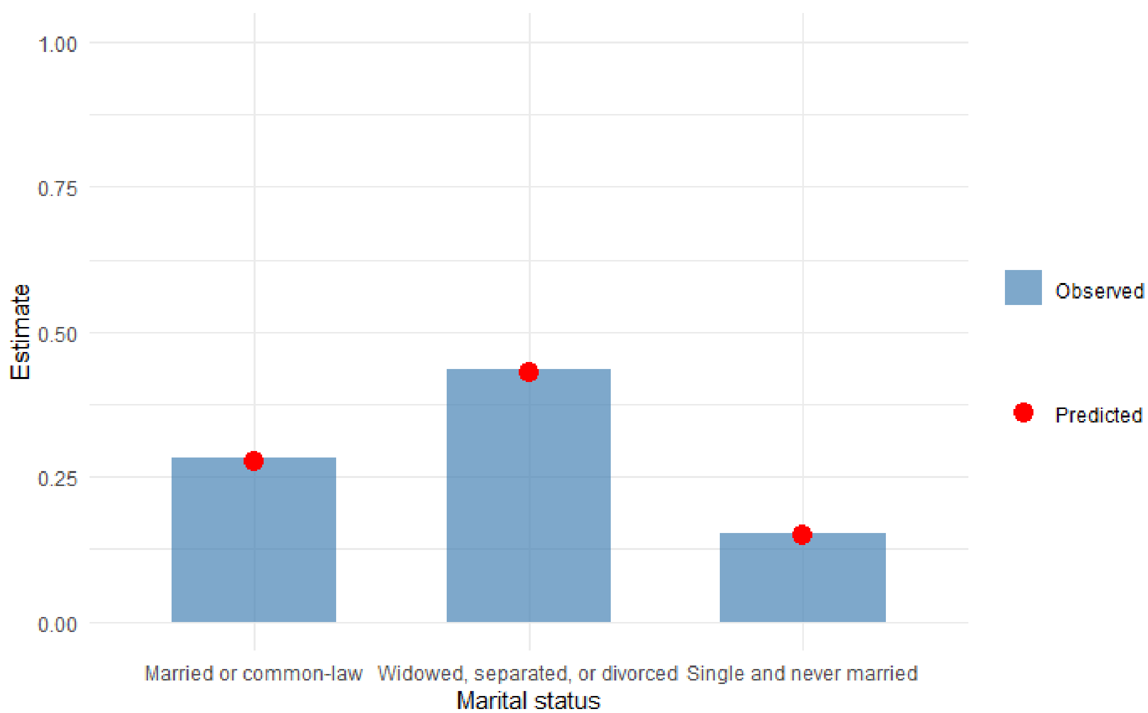
	Male		Female	
Variable	Full model	Reduced model	Full model	Reduced model
Intercept	-1.121341709	-1.844729679	-1.68856589	-1.266722704
First RCS (restricted cubic spline) component for age (Age)	0.120610603	0.070142811	0.123353526	0.171875158
Second RCS component for age (Age')	-0.191075217	0.036360089	-0.06815761	-0.124397394
Third RCS component for age (Age'')	0.617054045	-0.072202759	0.105235736	0.200828973
Widowed, separated, or divorced	0.011753056		0.019019769	
Single and never married	0.039808873		0.101933808	
Secondary school graduate only	0.037040512		0.142132526	
Never finished secondary school	0.346332376		0.106132074	
Working status	-0.13466716		0.100371978	
Self-rated mental health	-0.077297363		-0.165090454	
Self-perceived stress	-0.068451241		-0.024455701	
Sense of belonging	-0.120231019		0.089816155	
Hypertension family history	0.811156601	0.782228096	0.892403039	0.85999173
First RCS component for body mass index (BMI)	-0.117228769	-0.06420197	0.0126533	0.053660739
Second RCS component for body mass index (BMI')	0.248621592	0.191423433	-0.017505191	-0.080109062
Low-risk (former or light) drinker	0.18512661		-0.230831958	
Moderate drinker	0.601096708		0.306115634	
Heavy drinker	1.25731058		0.368089047	
First RCS component for physical activity minutes (Exercise)	0.007713149		-0.004821327	
Second RCS component for physical activity minutes (Exercise')	-0.011893271		0.008501162	
Former smoker	0.234713028		-0.597385571	
Current smoker	0.228513211		-0.637719482	
Sleep duration	-0.124109202		0.810701523	
Daily fruit and vegetable consumption	-0.00108793		-0.024468502	
Diabetes	1.726568032	1.50258208	1.874638573	1.494153995
Chronic kidney disease	-0.767294006		0.984301017	
Age:Sense of belonging	-0.054972746		-0.015929847	
Age':Sense of belonging	0.101922279		0.013528891	
Age'':Sense of belonging	-0.238999574		0.000928856	
Age:BMI	-0.02139886	-0.018665302	-0.004544447	-0.001968393
Age':BMI	0.045712387	0.036399545	0.027980957	0.021593308
Age'':BMI	-0.101684598	-0.07722547	-0.083259879	-0.068405591
Age:BMI'	0.023698803	0.021531623	-0.000706525	-0.004475157
Age':BMI'	-0.050398253	-0.040003965	-0.014938772	-0.003069774
Age'':BMI'	0.103656052	0.07560878	0.055094881	0.026362919
Age:Exercise	0.000353785		-0.000447063	
Age':Exercise	-0.002557437		0.000207842	
Age'':Exercise	0.008213978		0.000467554	
Age:Exercise'	-0.000556		0.000943675	

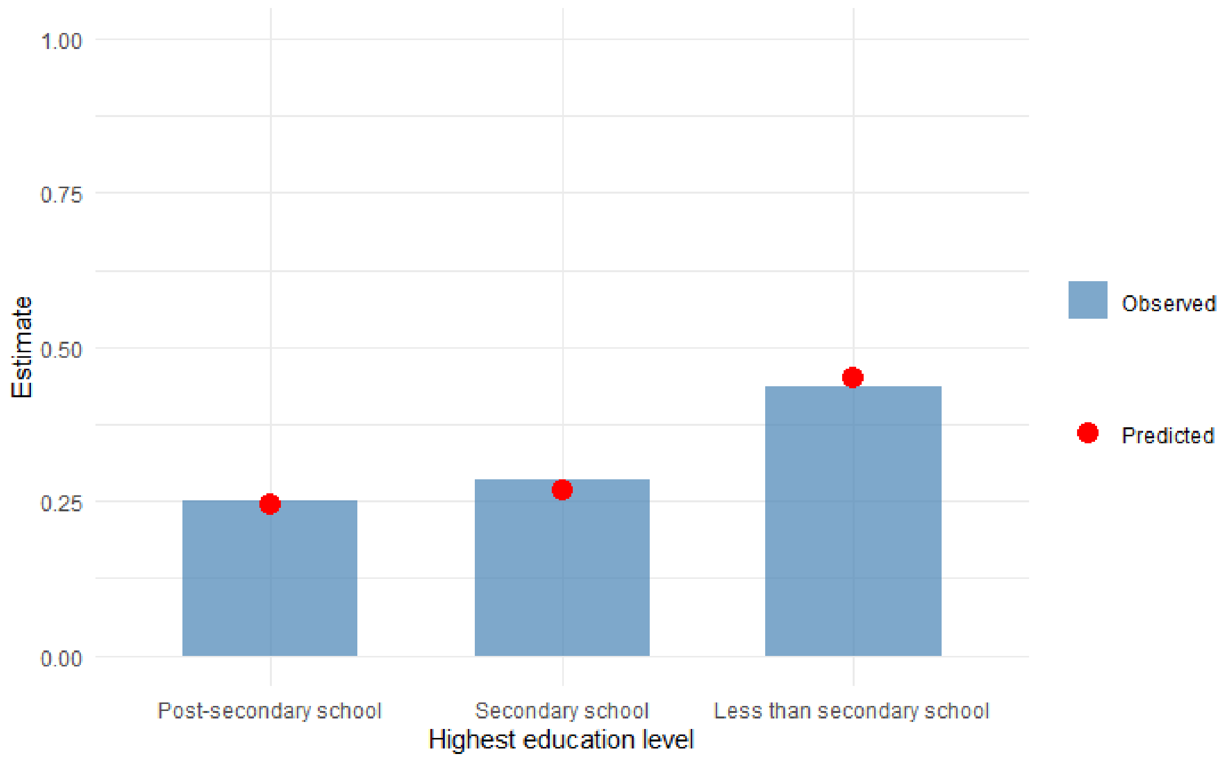
Age':Exercise'	0.0036823		-0.000968508	
Age'':Exercise'	-0.01185042		0.000820402	
Age:Former smoker	-0.017572272		-0.051530597	
Age':Former smoker	-0.062937645		0.129882254	
Age'':Former smoker	0.261326278		-0.274679026	
Age:Current smoker	0.029196794		-0.033225161	
Age':Current smoker	-0.108598324		0.13967307	
Age'':Current smoker	0.351105878		-0.417416334	
Age:Sleep	-0.019244631		0.045685775	
Age':Sleep	0.023972894		-0.15311149	
Age'':Sleep	-0.032741755		0.360599236	
Age:Diabetes	-0.093363163	-0.093051063	0.017223791	-0.024490926
Age':Diabetes	0.103215272	0.120165708	0.003858444	0.102039921
Age'':Diabetes	-0.260382646	-0.304303246	-0.158014951	-0.366964525
Age:Chronic kidney disease	-0.18195042		-0.087906113	
Age':Chronic kidney disease	0.386112756		0.054376039	
Age'':Chronic kidney disease	-0.853806739		0.002674929	

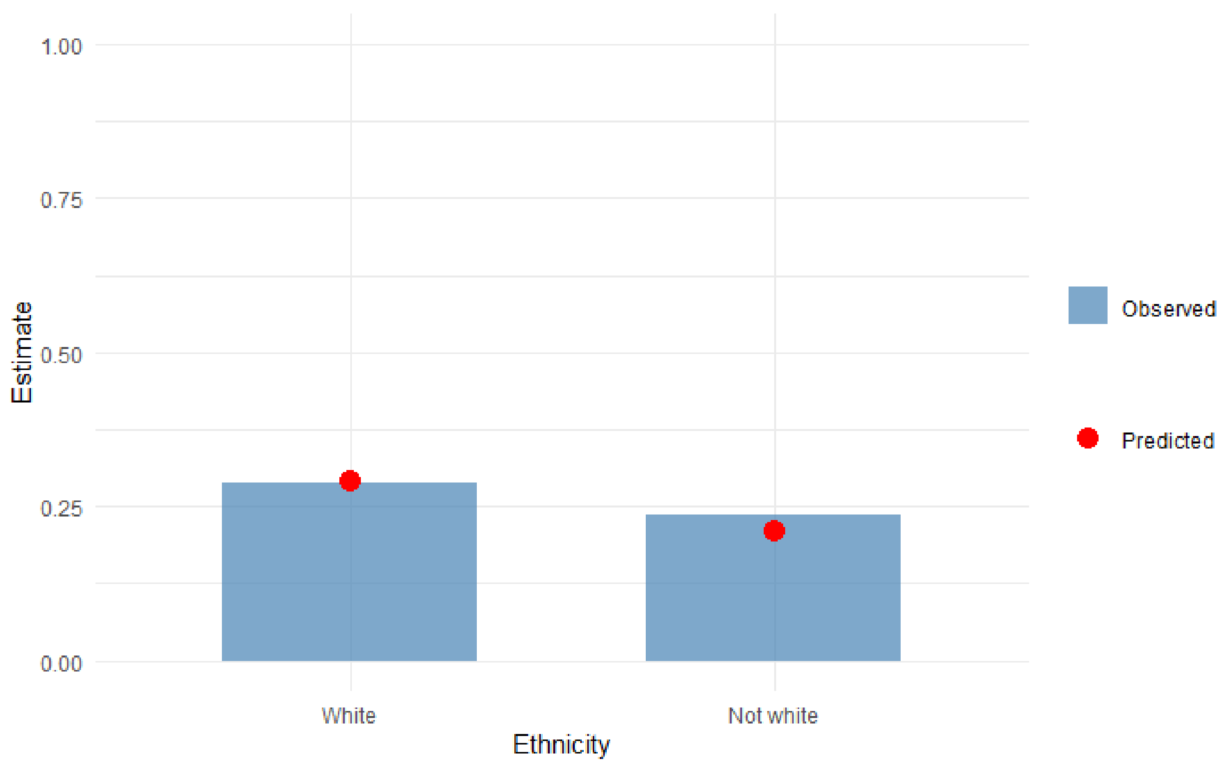
Appendix 7 – Calibration across subgroups for full models

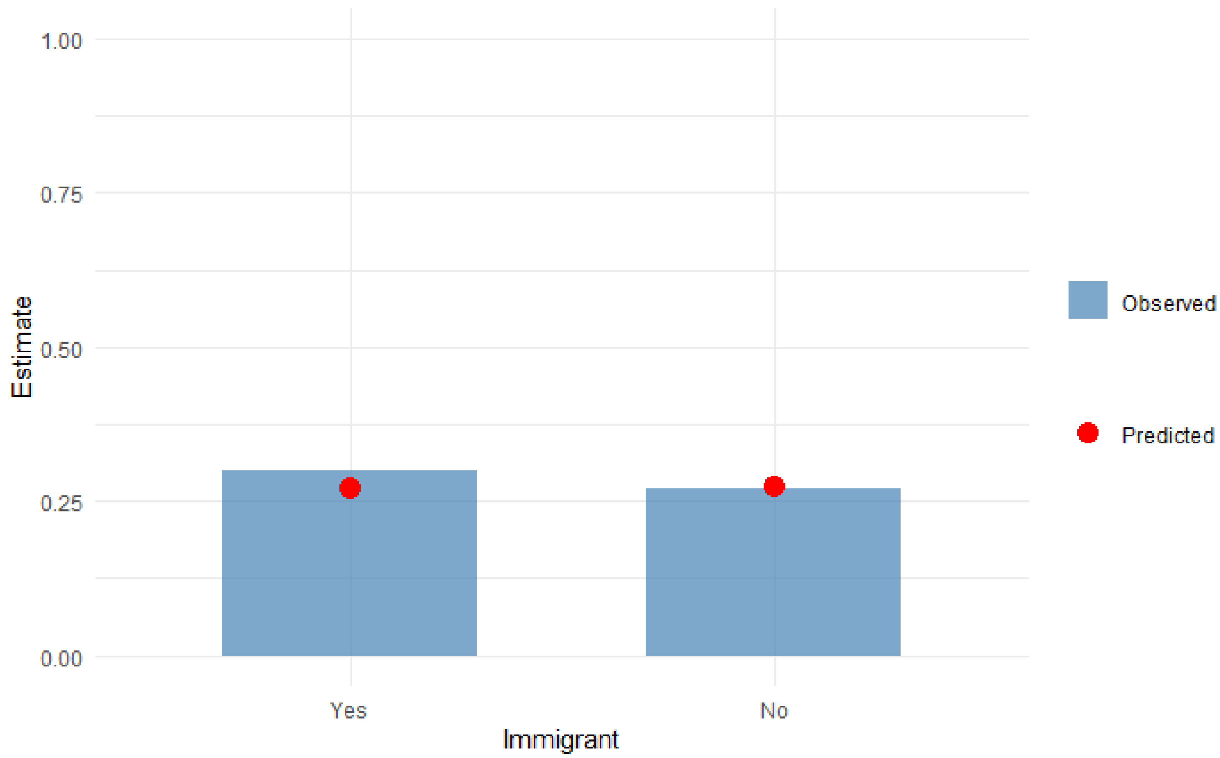
Male Full Model:
X – excluded subgroup with observed estimate less than 5%
*** – subgroup with difference between observed and predicted estimates over 20%**

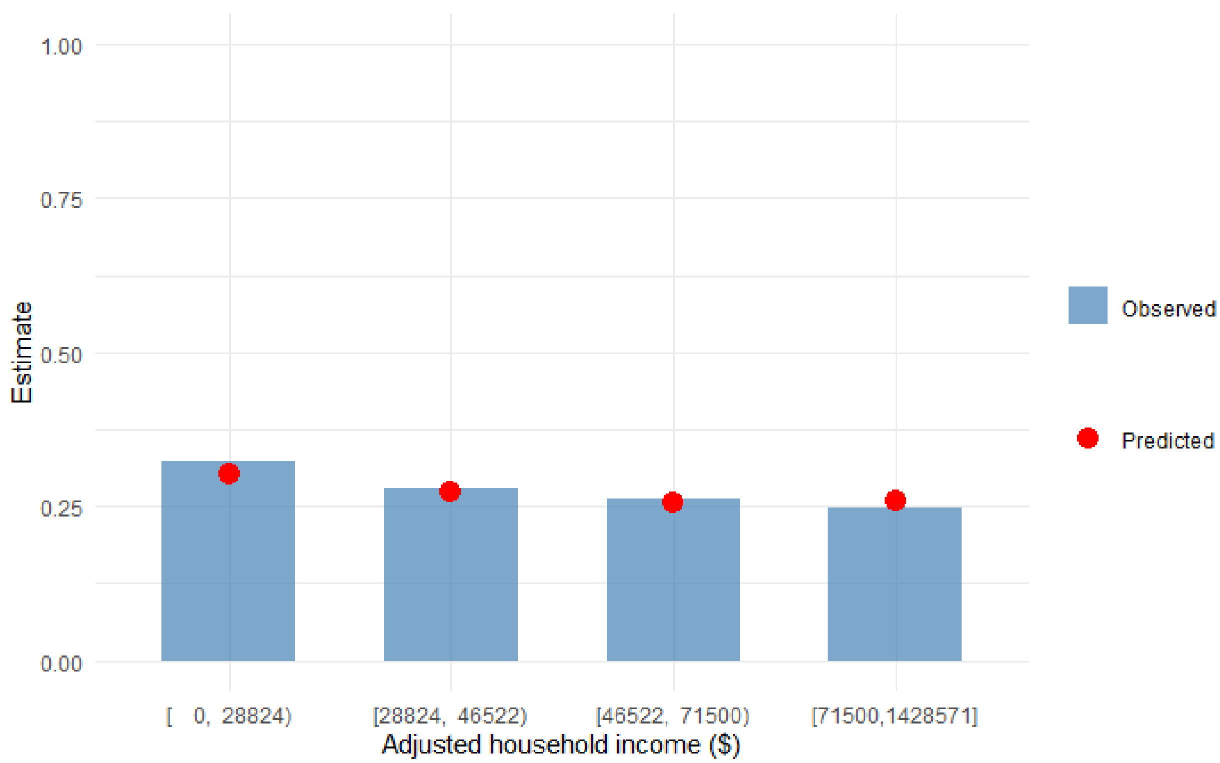


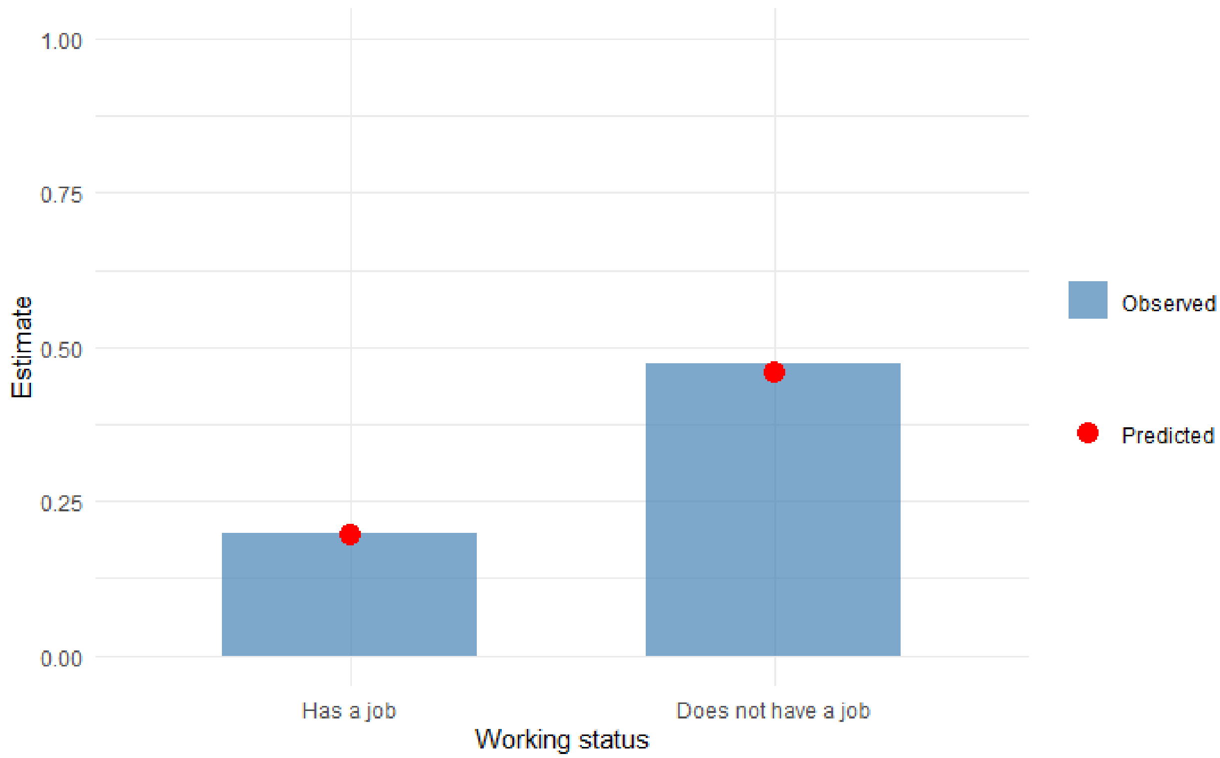



1.00
0.75
0.50
0.25
0.00
Estimate
Post-secondary school
Secondary school
Less than secondary school
Highest education level
Observed
Predicted

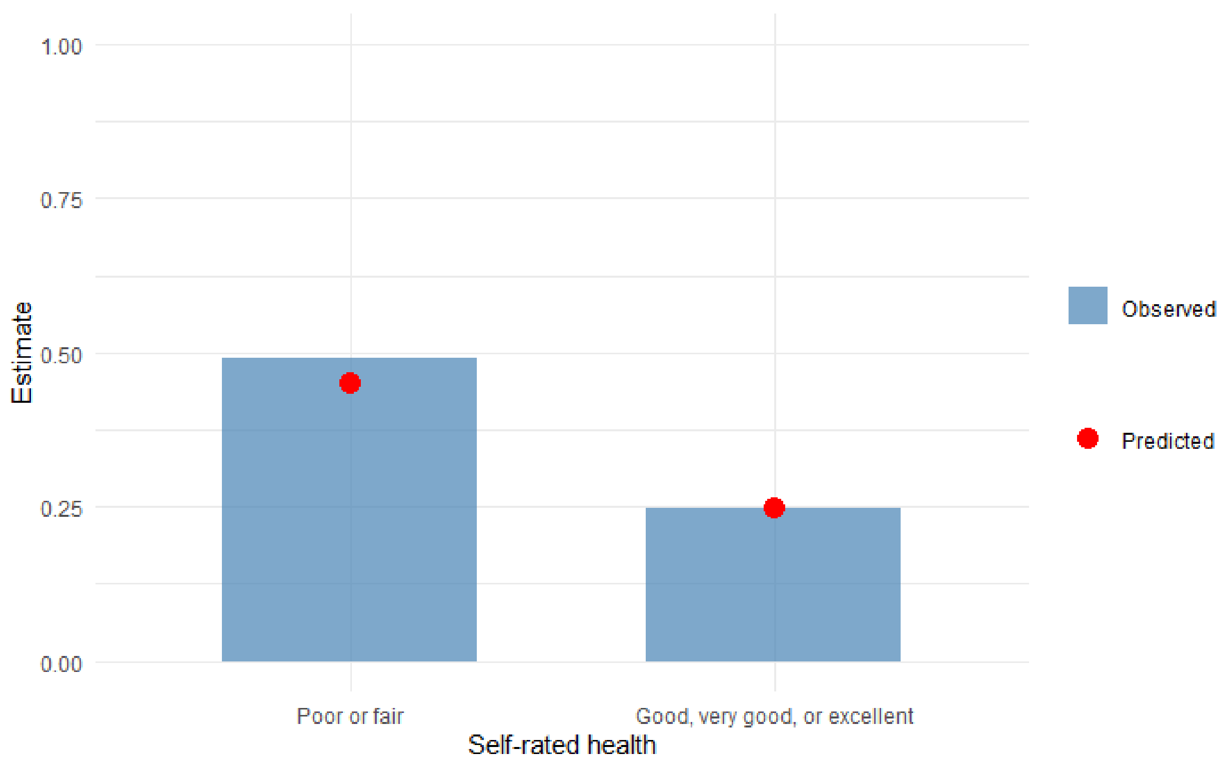

1.00
0.75
0.50
0.25
0.00
Estimate
White
Not white
Ethnicity
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
Immigrant
Observed
Predicted

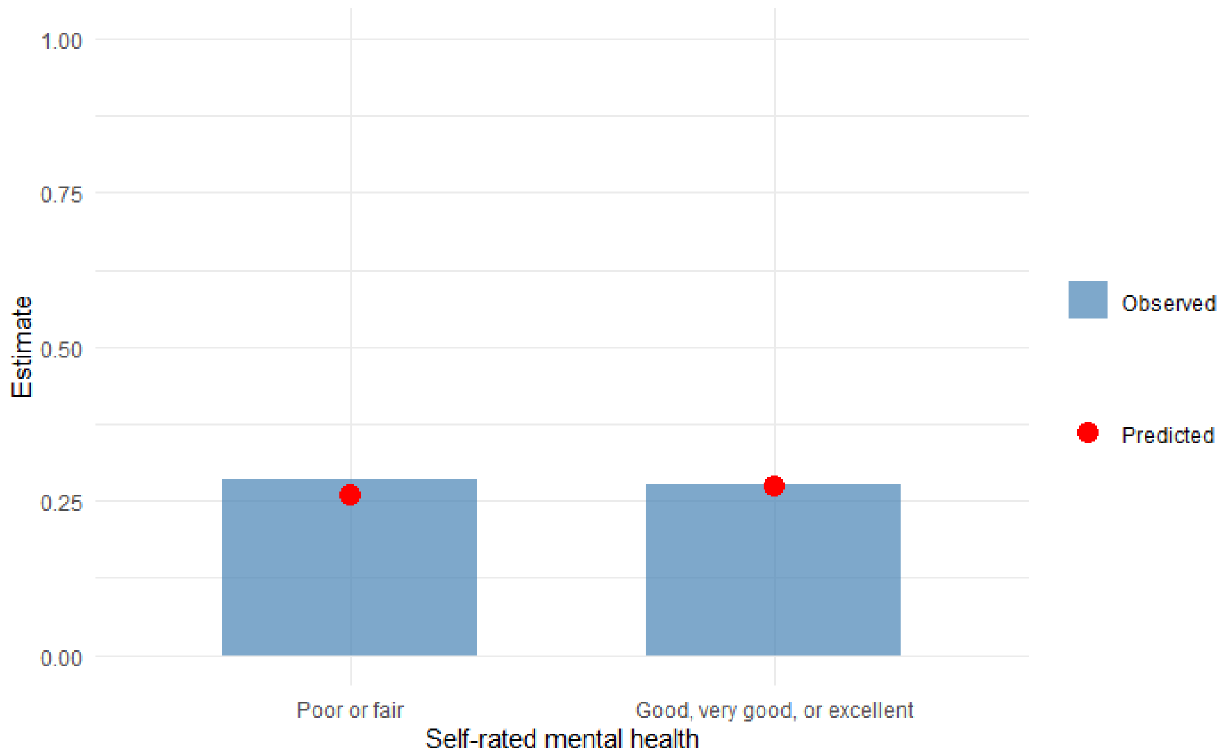

1.00
0.75
0.50
0.25
0.00
Estimate
[0, 28824)
[28824, 46522)
[46522, 71500)
[71500,1428571]
Adjusted household income ($)
Observed
Predicted

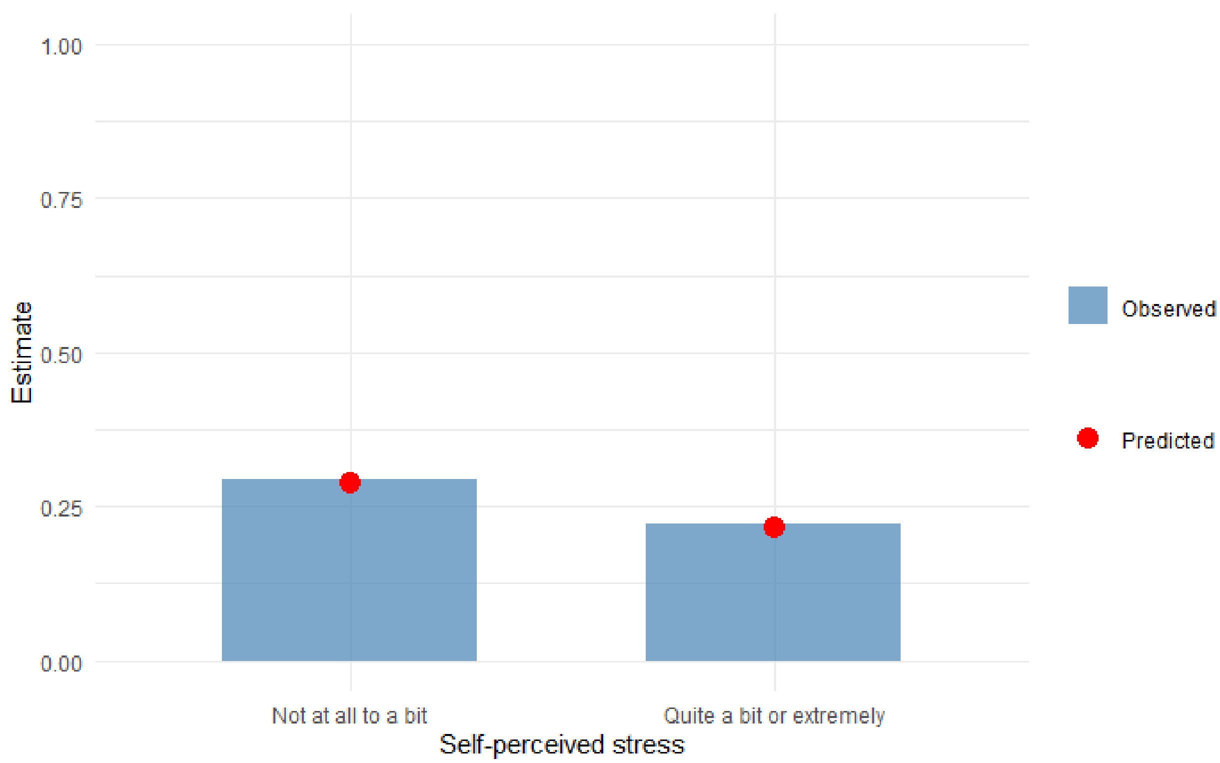


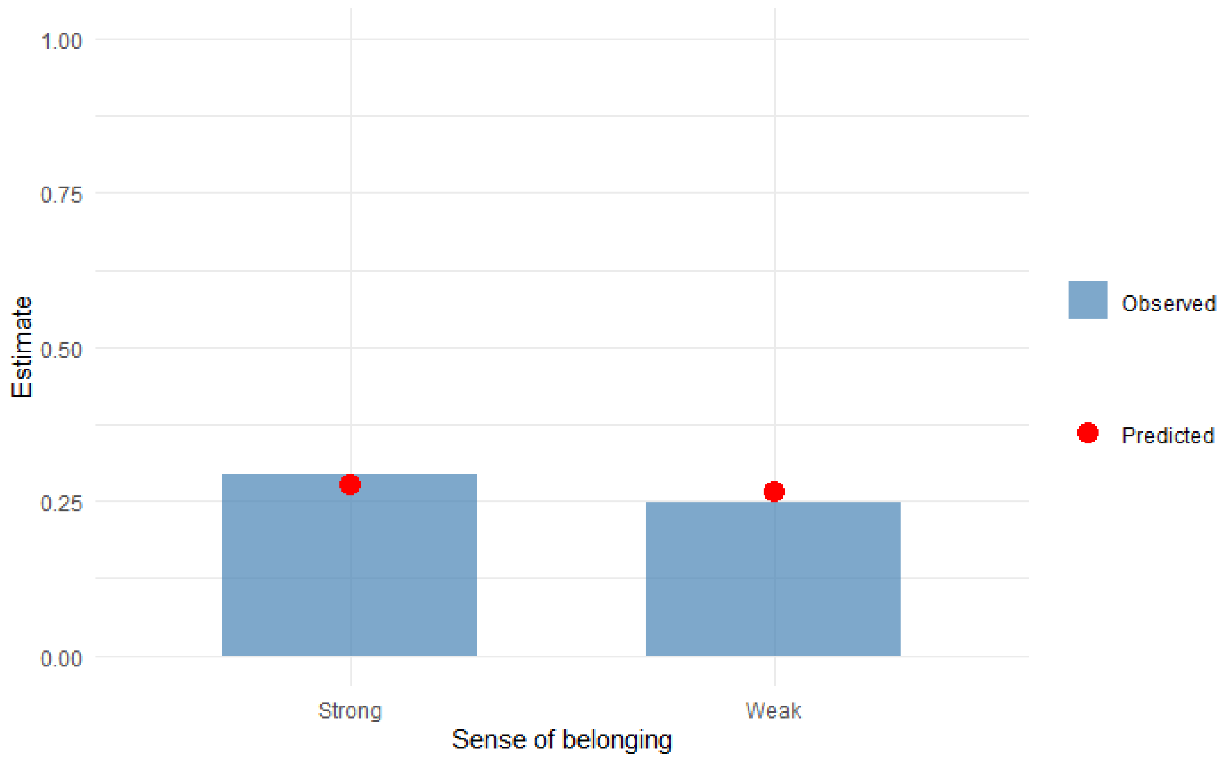
1.00
0.75
0.50
0.25
0.00
Estimate
Has a job
Does not have a job
Working status
Observed
Predicted



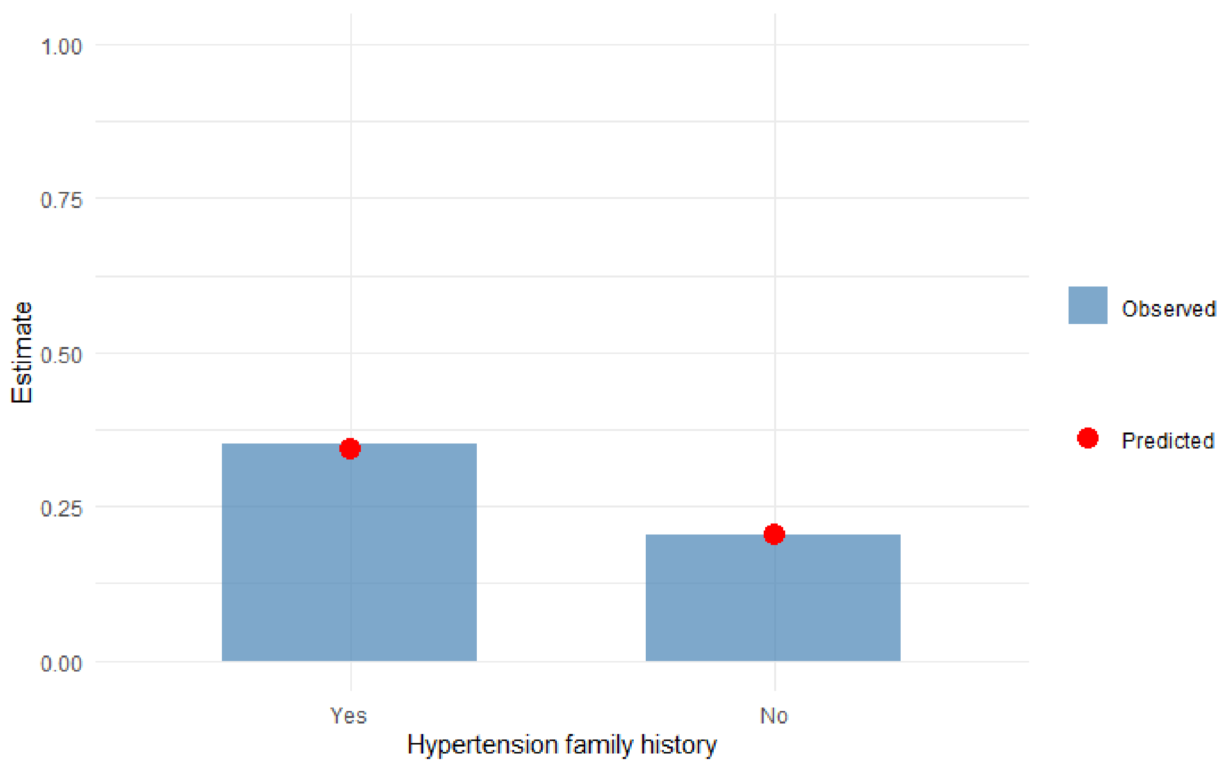
1.00
0.75
0.50
0.25
0.00
Estimate
Poor or fair
Good, very good, or excellent
Self-rated health
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
Poor or fair
Good, very good, or excellent
Self-rated mental health
Observed
Predicted

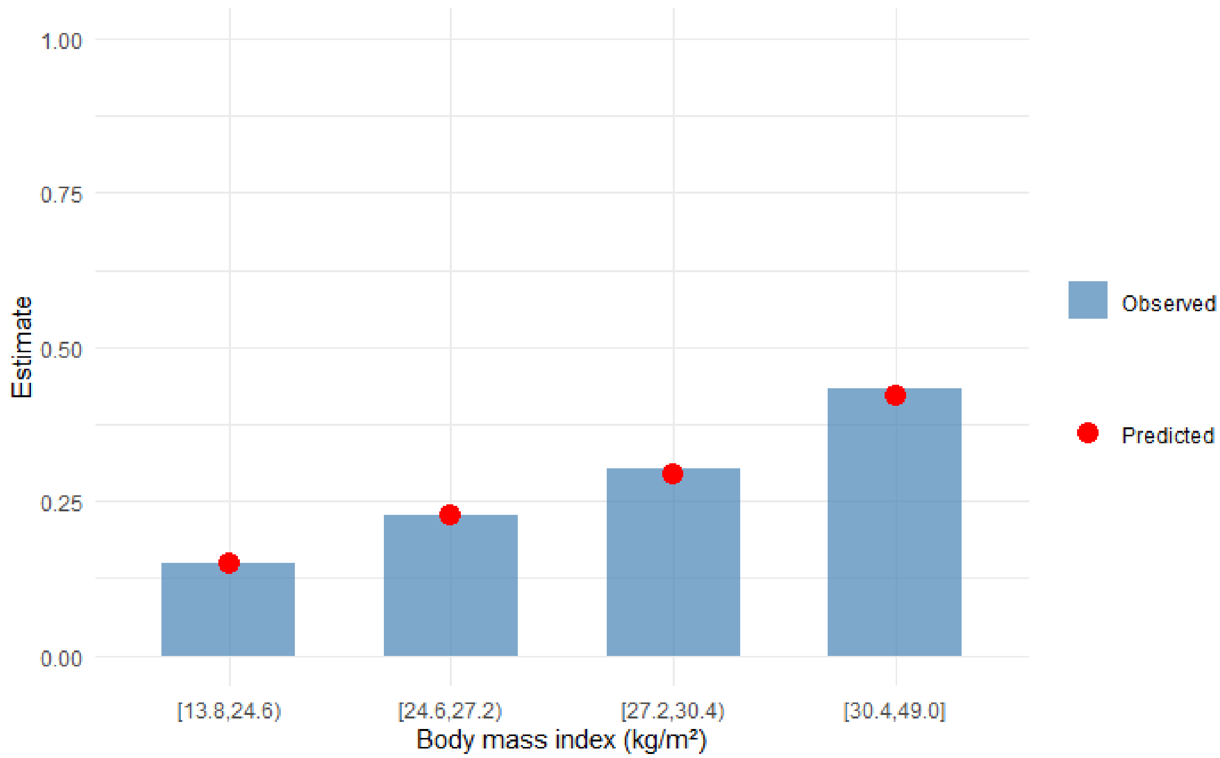

1.00
0.75
0.50
0.25
0.00
Estimate
Not at all to a bit
Quite a bit or extremely
Self-perceived stress
Observed
Predicted

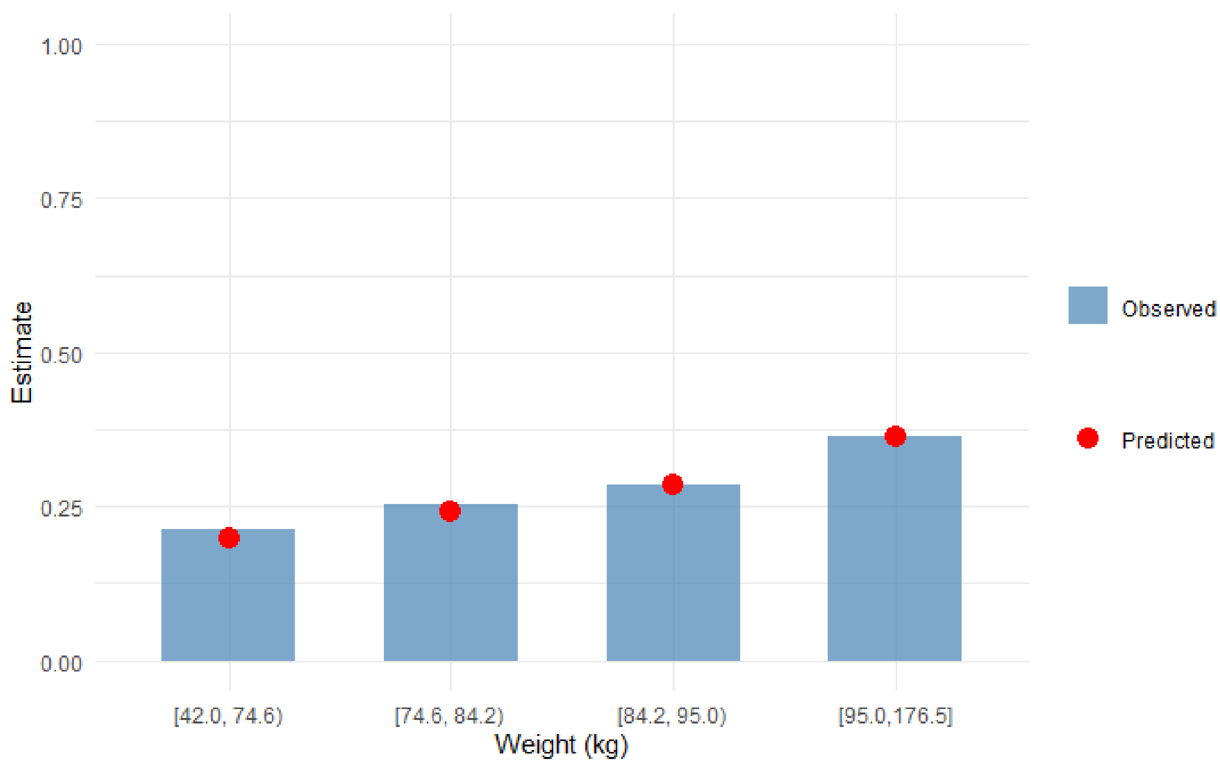


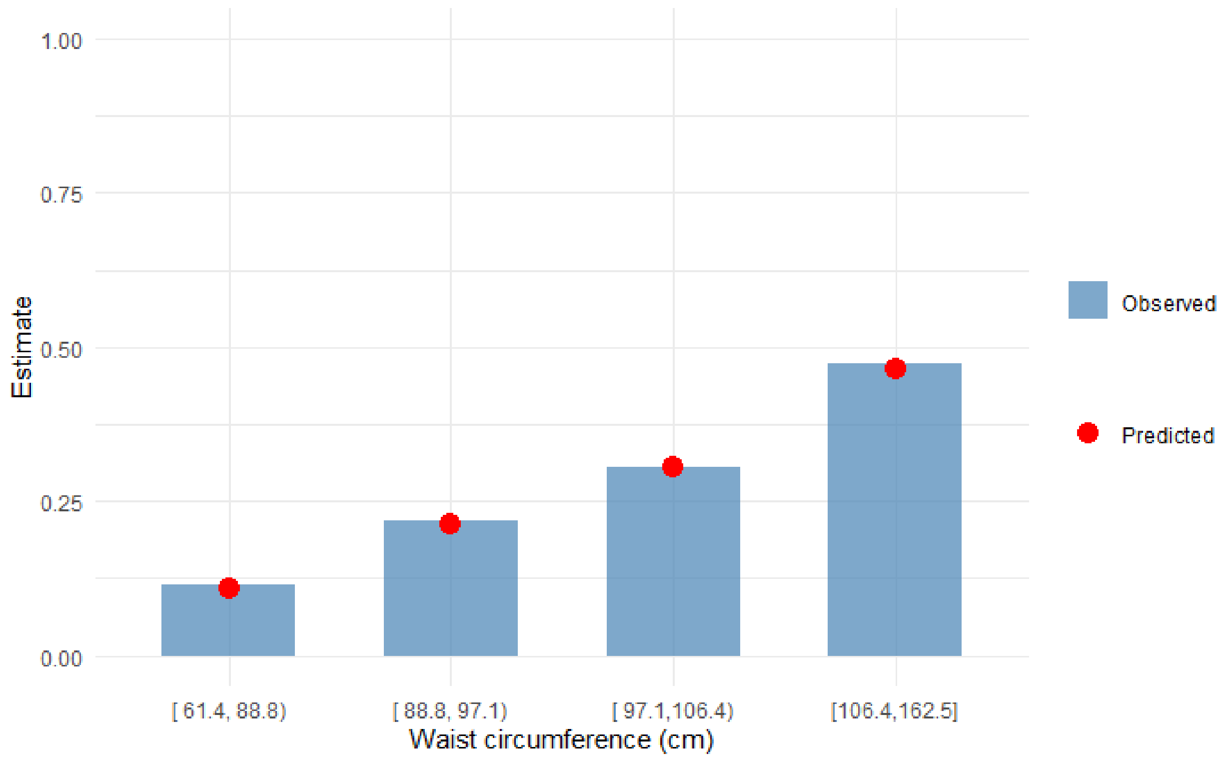
1.00
0.75
0.50
0.25
0.00
Estimate
Strong
Weak
Sense of belonging
Observed
Predicted



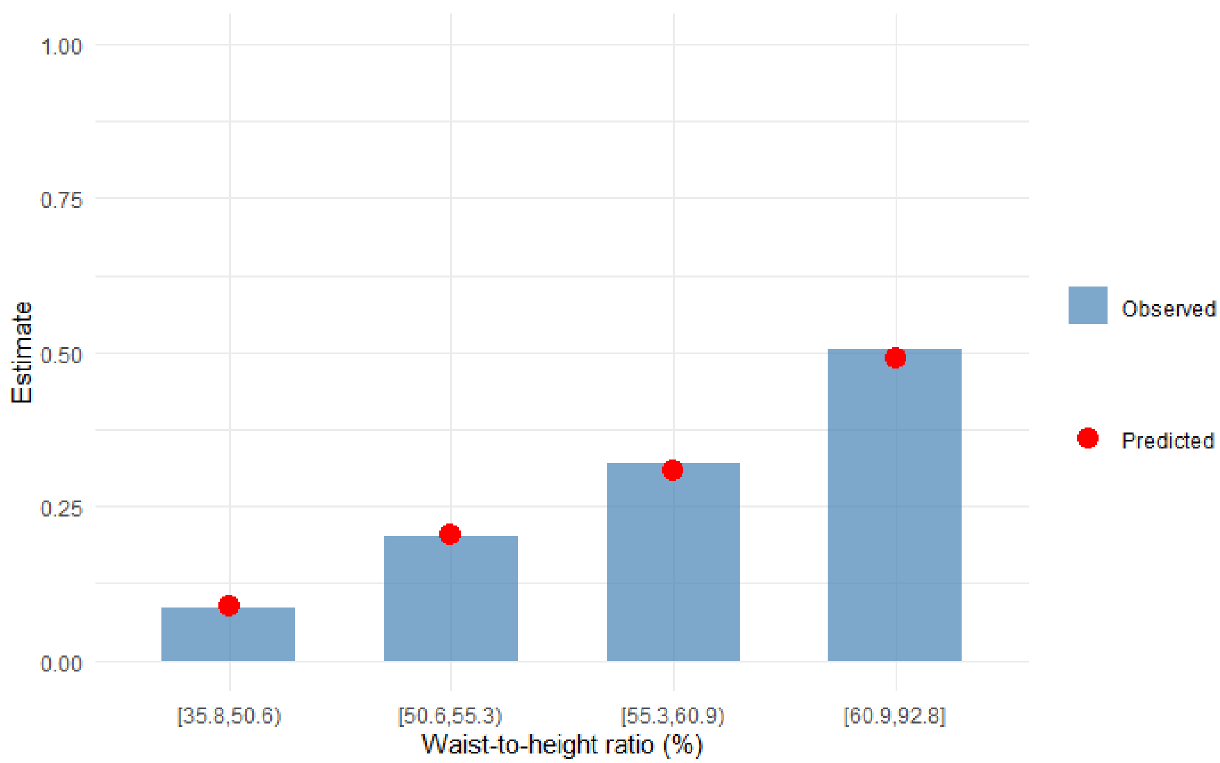
1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
Hypertension family history
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
[13.8,24.6)
[24.6,27.2)
[27.2,30.4)
[30.4,49.0]
Body mass index (kg/m²)
Observed
Predicted

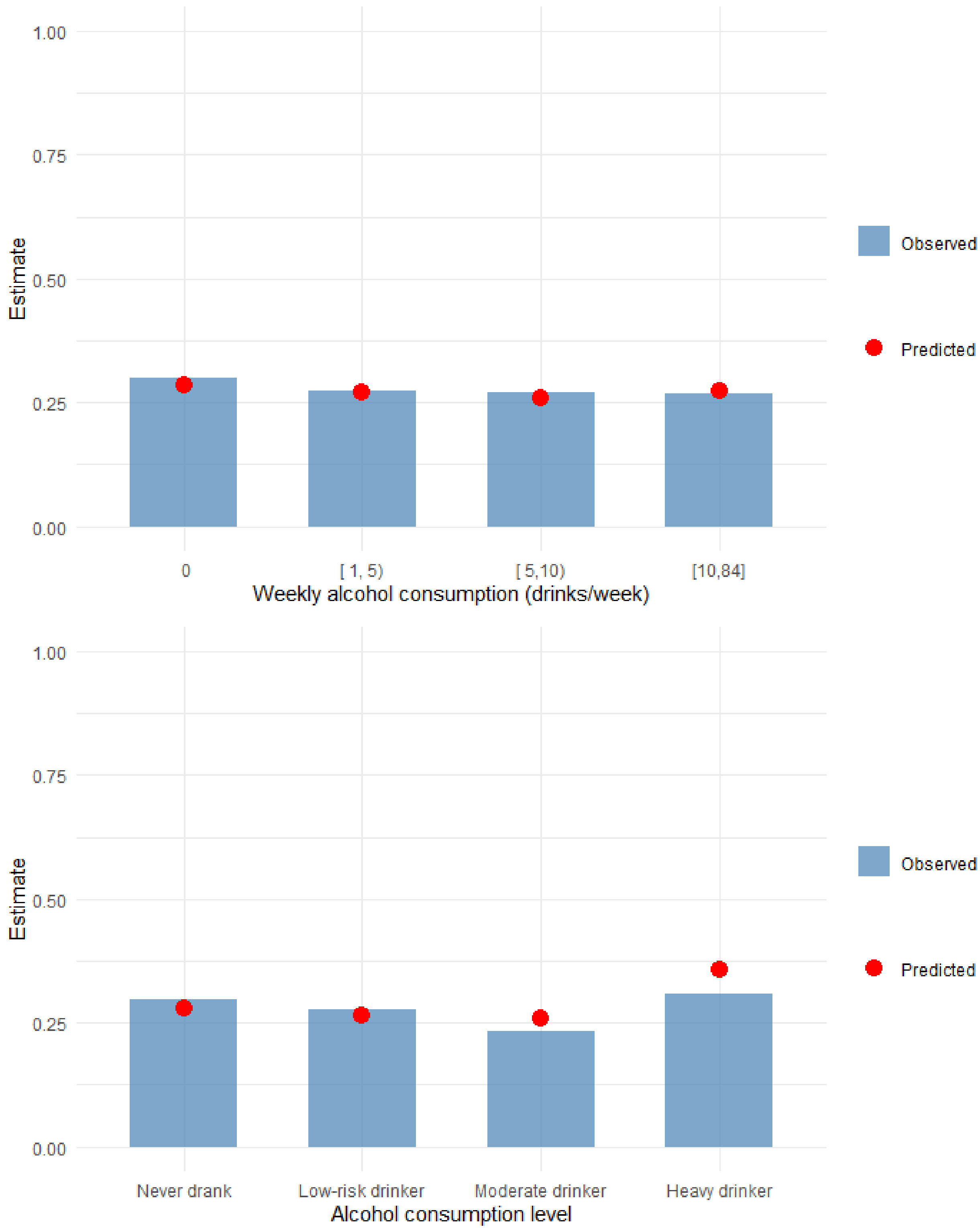

1.00
0.75
0.50
0.25
0.00
Estimate
[42.0, 74.6)
[74.6, 84.2)
[84.2, 95.0)
[95.0,176.5]
Weight (kg)
Observed
Predicted



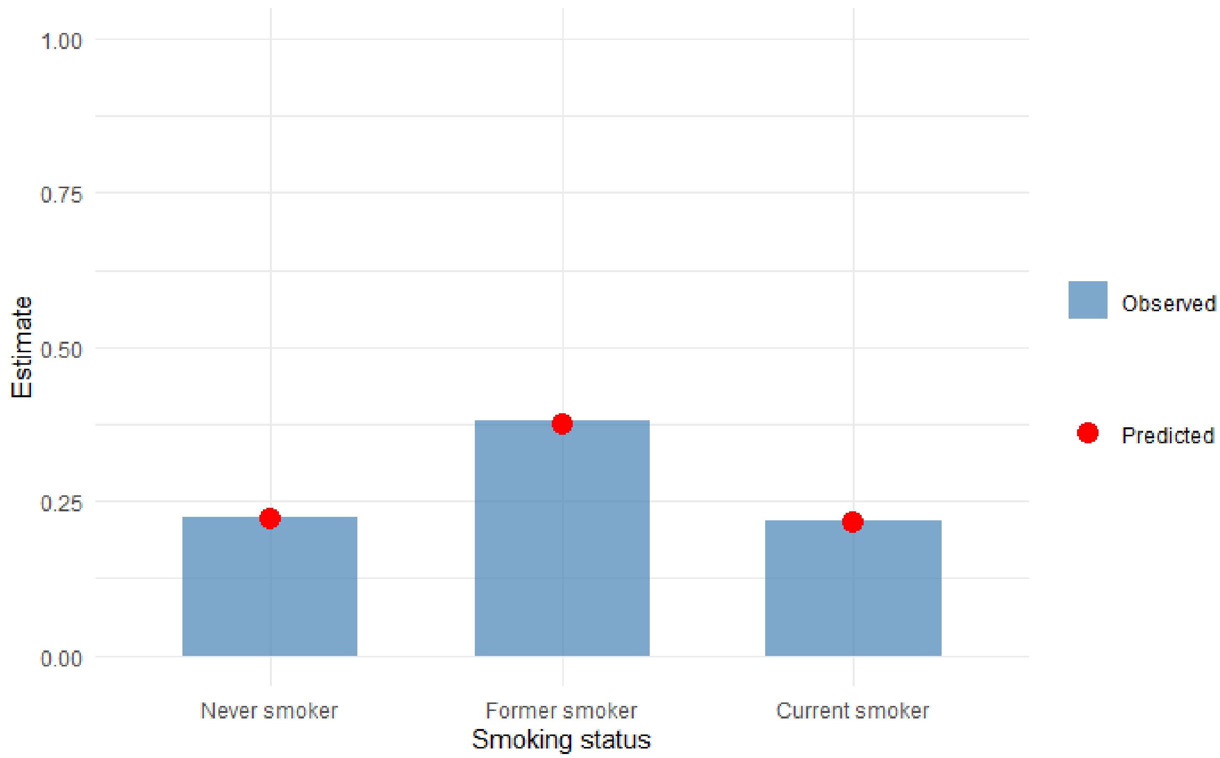
1.00
0.75
0.50
0.25
0.00
Estimate
[61.4, 88.8)
[88.8, 97.1)
[97.1,106.4)
[106.4,162.5]
Waist circumference (cm)
Observed
Predicted



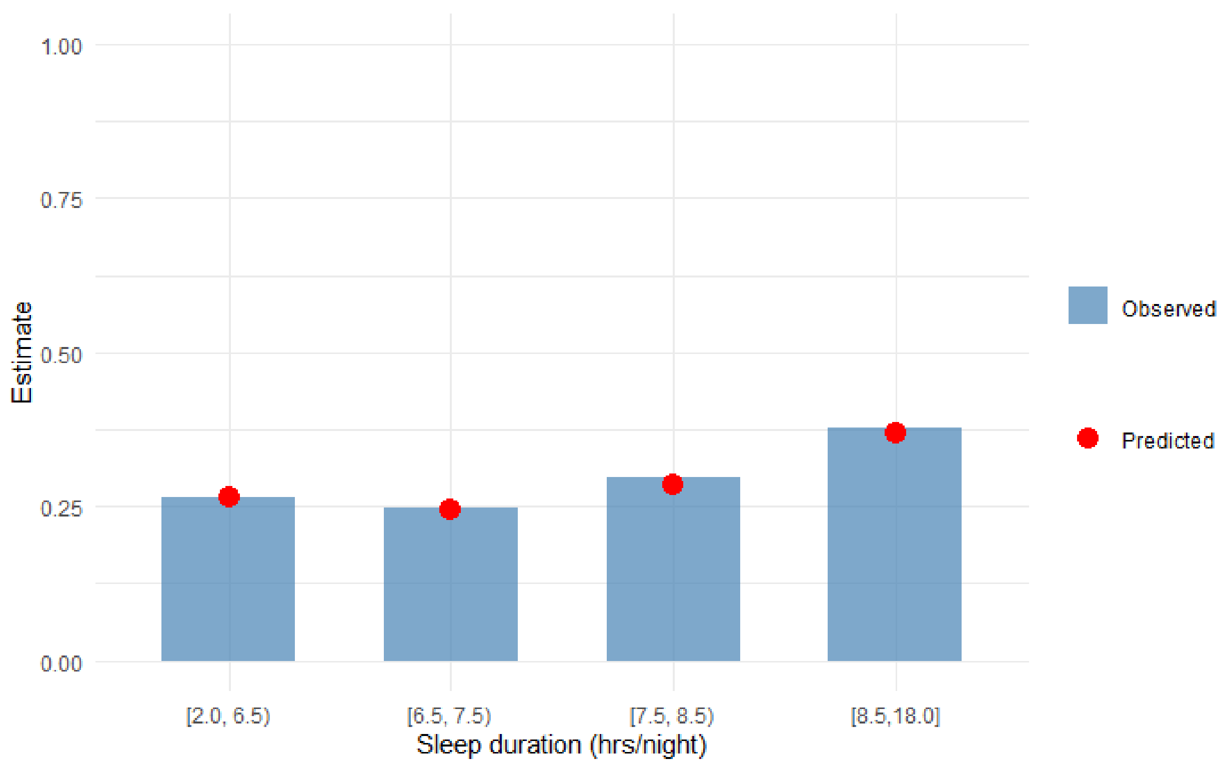
1.00
0.75
0.50
0.25
0.00
Estimate
[35.8,50.6)
[50.6,55.3)
[55.3,60.9)
[60.9,92.8]
Waist-to-height ratio (%)
Observed
Predicted



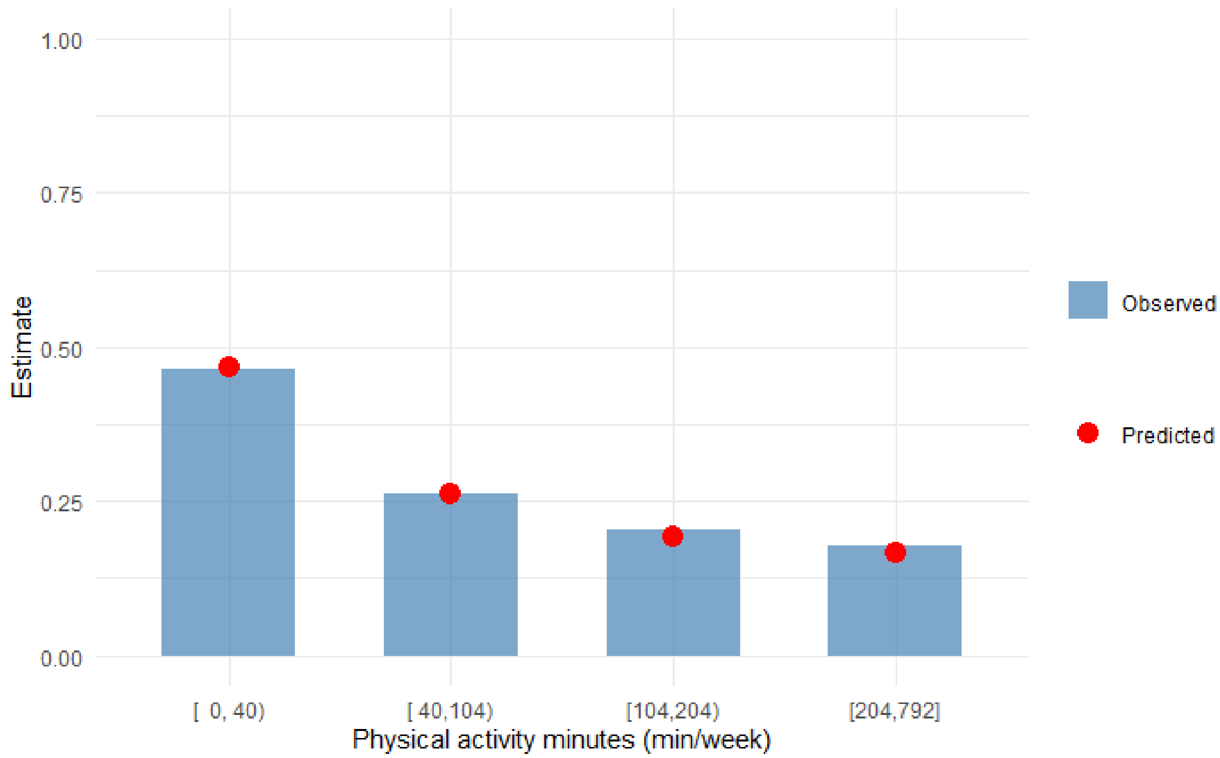
1.00
0.75
0.50
0.25
0.00
Estimate
0
[1, 5)
[5,10)
[10,84]
Weekly alcohol consumption (drinks/week)
Observed
Predicted
1.00
0.75
0.50
0.25
0.00
Estimate
Never drank
Low-risk drinker
Moderate drinker
Heavy drinker
Alcohol consumption level
Observed
Predicted



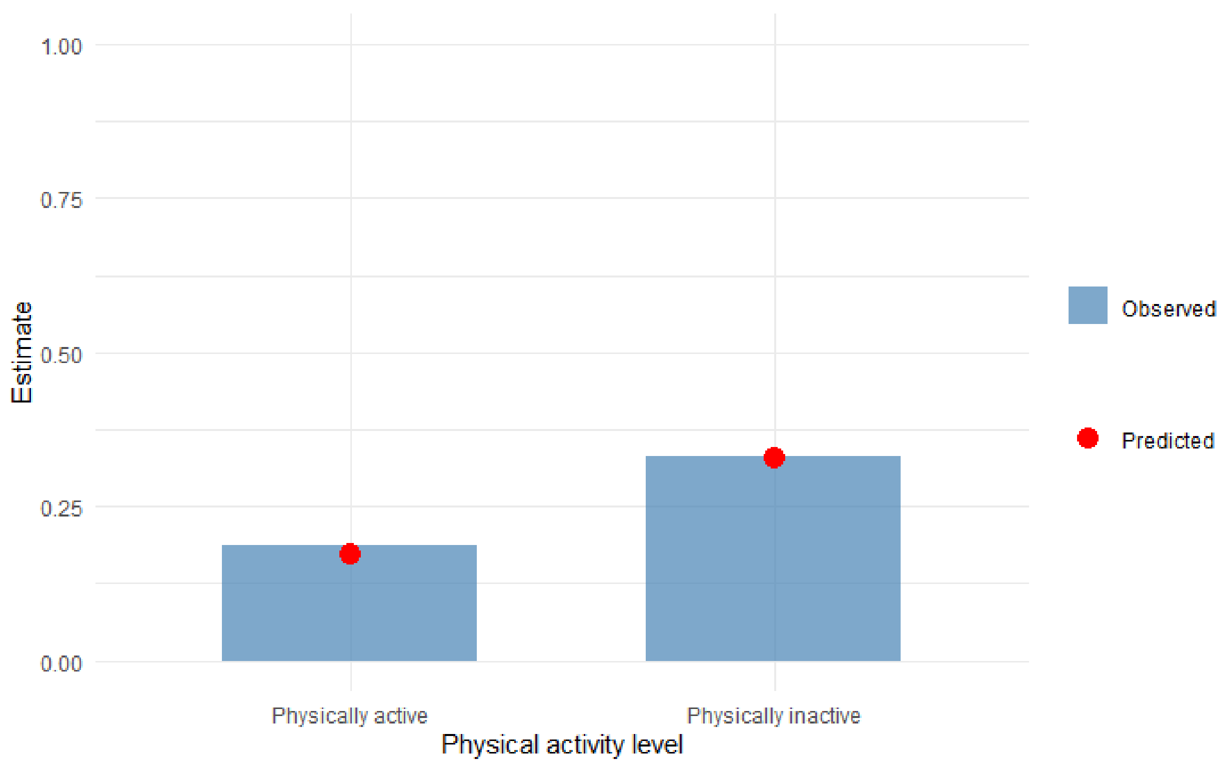
Estimate
1.00
0.75
0.50
0.25
0.00
Never smoker
Former smoker
Current smoker
Smoking status
Observed
Predicted



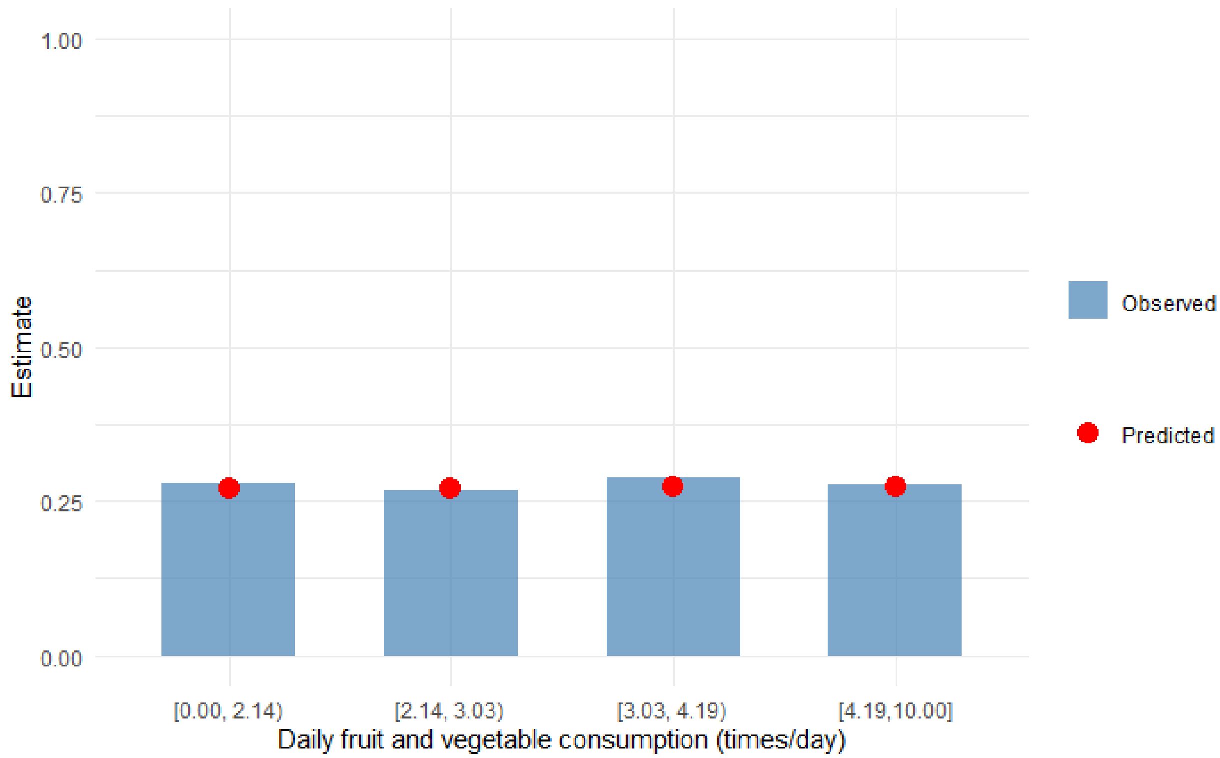
Estimate
1.00
0.75
0.50
0.25
0.00
[2.0, 6.5)
[6.5, 7.5)
[7.5, 8.5)
[8.5,18.0]
Sleep duration (hrs/night)
Observed
Predicted

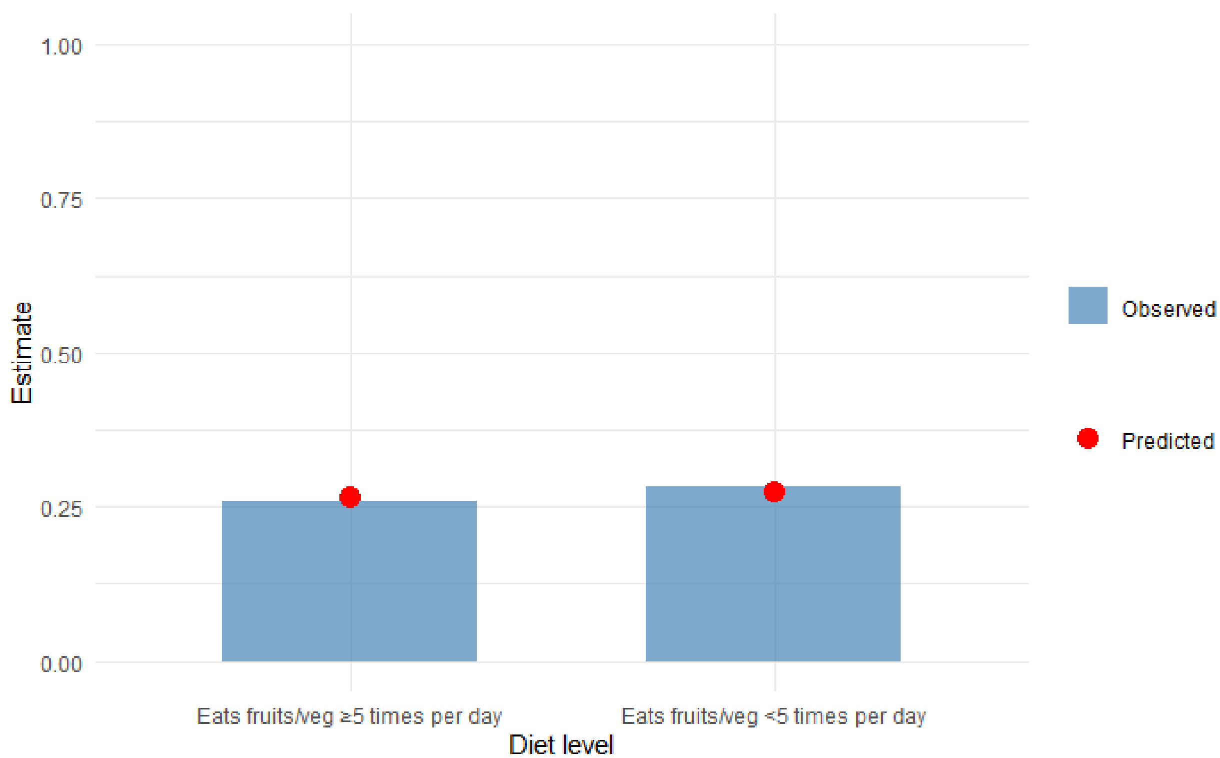


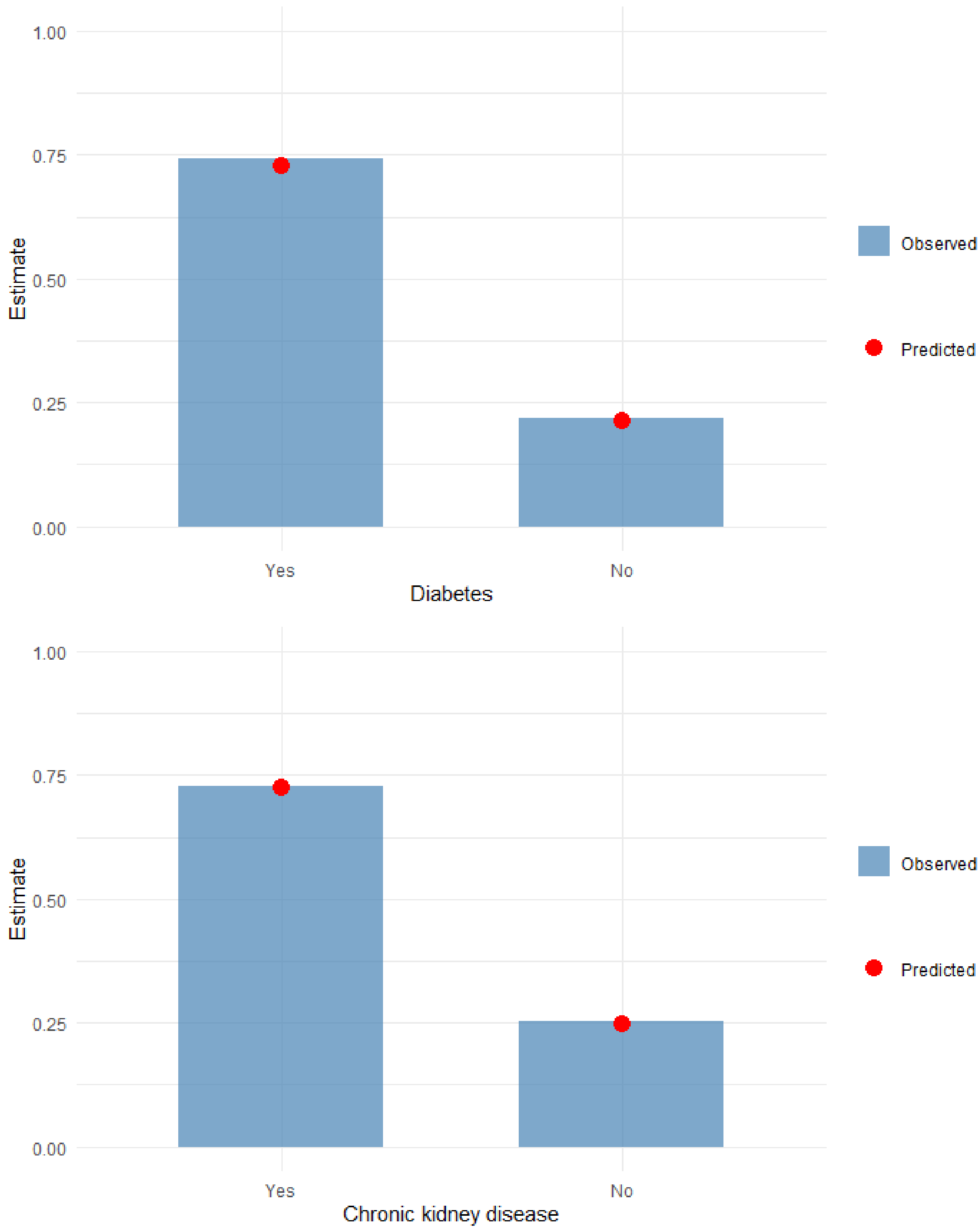
1.00
0.75
0.50
0.25
0.00
Estimate
[0, 40)
[40,104)
[104,204)
[204,792]
Physical activity minutes (min/week)
Observed
Predicted

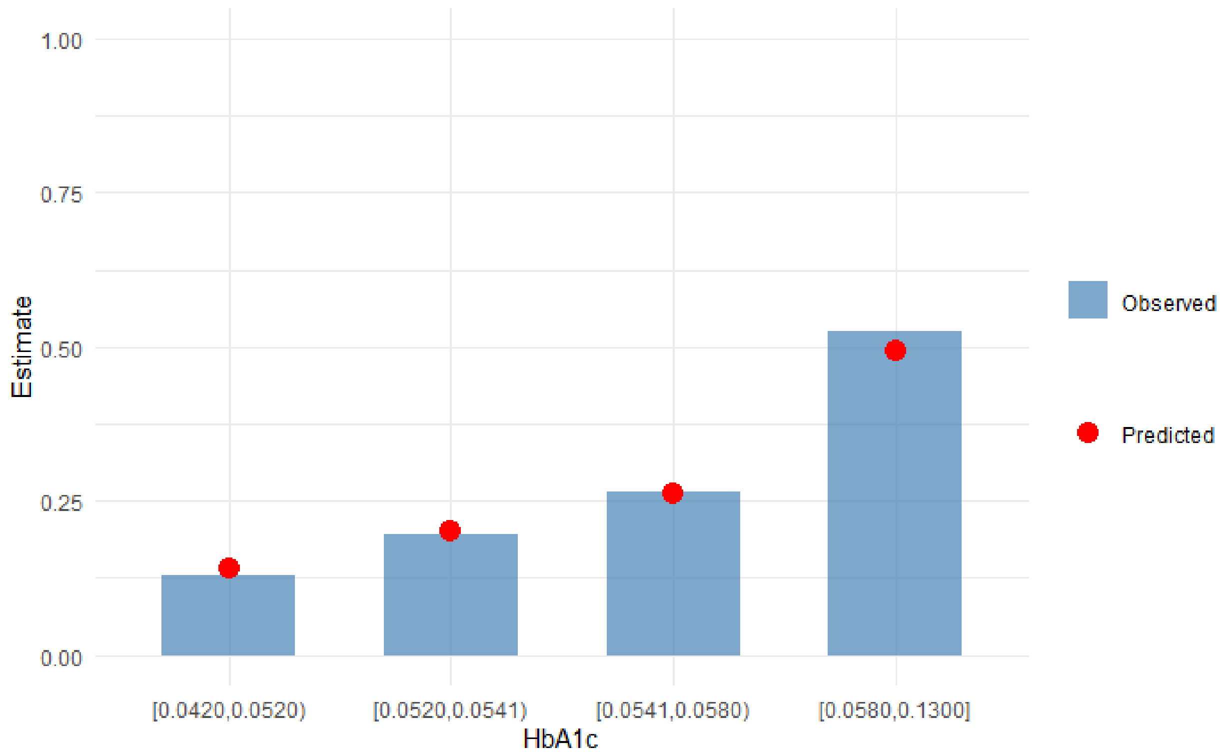


1.00
0.75
0.50
0.25
0.00
Estimate
Physically active
Physically inactive
Physical activity level
Observed
Predicted

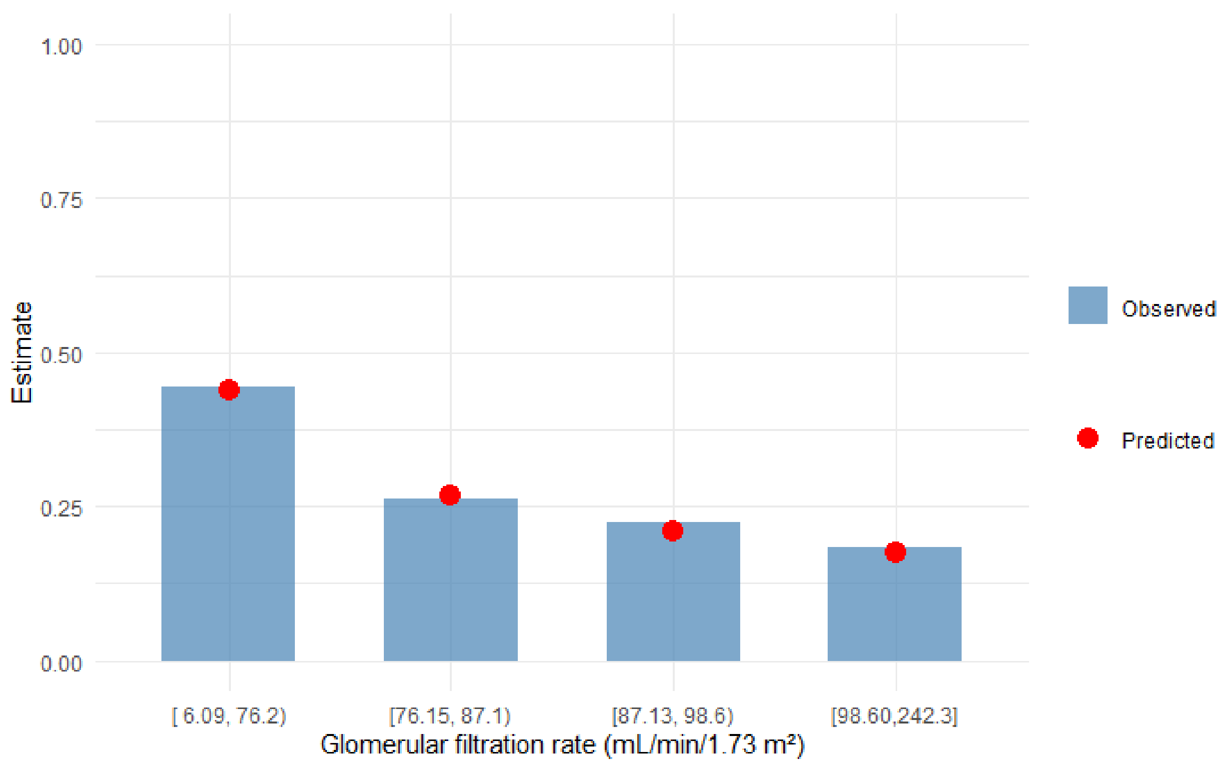

1.00
0.75
0.50
0.25
0.00
Estimate
[0.00, 2.14)
[2.14, 3.03)
[3.03, 4.19)
[4.19,10.00]
Daily fruit and vegetable consumption (times/day)
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
Eats fruits/veg ≥5 times per day
Eats fruits/veg <5 times per day
Diet level
Observed
Predicted

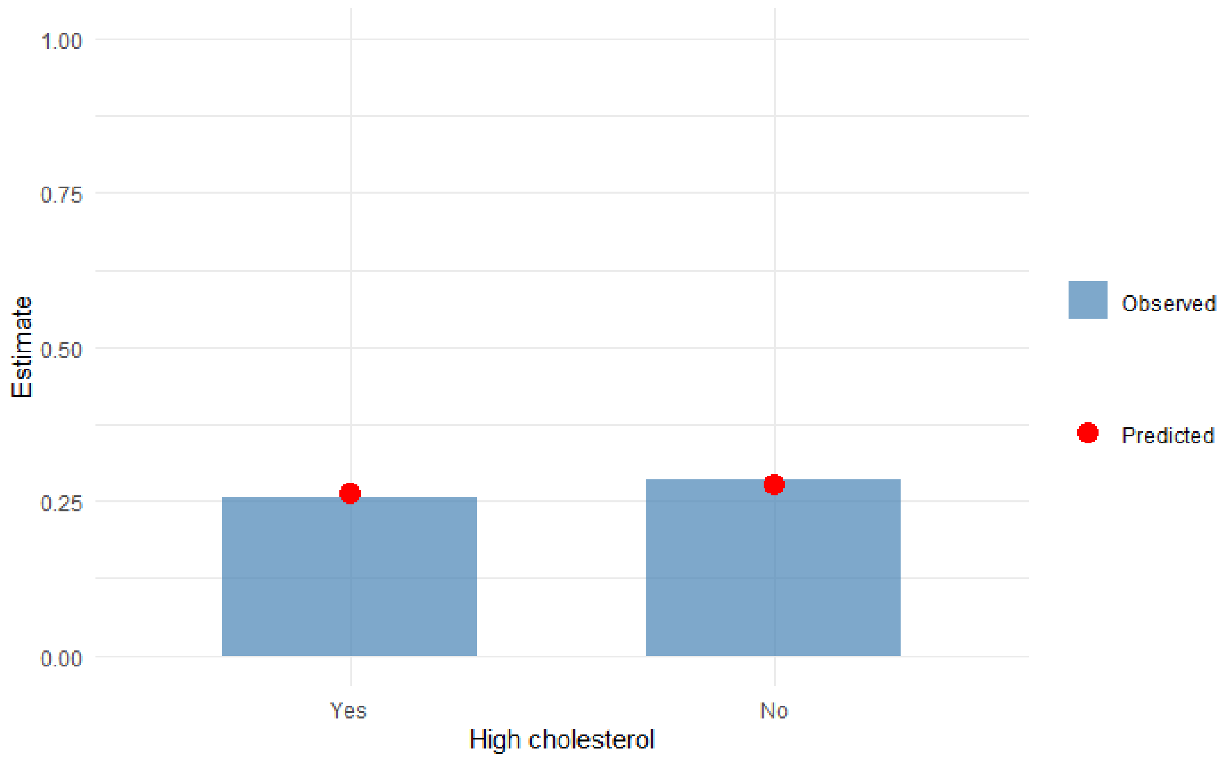

Estimate
1.00
0.75
0.50
0.25
0.00
Yes
No
Diabetes
Observed
Predicted
Estimate
1.00
0.75
0.50
0.25
0.00
Yes
No
Chronic kidney disease
Observed
Predicted

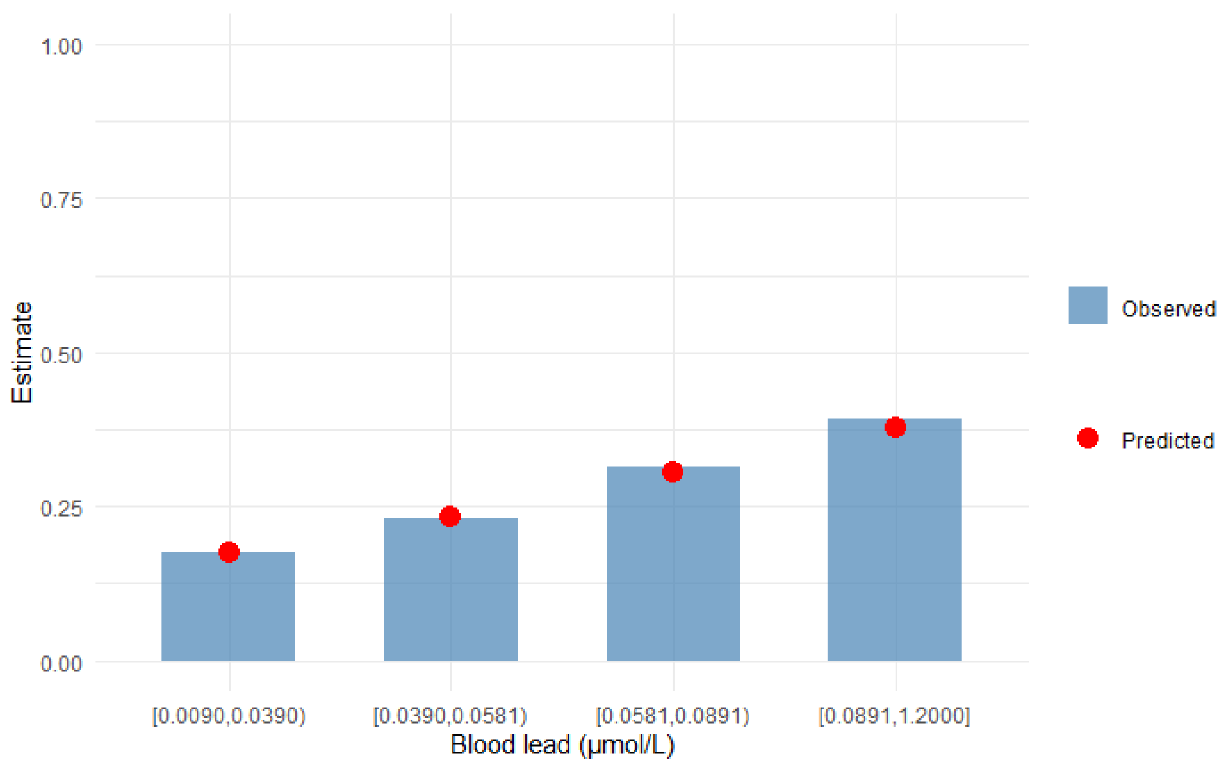


1.00
0.75
0.50
0.25
0.00
Estimate
Observed
Predicted
[0.0420,0.0520)
[0.0520,0.0541)
[0.0541,0.0580)
[0.0580,0.1300]
HbA1c

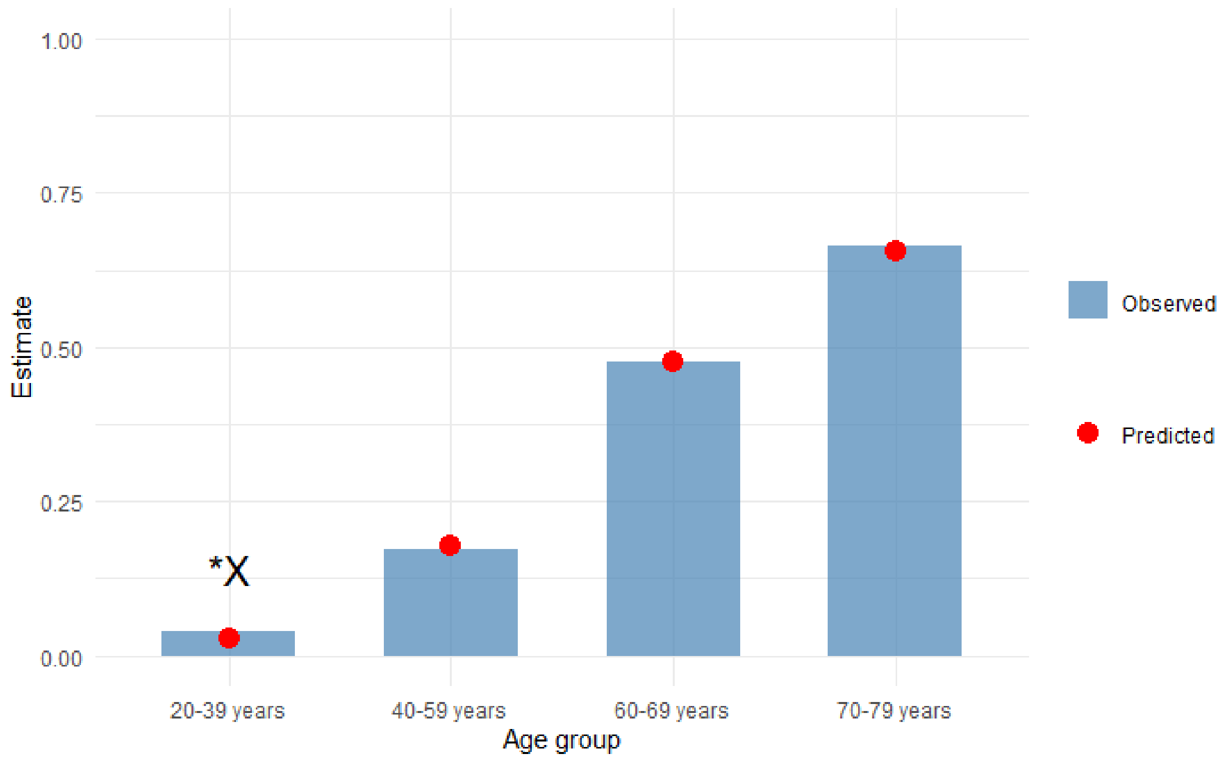


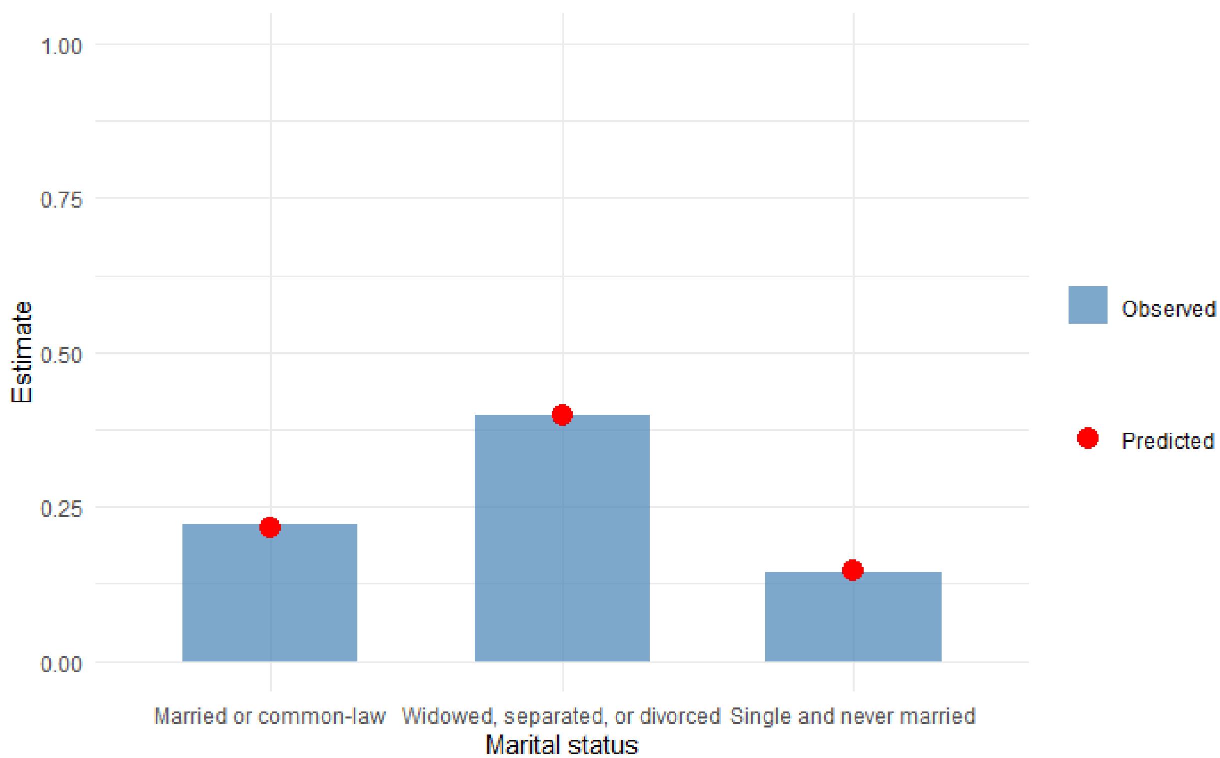
1.00
0.75
0.50
0.25
0.00
Estimate
Observed
Predicted
[6.09, 76.2)
[76.15, 87.1)
[87.13, 98.6)
[98.60,242.3]
Glomerular filtration rate (mL/min/1.73 m²)

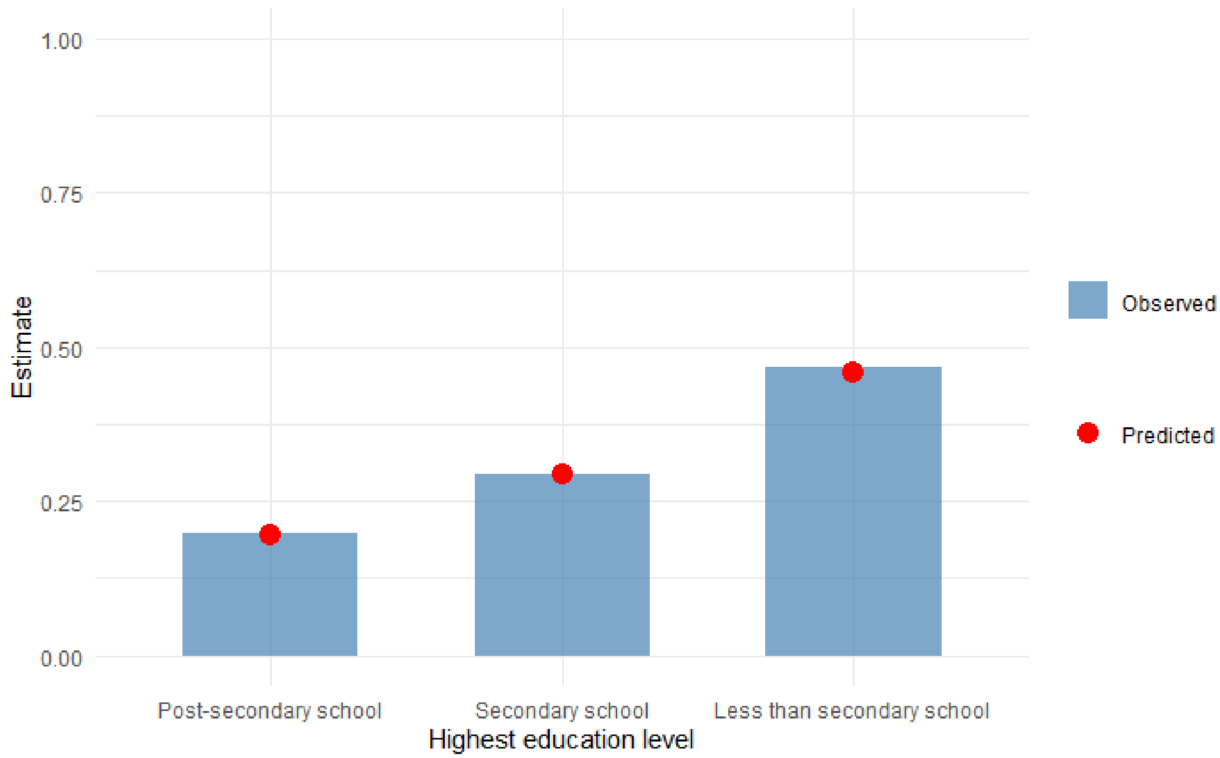

1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
High cholesterol
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
[0.0090,0.0390)
[0.0390,0.0581)
[0.0581,0.0891)
[0.0891,1.2000]
Blood lead (μmol/L)
Observed
Predicted

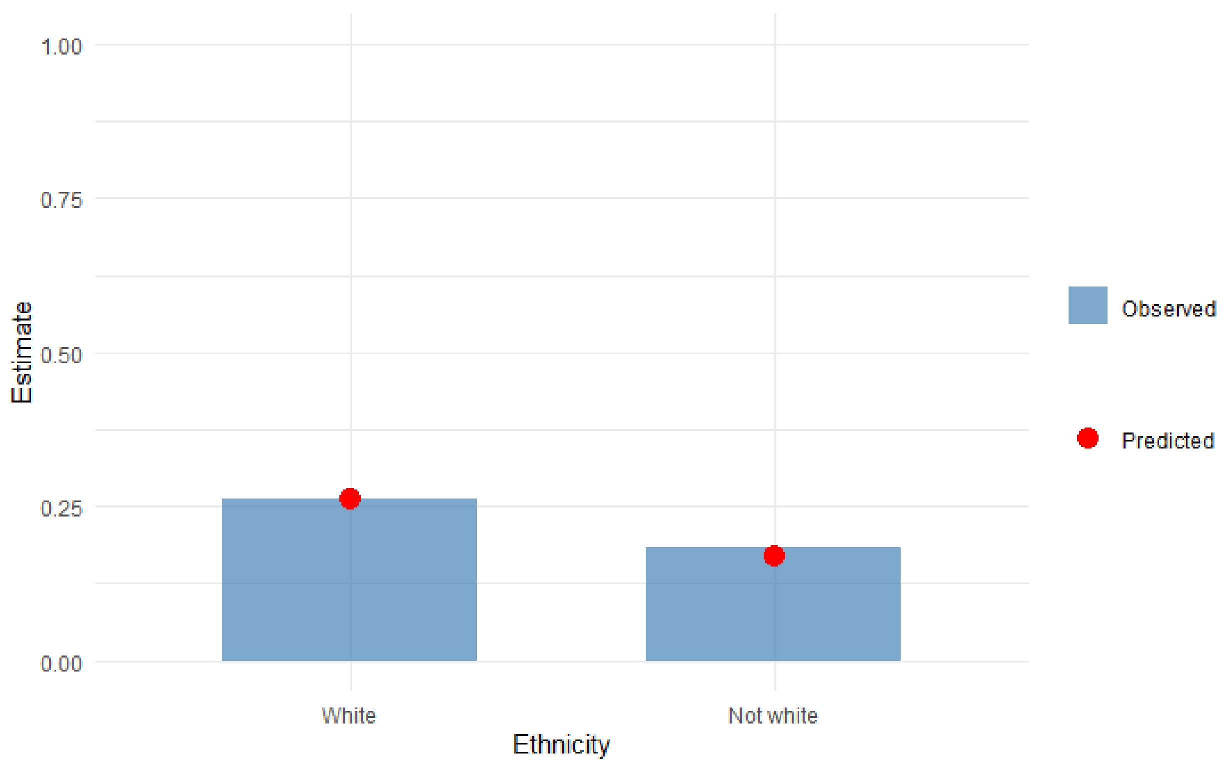
Female Full Model:
X – excluded subgroup with observed estimate less than 5%
*** – subgroup with difference between observed and predicted estimates over 20%**



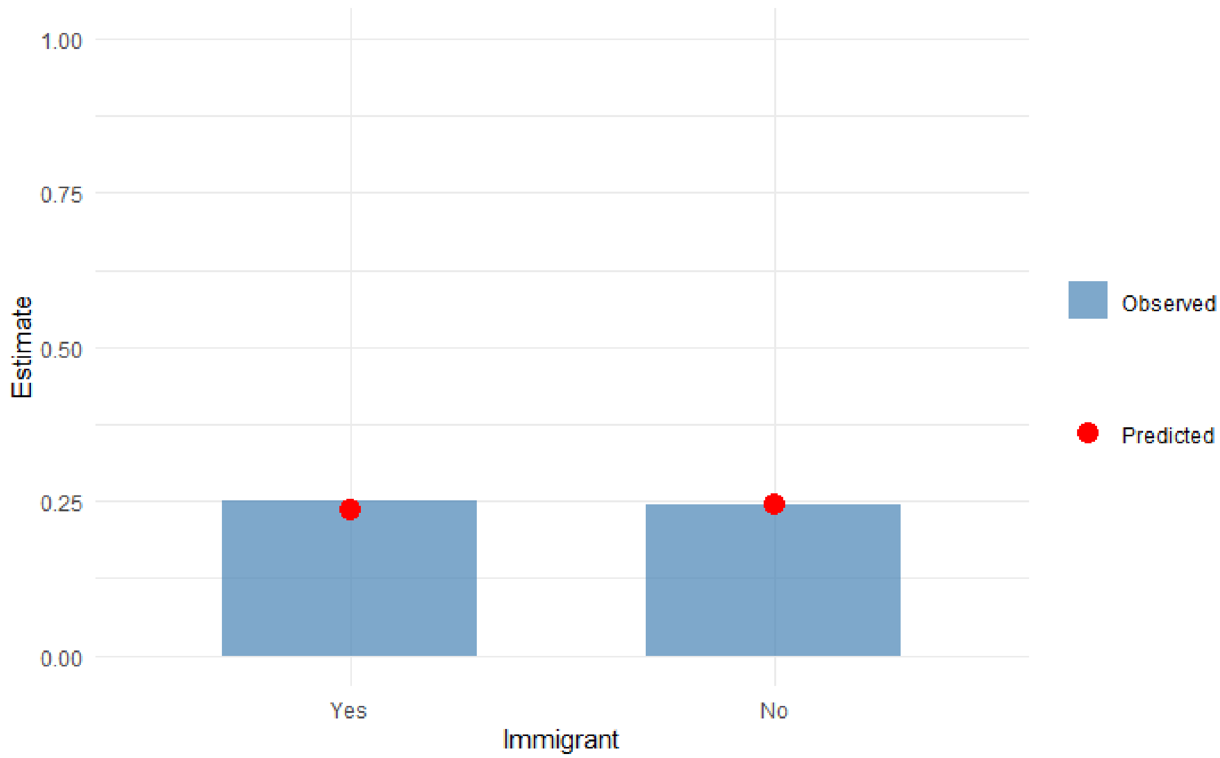




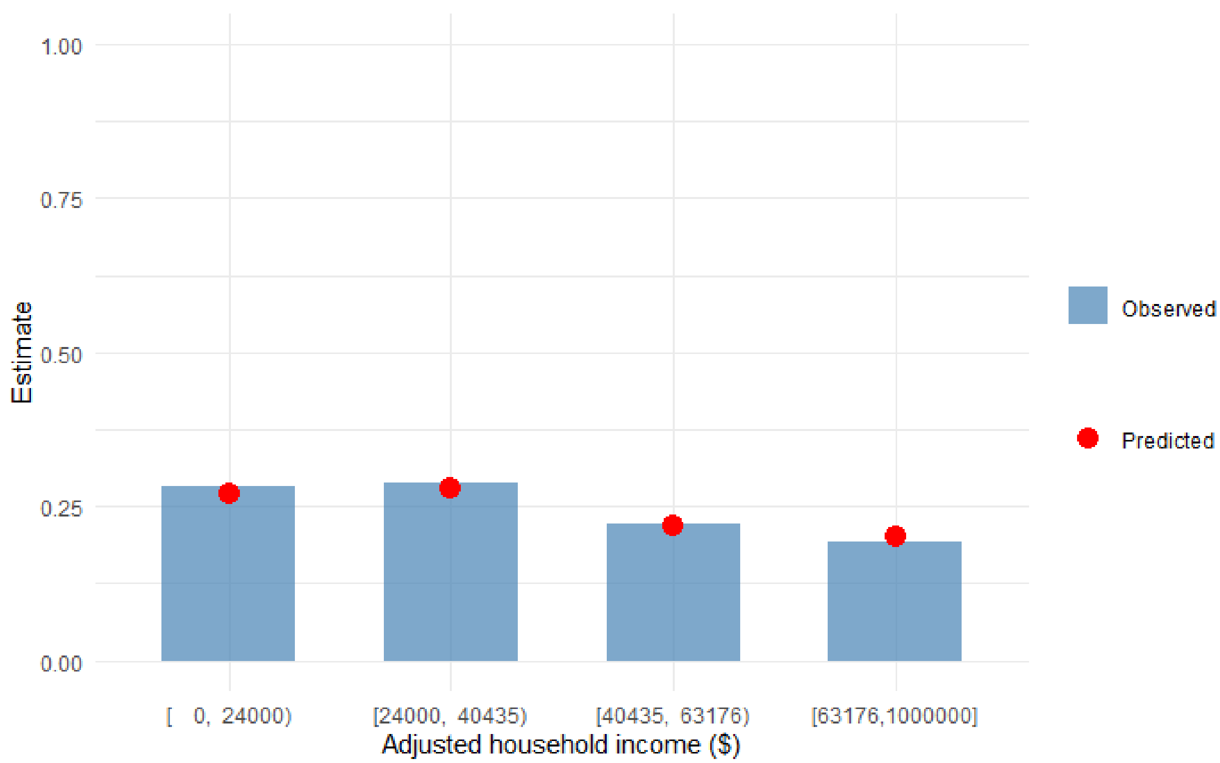
1.00
0.75
0.50
0.25
0.00
Estimate
Post-secondary school
Secondary school
Less than secondary school
Highest education level
Observed
Predicted



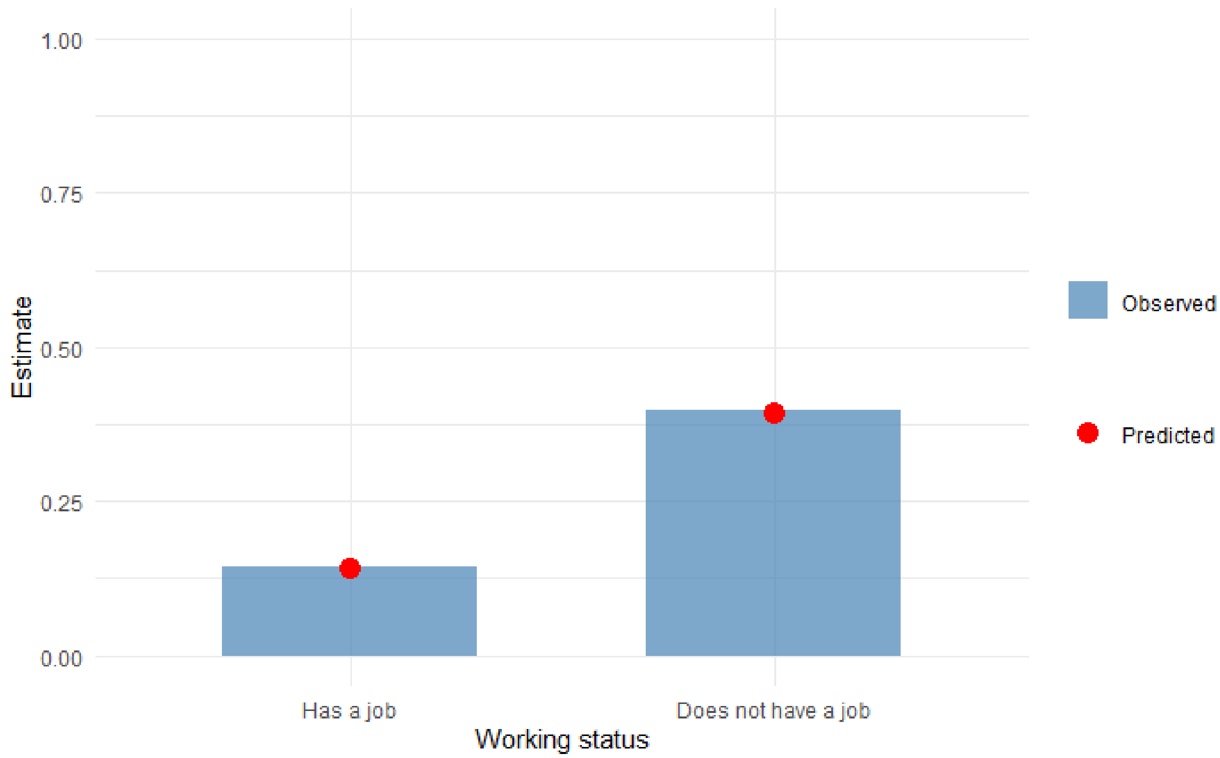
1.00
0.75
0.50
0.25
0.00
Estimate
White
Not white
Ethnicity
Observed
Predicted

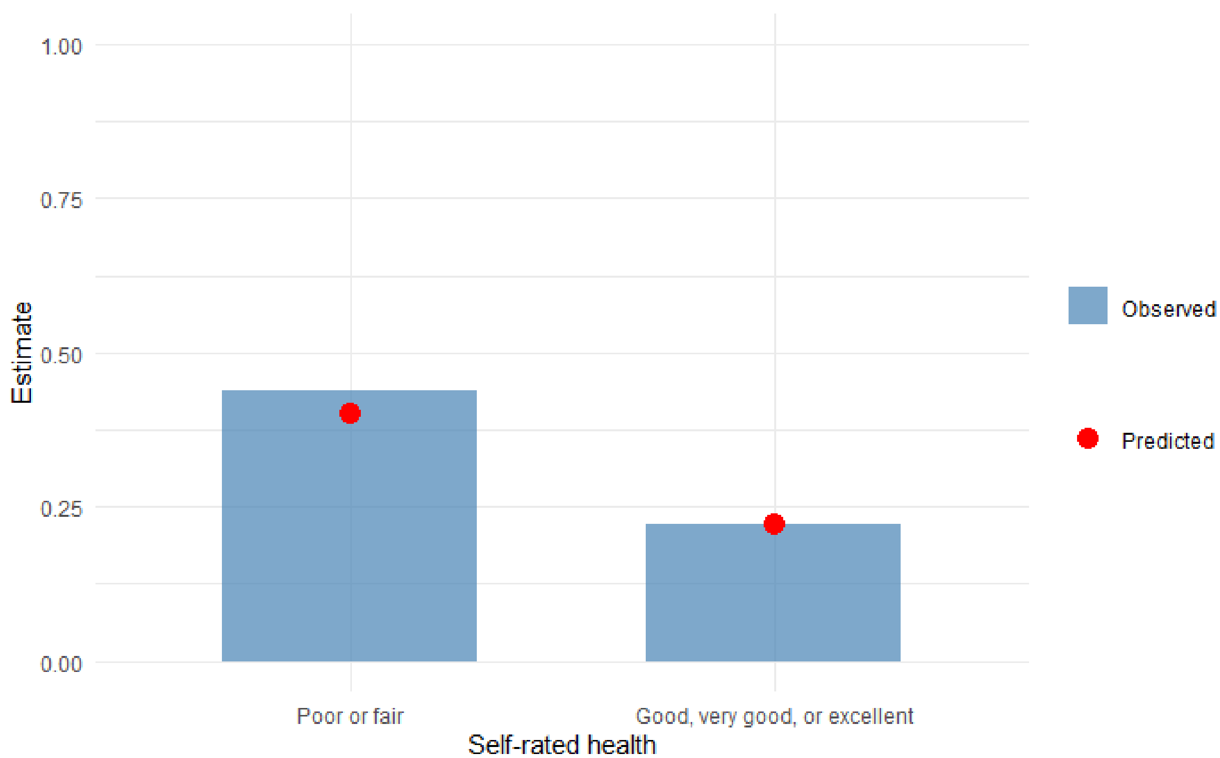


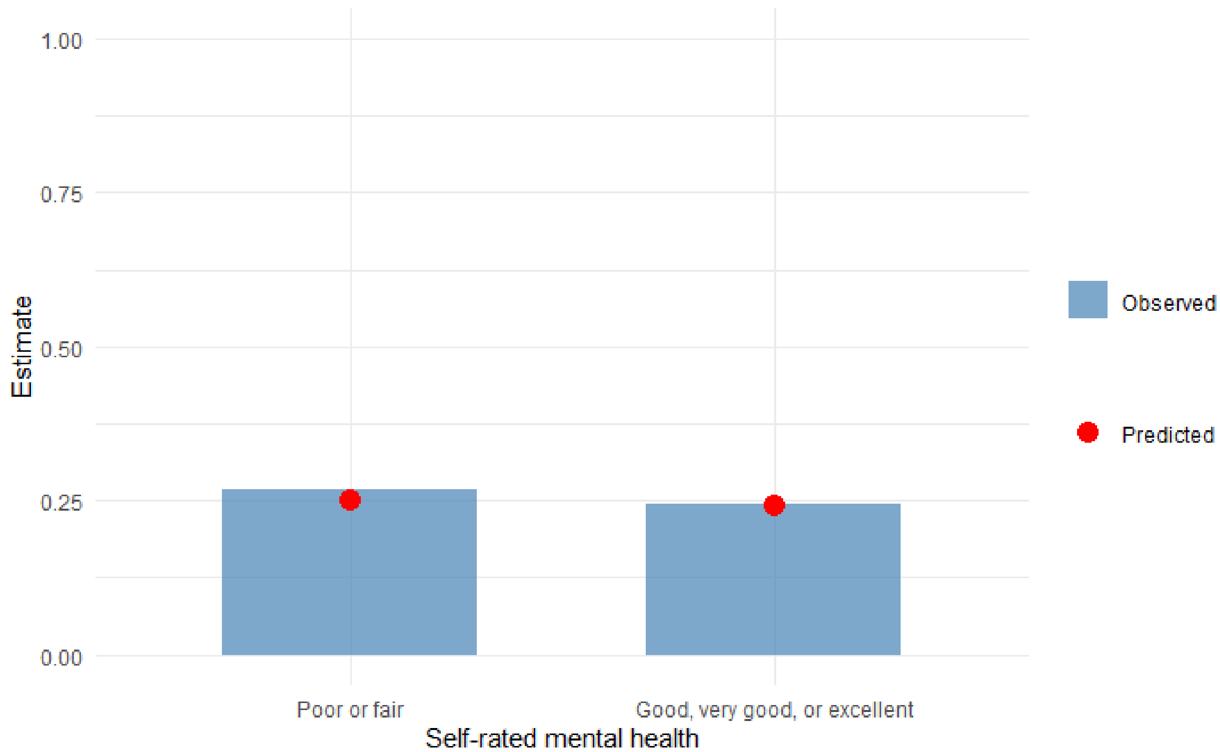
1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
Immigrant
Observed
Predicted

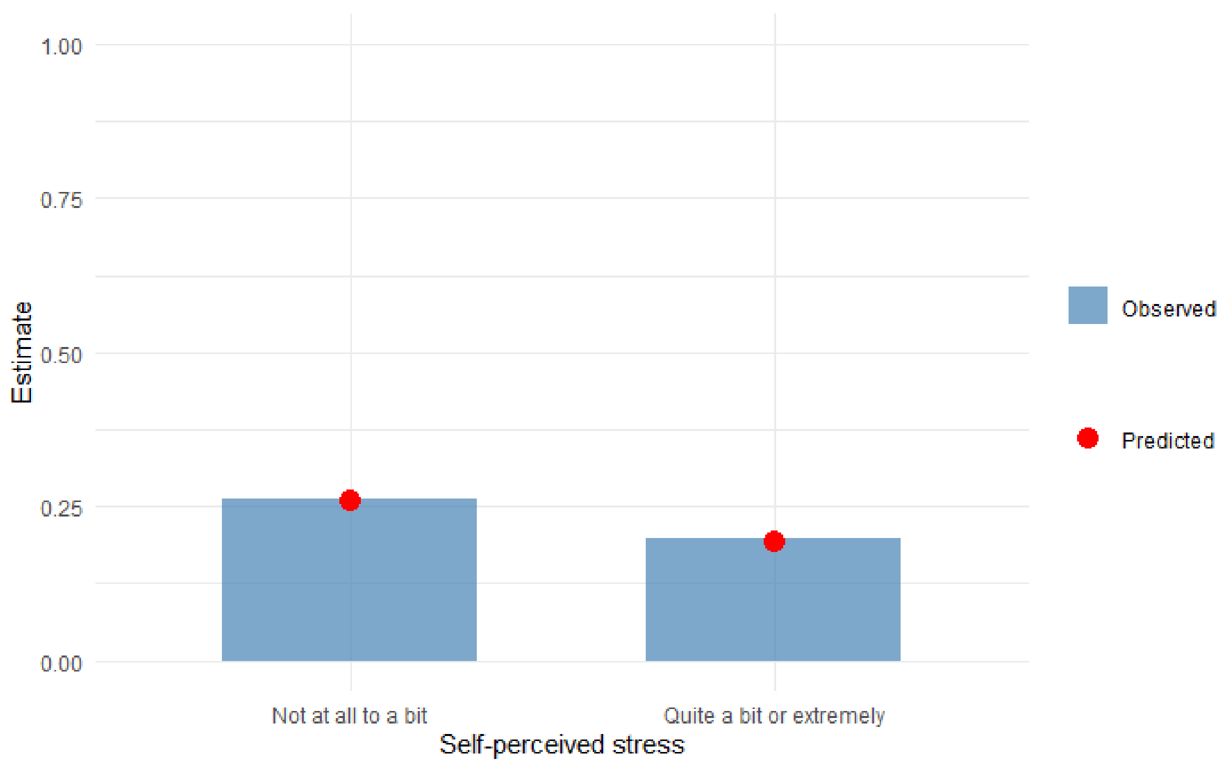


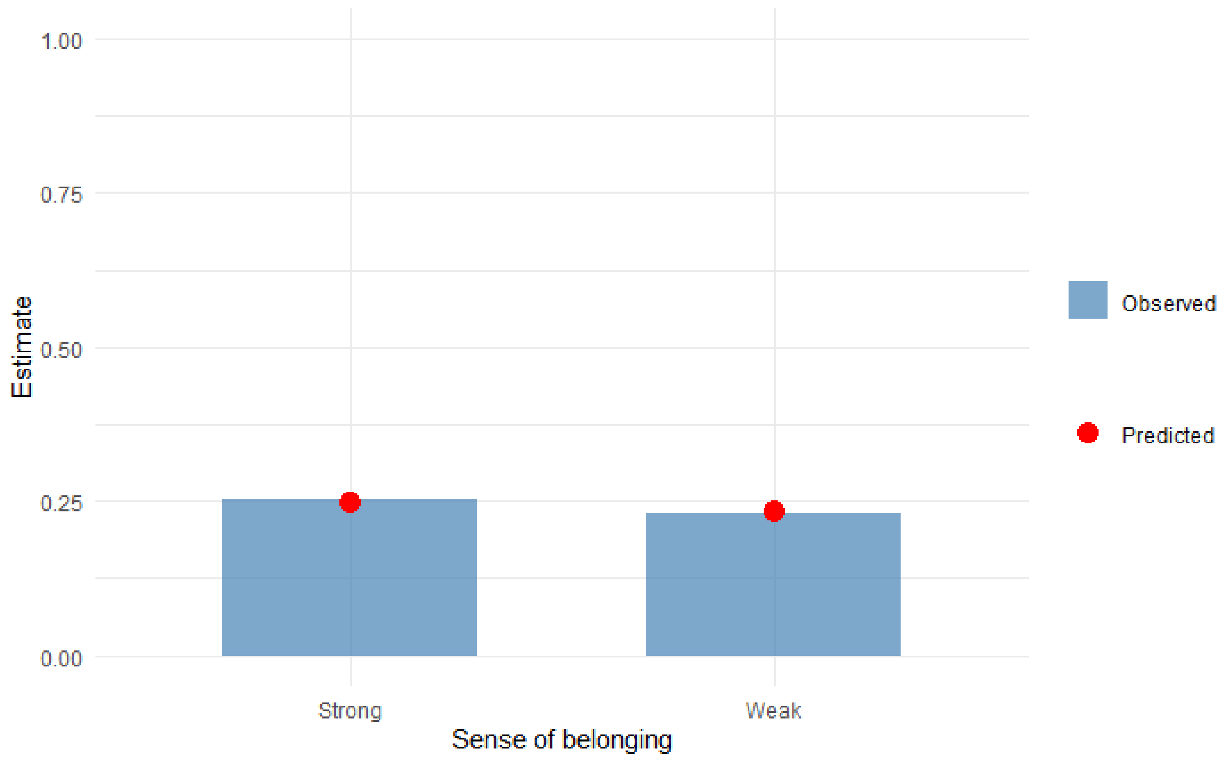
1.00
0.75
0.50
0.25
0.00
Estimate
[0, 24000)
[24000, 40435)
[40435, 63176)
[63176,1000000]
Adjusted household income ($)
Observed
Predicted

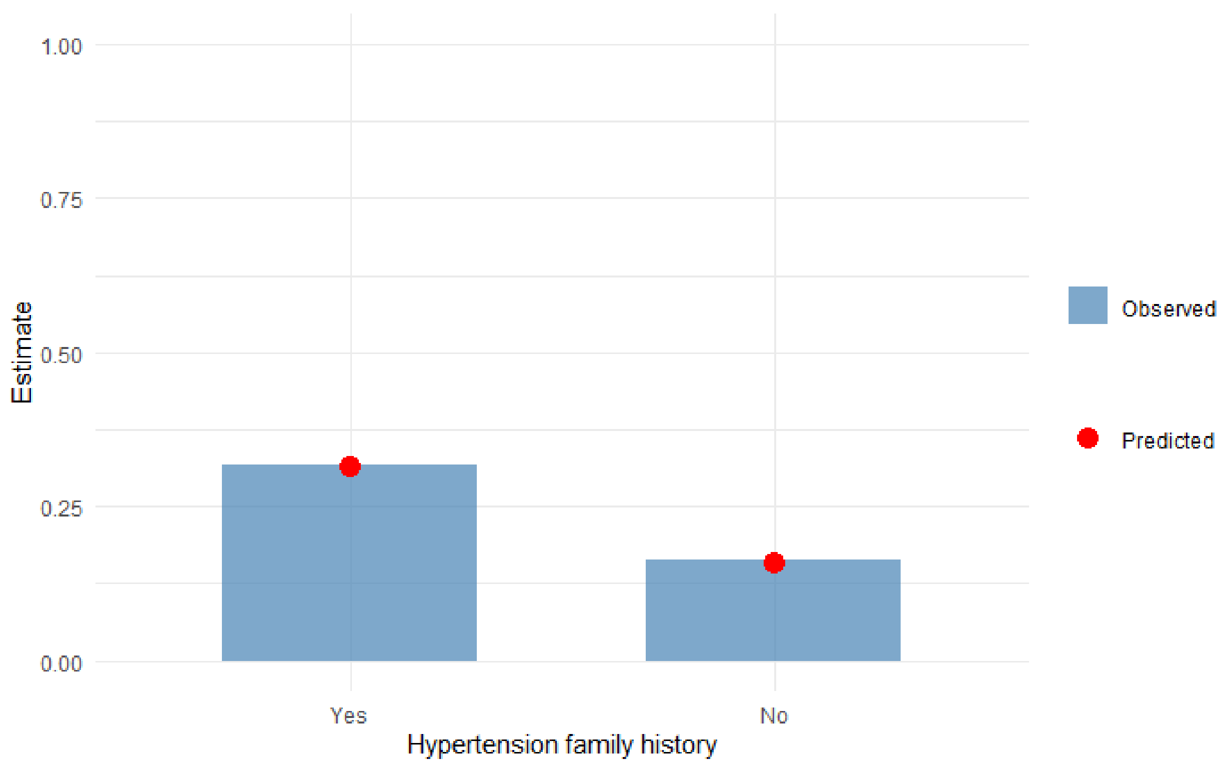

1.00
0.75
0.50
0.25
0.00
Estimate
Has a job
Does not have a job
Working status
Observed
Predicted

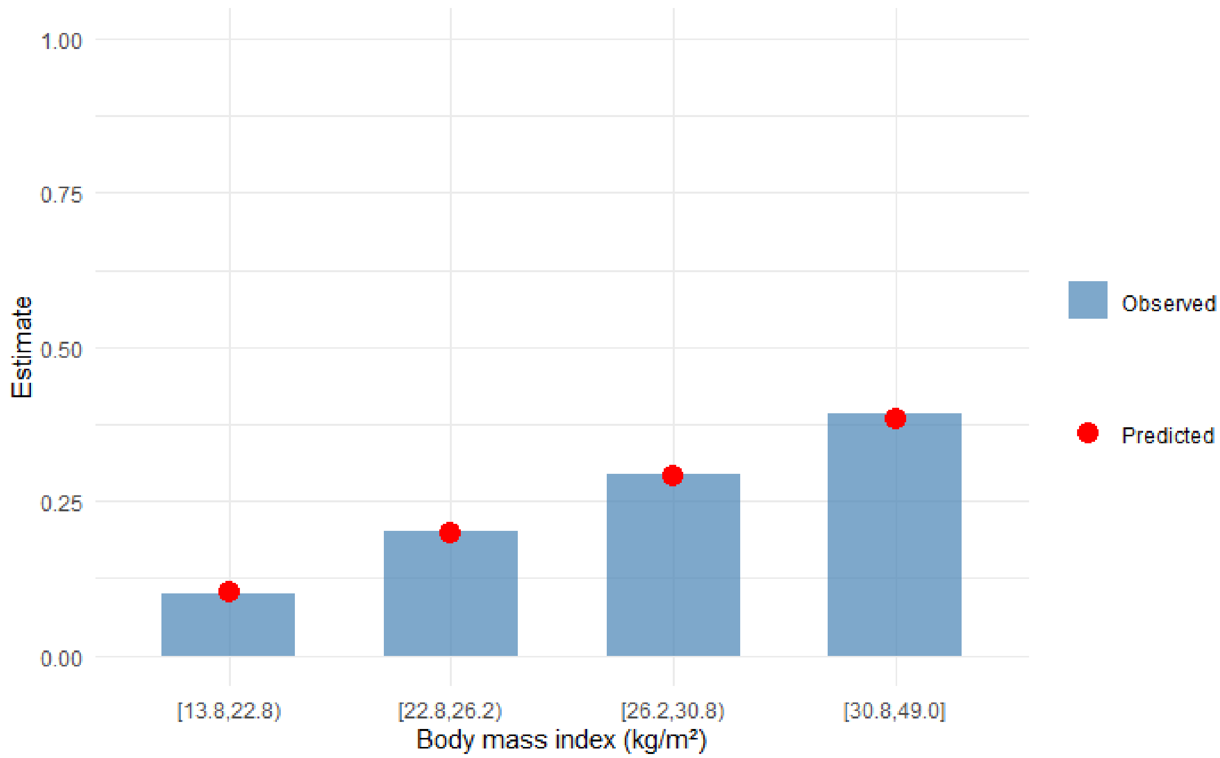

1.00
0.75
0.50
0.25
0.00
Estimate
Poor or fair
Good, very good, or excellent
Self-rated health
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
Poor or fair
Good, very good, or excellent
Self-rated mental health
Observed
Predicted

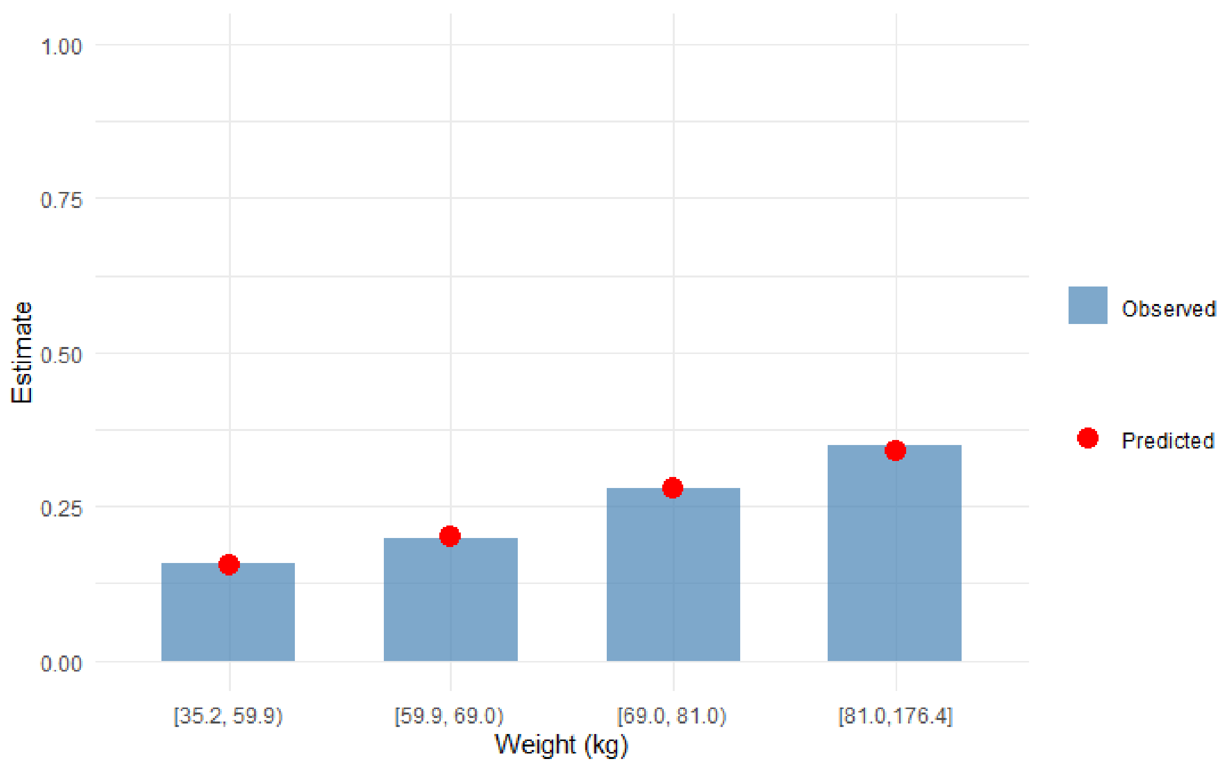

1.00
0.75
0.50
0.25
0.00
Estimate
Not at all to a bit
Quite a bit or extremely
Self-perceived stress
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
Strong
Weak
Sense of belonging
Observed
Predicted

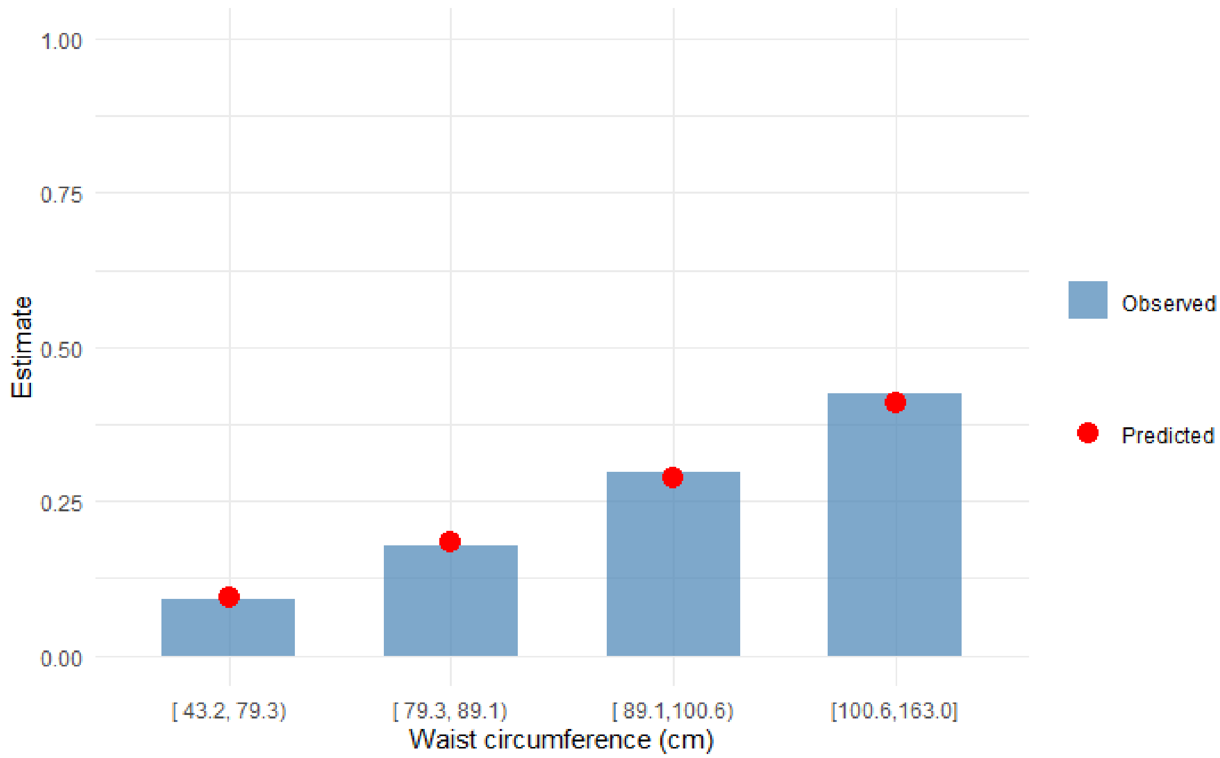

1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
Hypertension family history
Observed
Predicted

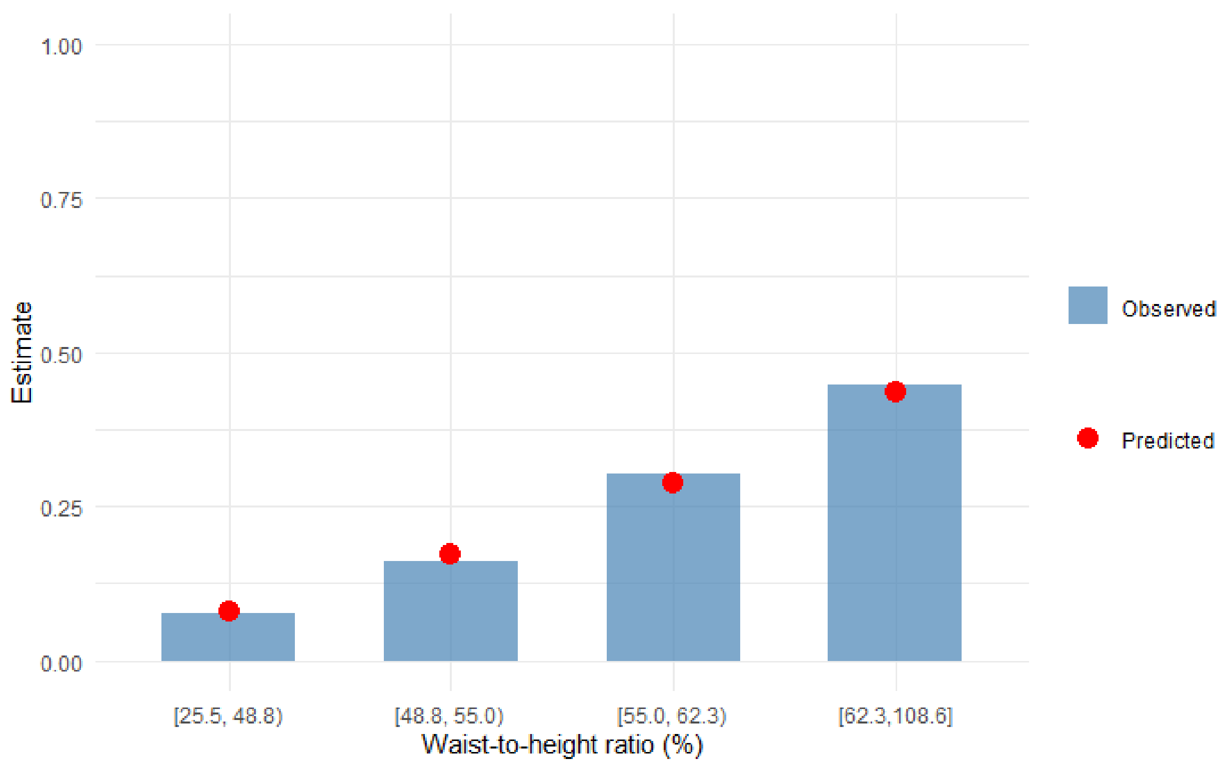


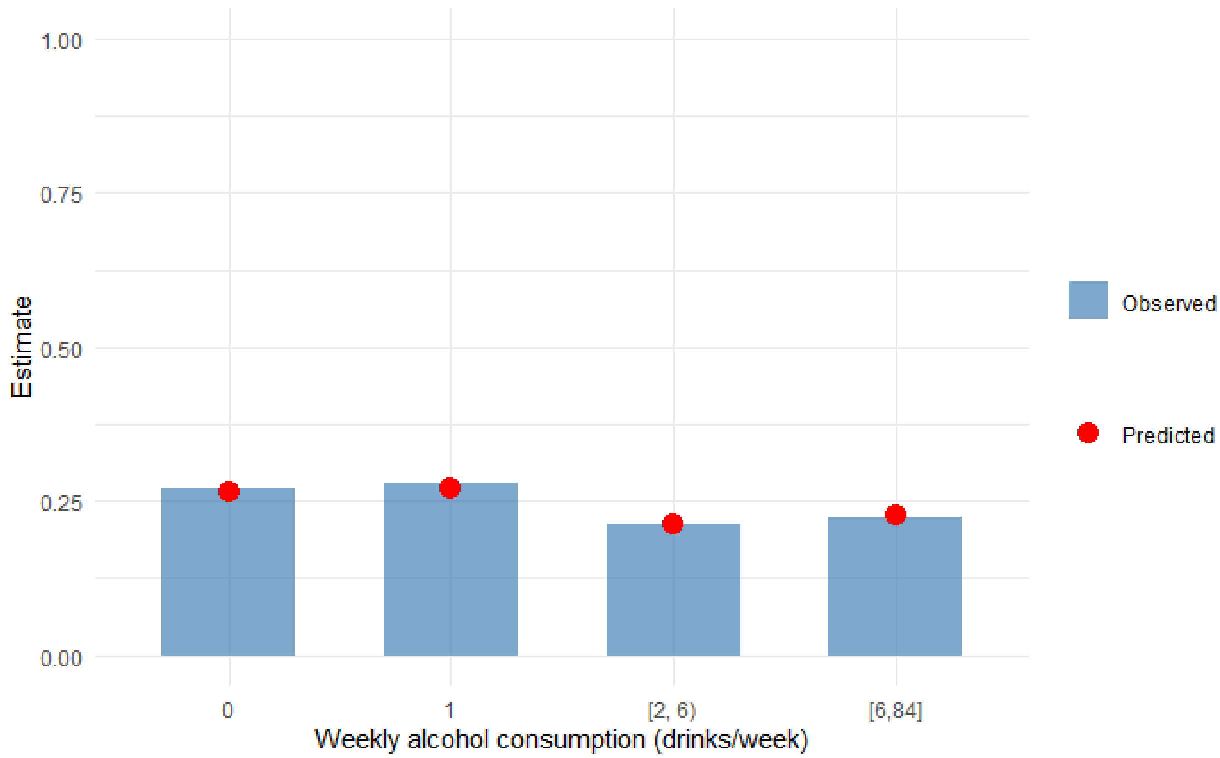
1.00
0.75
0.50
0.25
0.00
Estimate
[13.8,22.8)
[22.8,26.2)
[26.2,30.8)
[30.8,49.0]
Body mass index (kg/m²)
Observed
Predicted

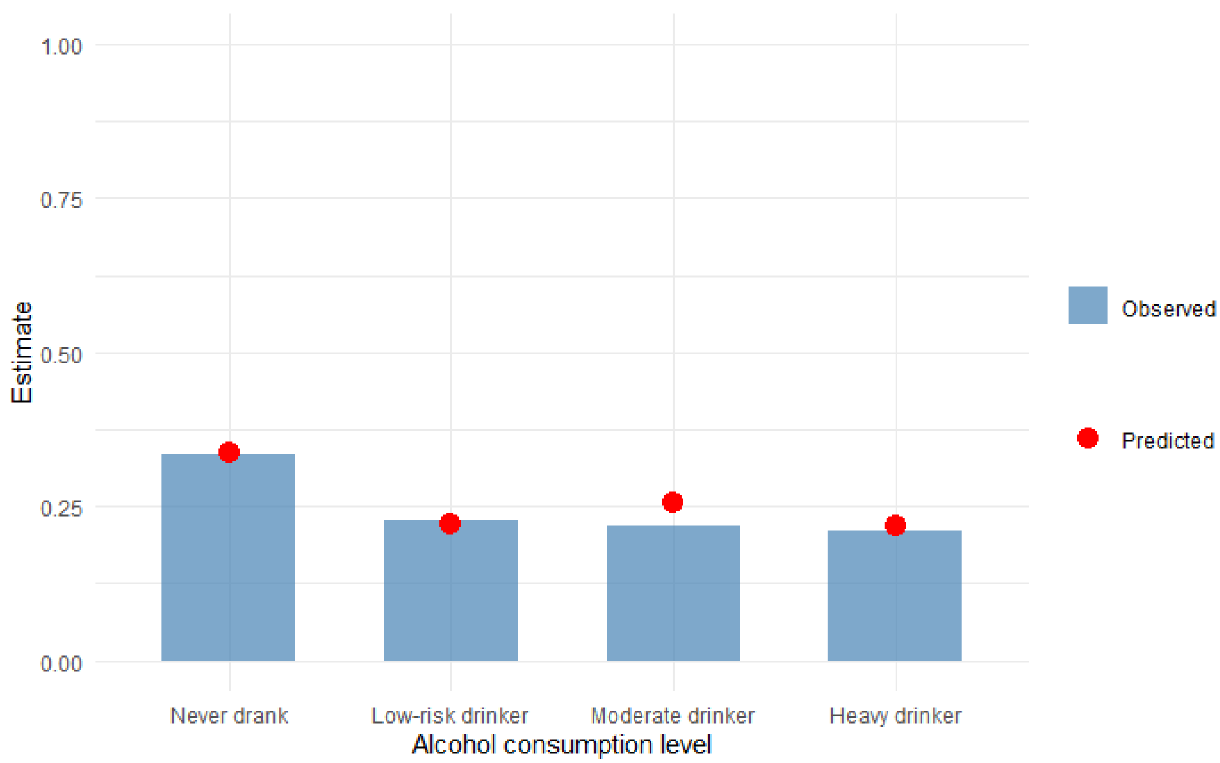


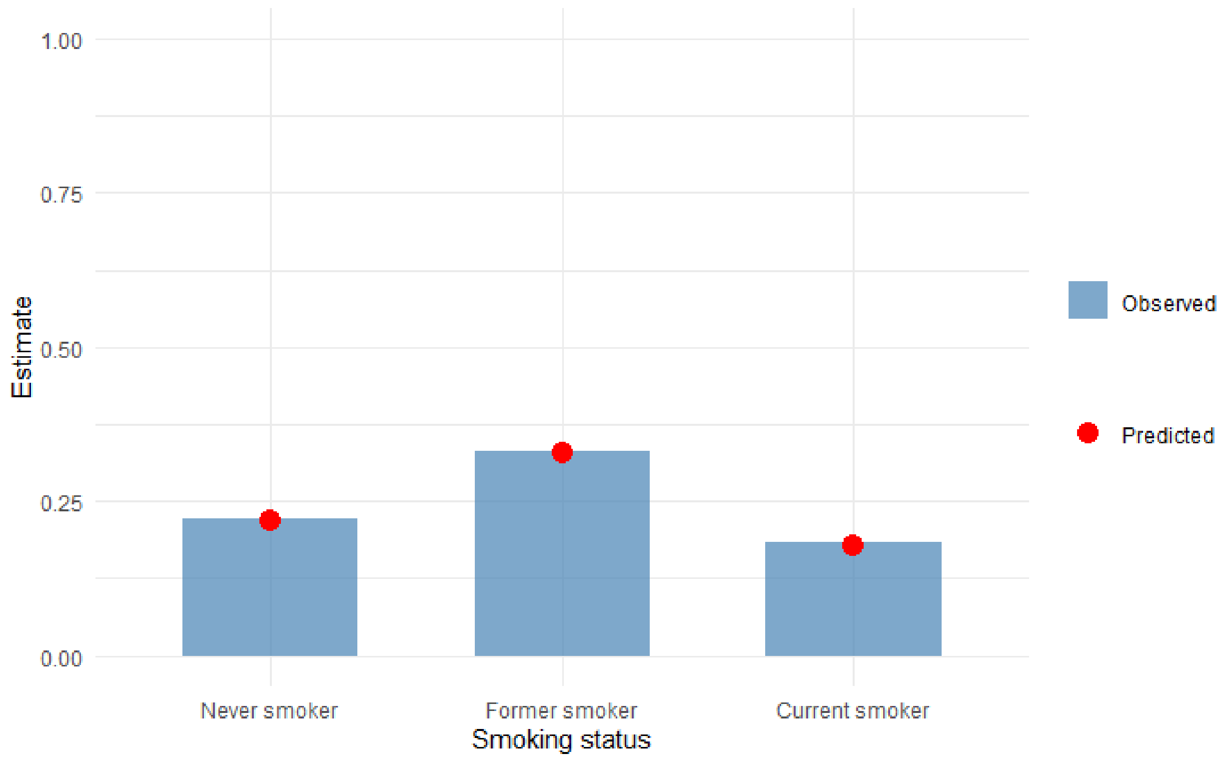
1.00
0.75
0.50
0.25
0.00
Estimate
[35.2, 59.9)
[59.9, 69.0)
[69.0, 81.0)
[81.0,176.4]
Weight (kg)
Observed
Predicted

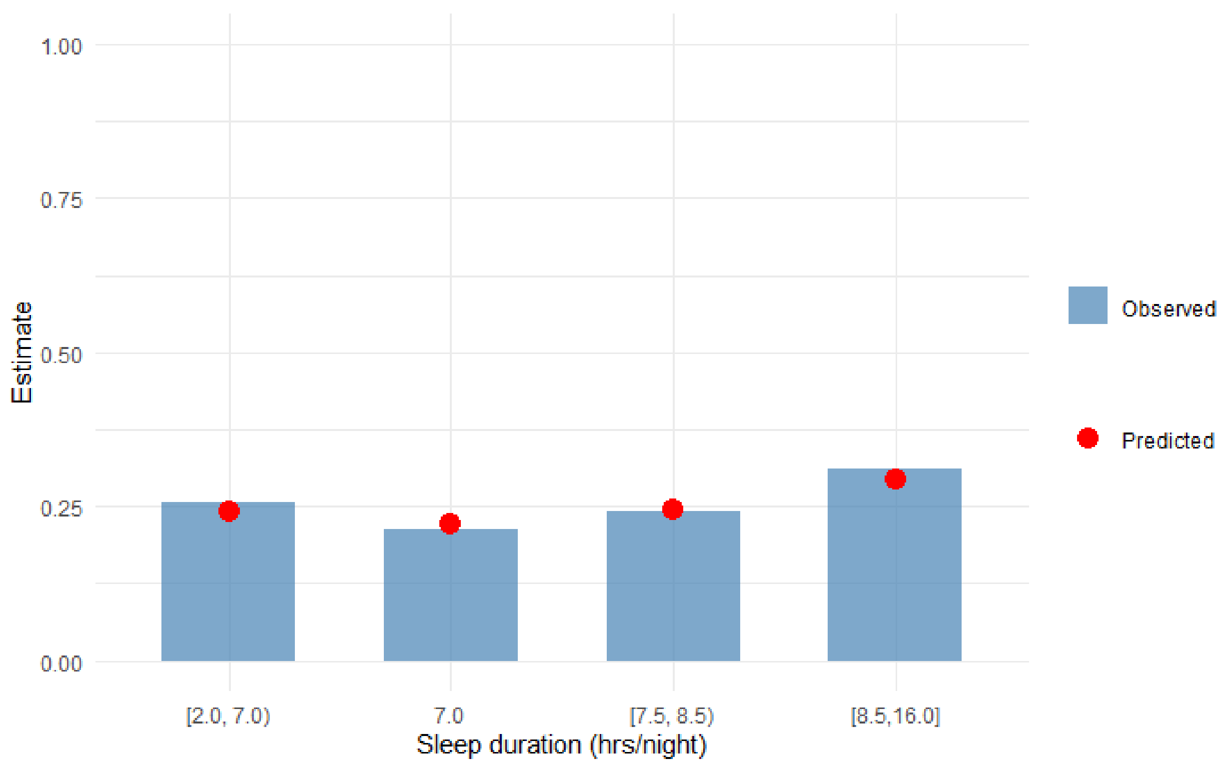

1.00
0.75
0.50
0.25
0.00
Estimate
[43.2, 79.3)
[79.3, 89.1)
[89.1,100.6)
[100.6,163.0]
Waist circumference (cm)
Observed
Predicted

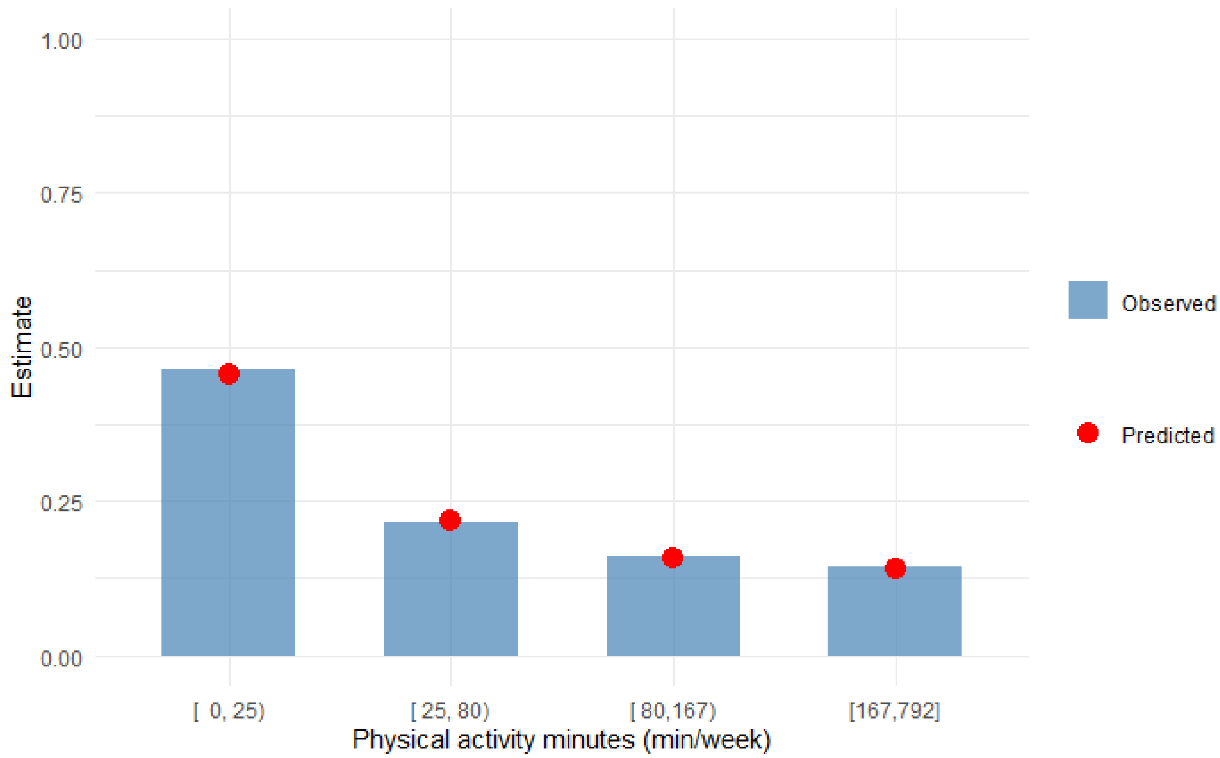

1.00
0.75
0.50
0.25
0.00
Estimate
[25.5, 48.8)
[48.8, 55.0)
[55.0, 62.3)
[62.3,108.6]
Waist-to-height ratio (%)
Observed
Predicted

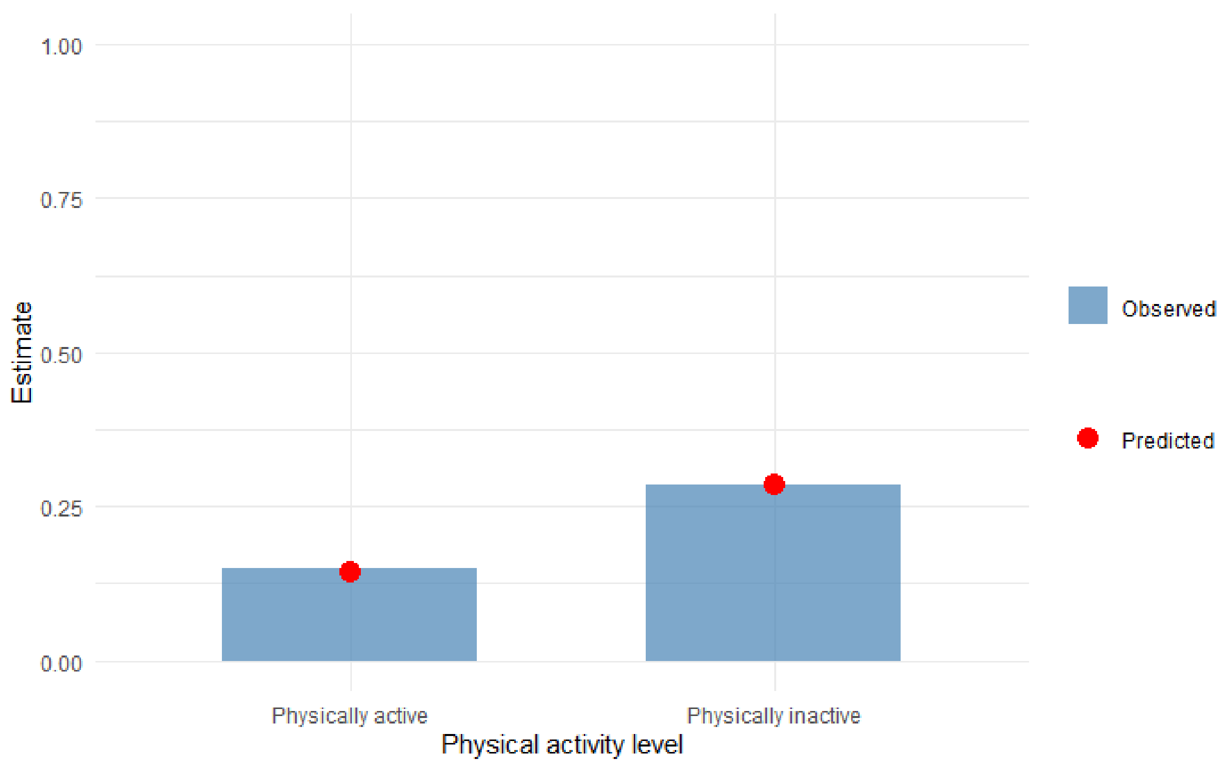

1.00
0.75
0.50
0.25
0.00
Estimate
0
1
[2, 6)
[6,84]
Weekly alcohol consumption (drinks/week)
Observed
Predicted

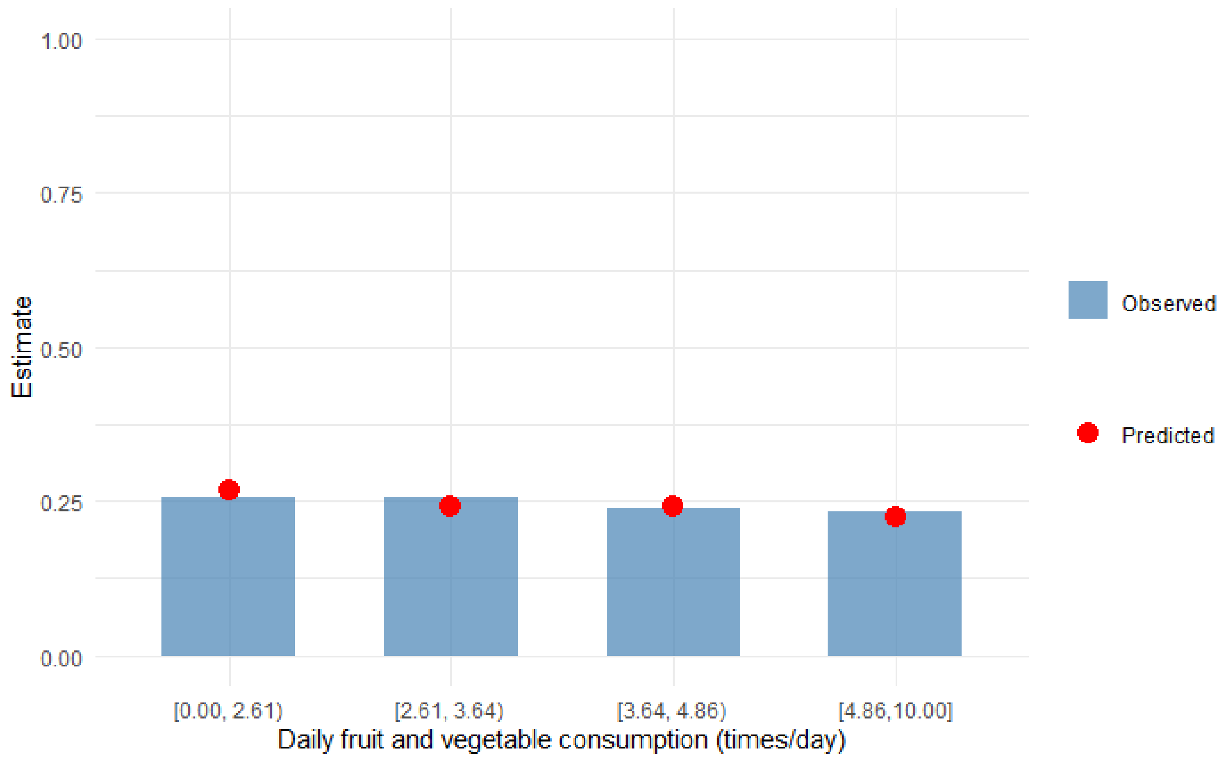

1.00
0.75
0.50
0.25
0.00
Estimate
Never drank
Low-risk drinker
Moderate drinker
Heavy drinker
Alcohol consumption level
Observed
Predicted

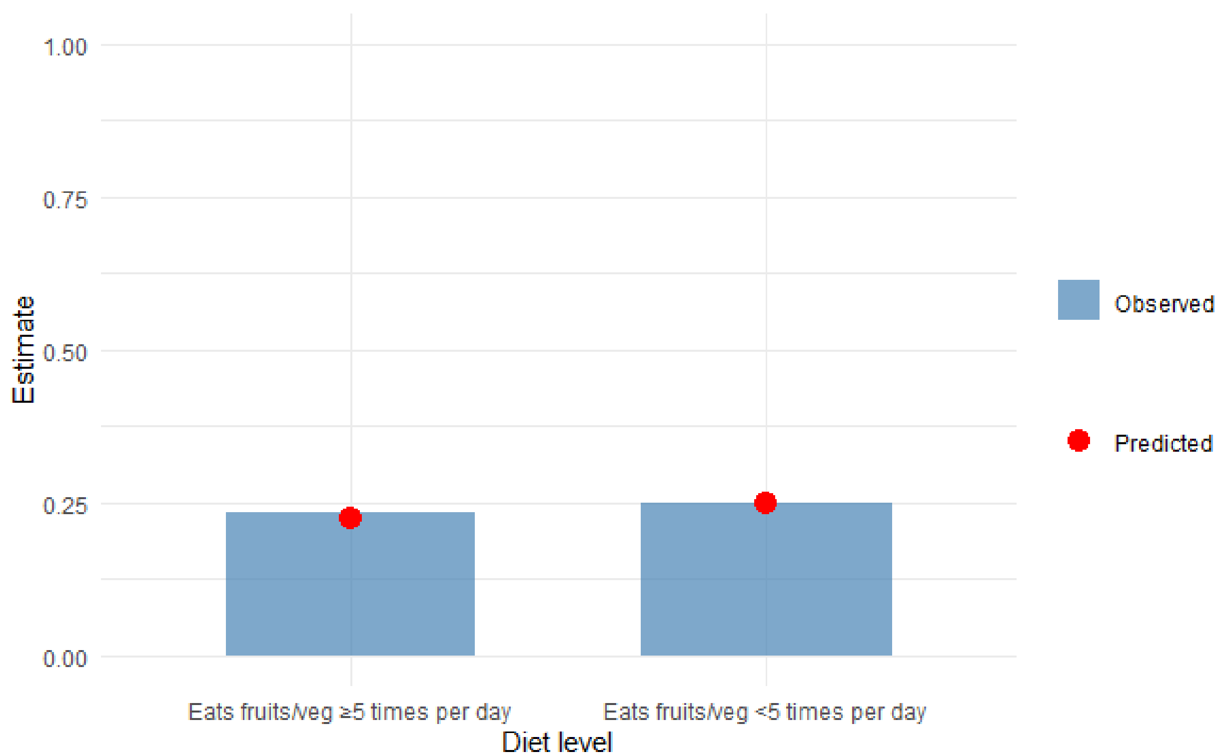

Estimate
1.00
0.75
0.50
0.25
0.00
Never smoker
Former smoker
Current smoker
Smoking status
Observed
Predicted

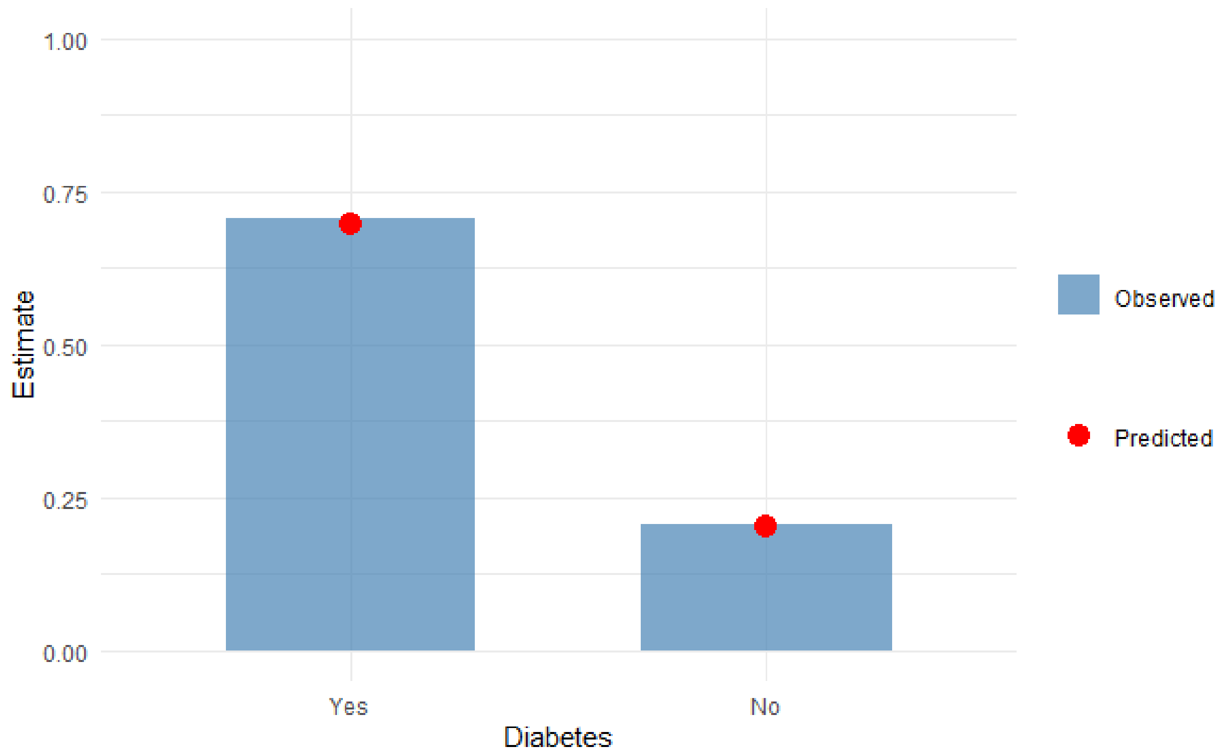

Estimate
1.00
0.75
0.50
0.25
0.00
[2.0, 7.0)
7.0
[7.5, 8.5)
[8.5,16.0]
Sleep duration (hrs/night)
Observed
Predicted

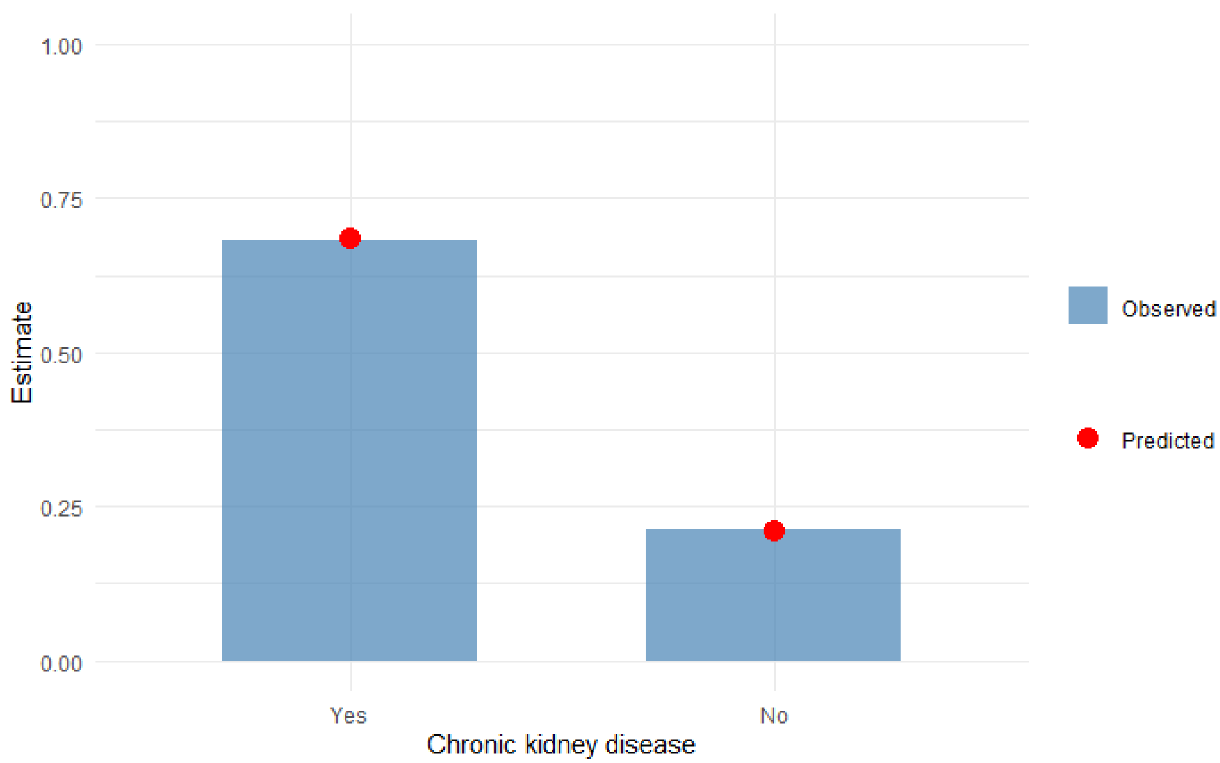

1.00
0.75
0.50
0.25
0.00
Estimate
[0, 25)
[25, 80)
[80,167)
[167,792]
Physical activity minutes (min/week)
Observed
Predicted

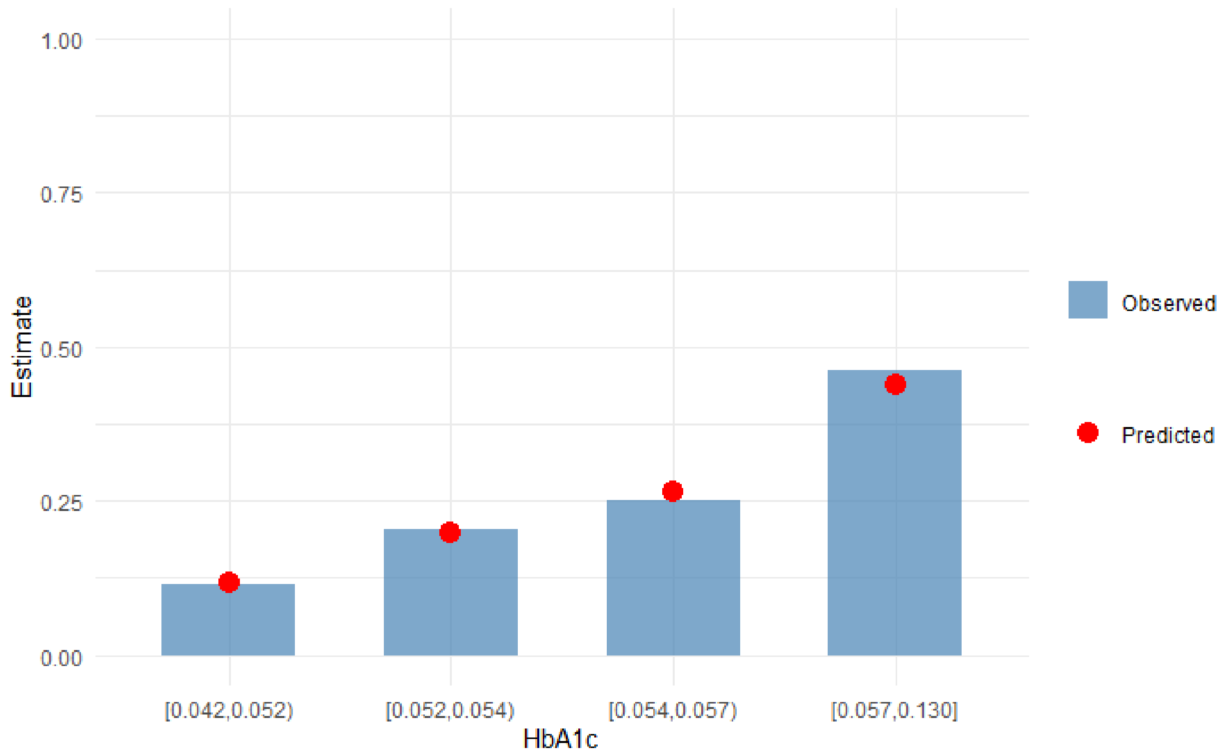

1.00
0.75
0.50
0.25
0.00
Estimate
Physically active
Physically inactive
Physical activity level
Observed
Predicted

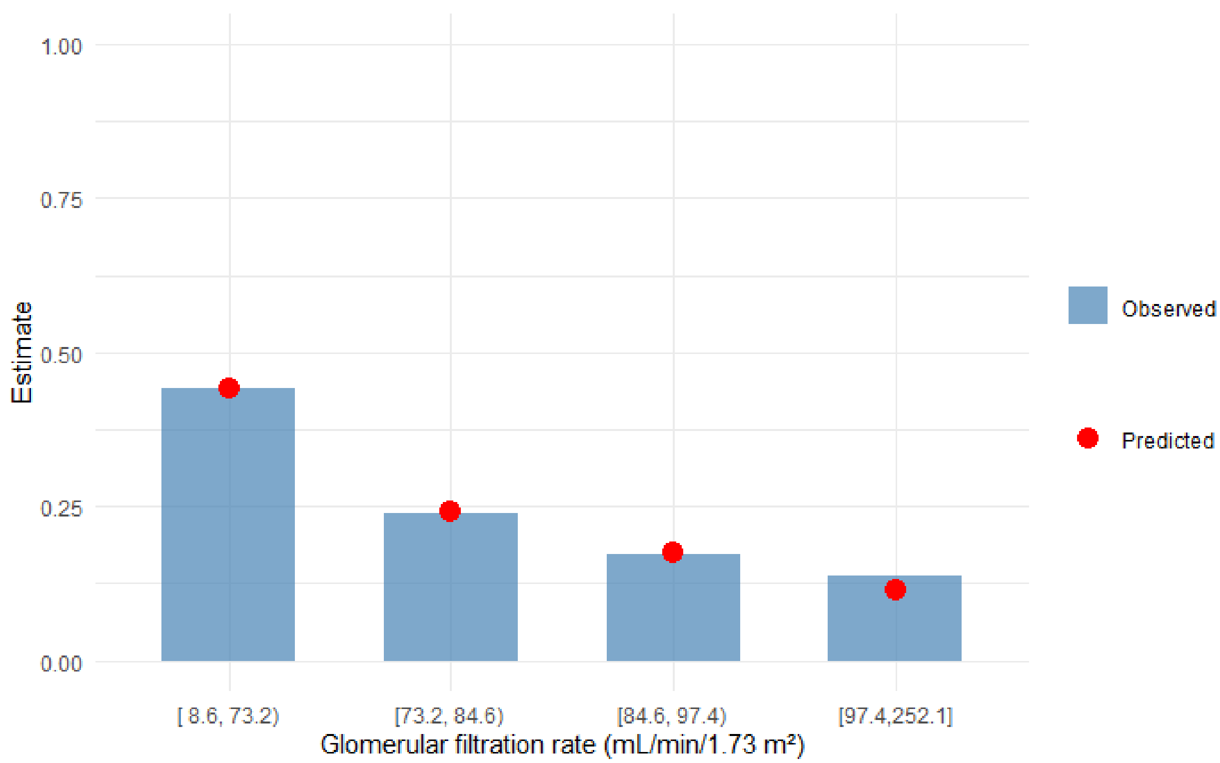

1.00
0.75
0.50
0.25
0.00
Estimate
Observed
Predicted
[0.00, 2.61)
[2.61, 3.64)
[3.64, 4.86)
[4.86,10.00]
Daily fruit and vegetable consumption (times/day)

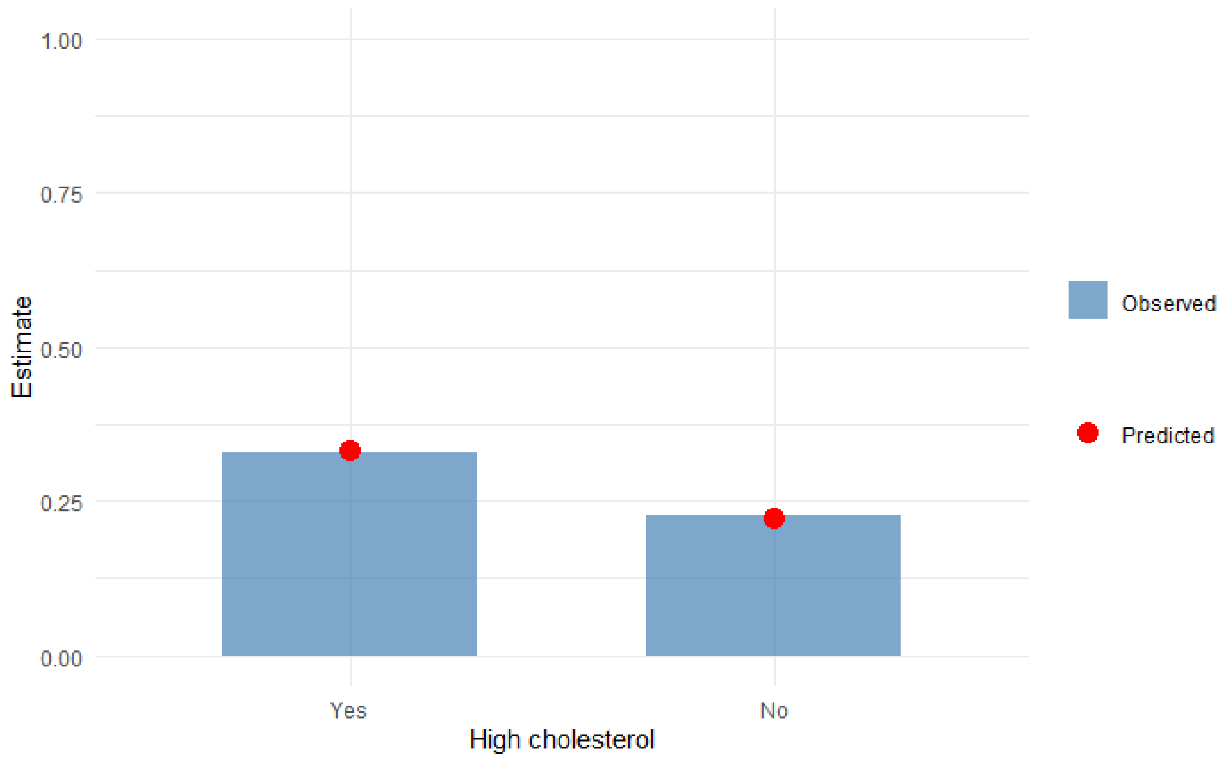

1.00
0.75
0.50
0.25
0.00
Estimate
Observed
Predicted
Eats fruits/veg ≥5 times per day
Eats fruits/veg <5 times per day
Diet level

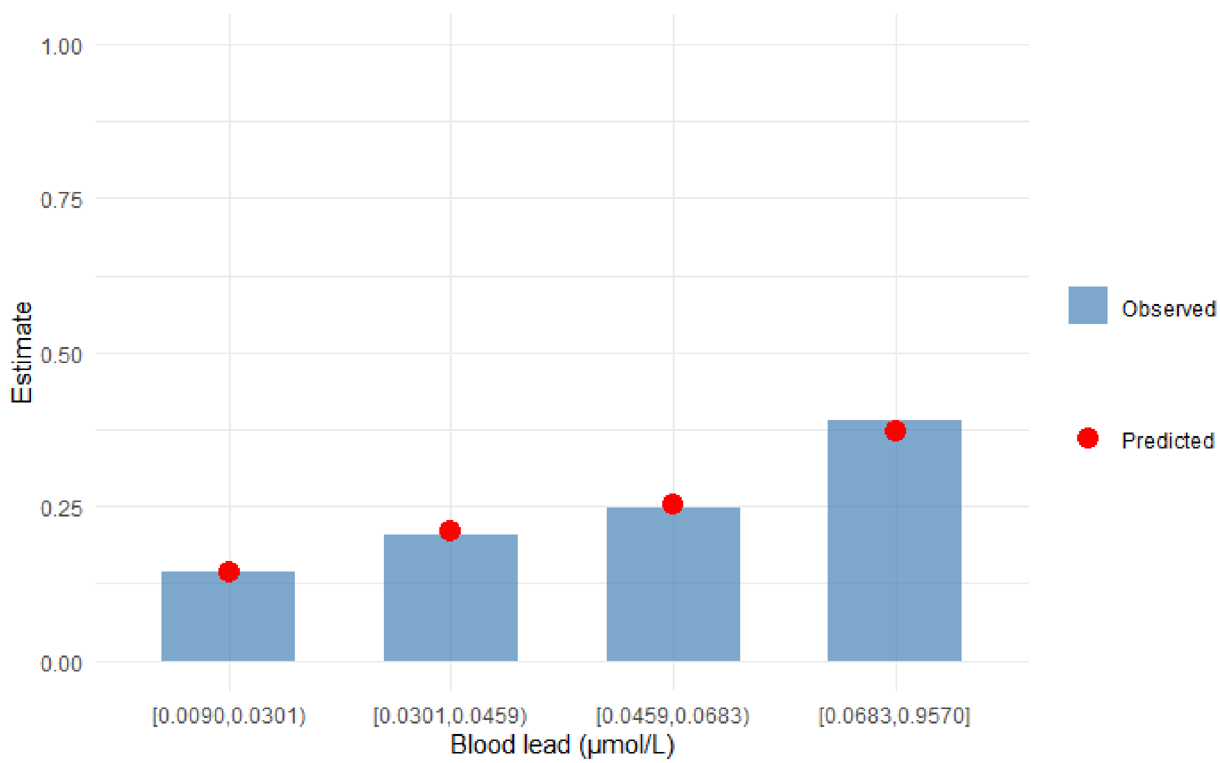

1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
Diabetes
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
Chronic kidney disease
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
[0.042,0.052)
[0.052,0.054)
[0.054,0.057)
[0.057,0.130]
HbA1c
Observed
Predicted

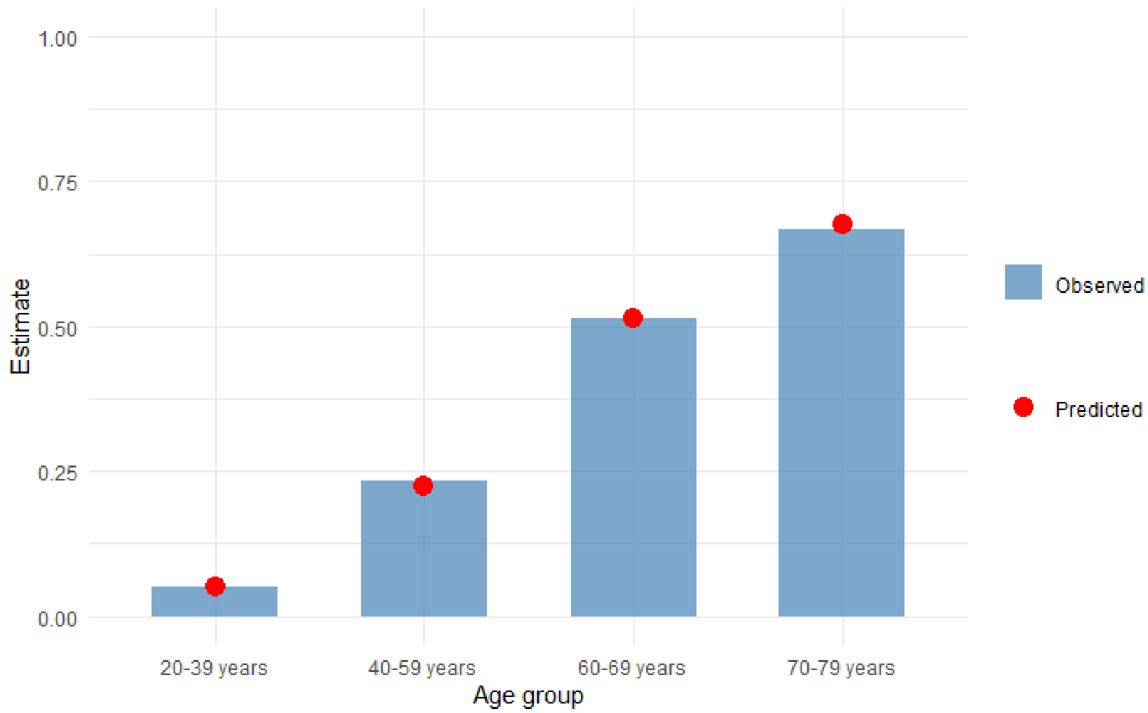

1.00
0.75
0.50
0.25
0.00
Estimate
[8.6, 73.2)
[73.2, 84.6)
[84.6, 97.4)
[97.4,252.1]
Glomerular filtration rate (mL/min/1.73 m²)
Observed
Predicted

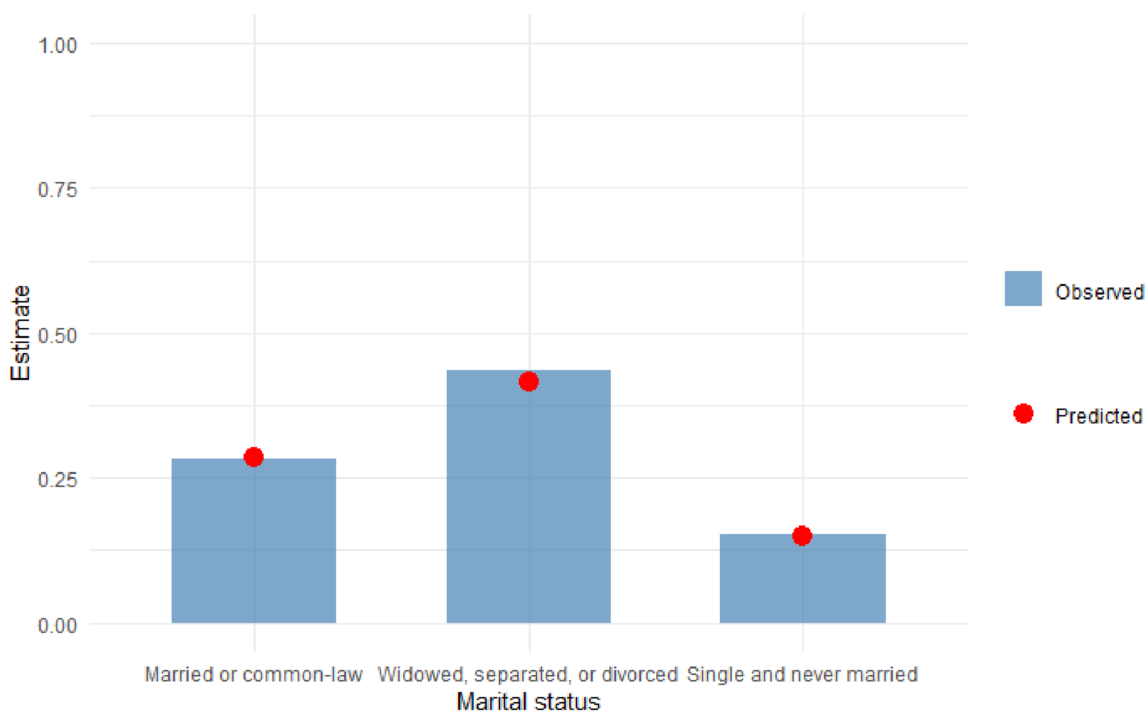

1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
High cholesterol
Observed
Predicted

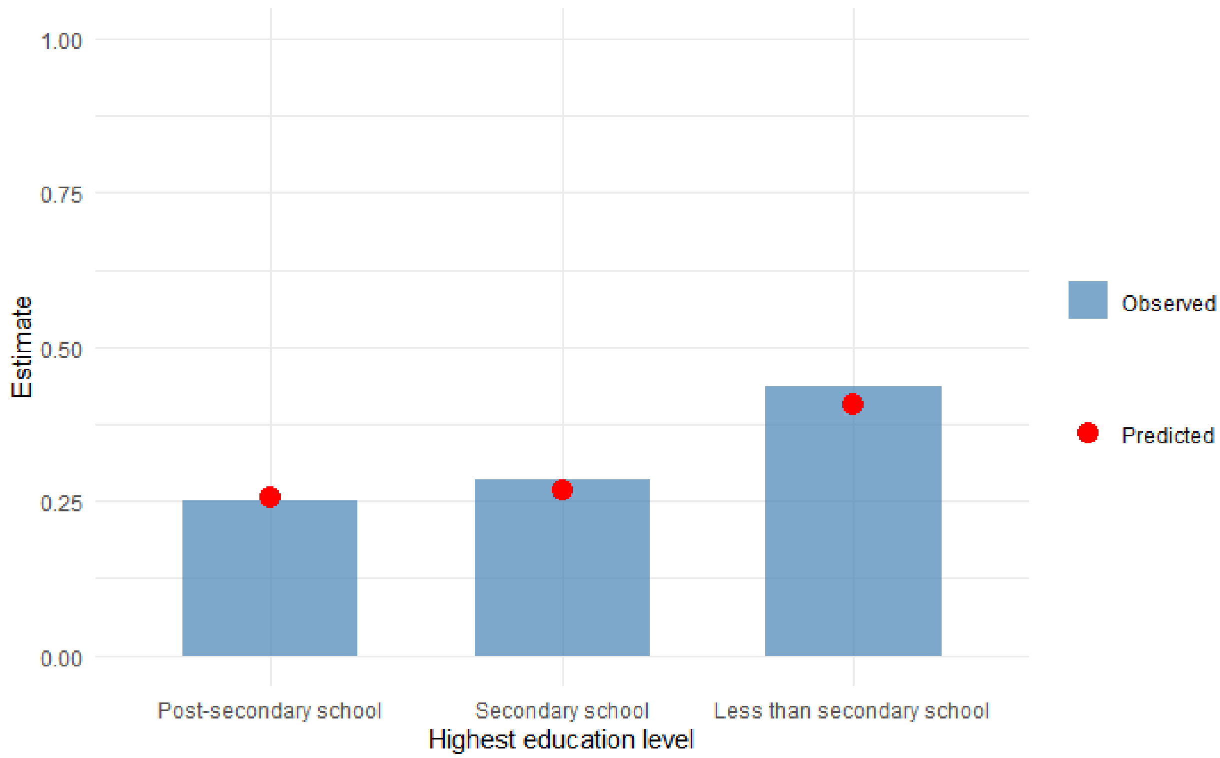

1.00
0.75
0.50
0.25
0.00
Estimate
[0.0090,0.0301)
[0.0301,0.0459)
[0.0459,0.0683)
[0.0683,0.9570]
Blood lead (μmol/L)
Observed
Predicted

Appendix 8 – Calibration across subgroups for reduced models

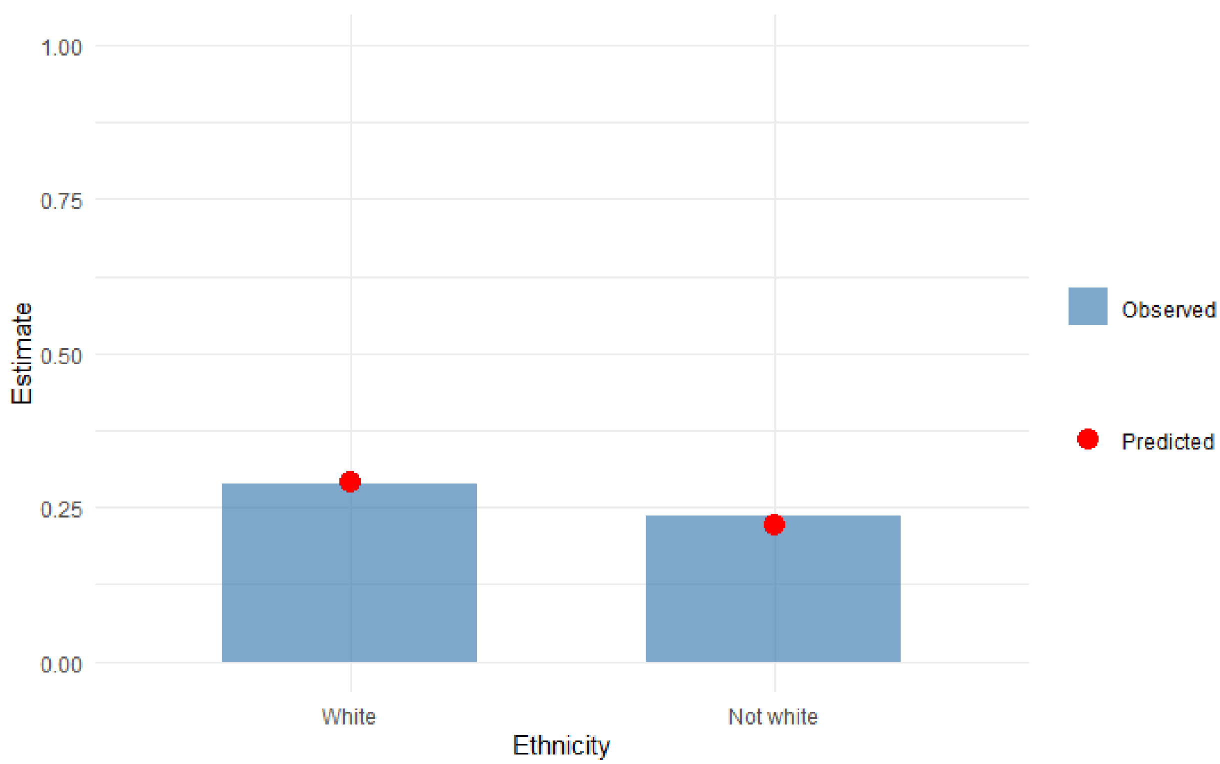
Male Reduced Model:
X – excluded subgroup with observed estimate less than 5%
*** – subgroup with difference between observed and predicted estimates over 20%**



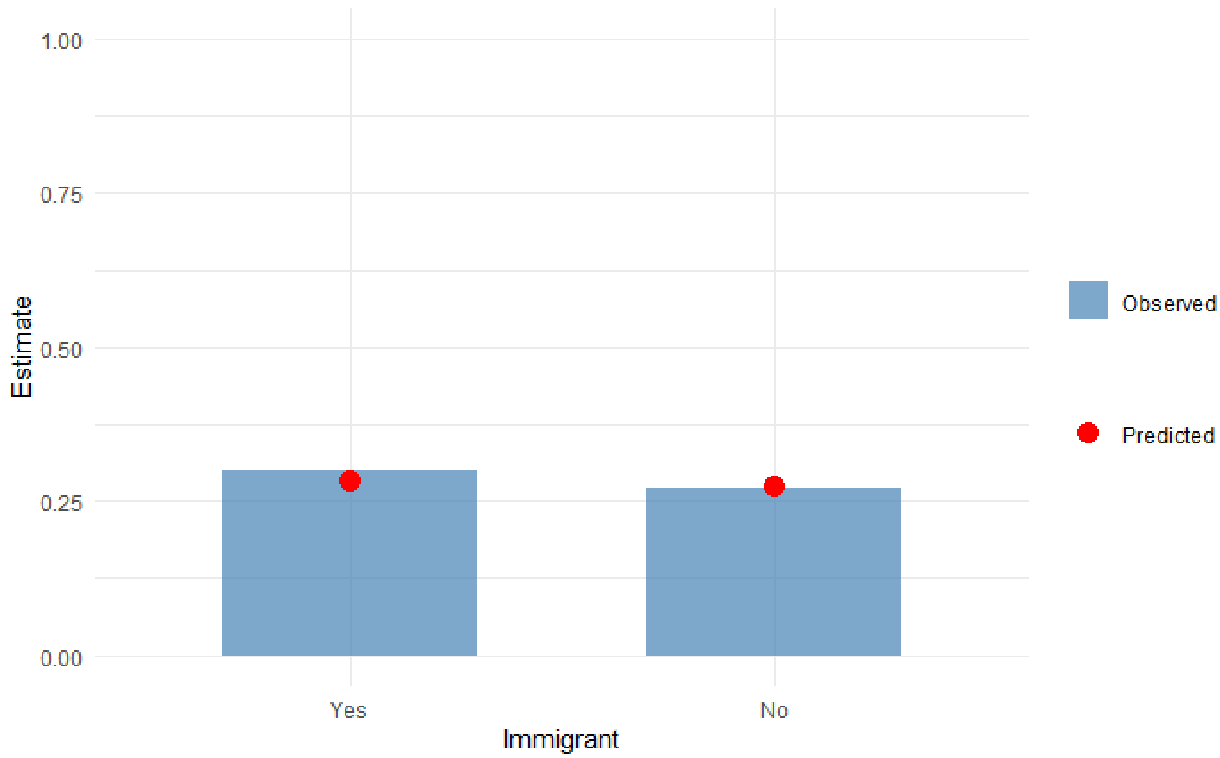


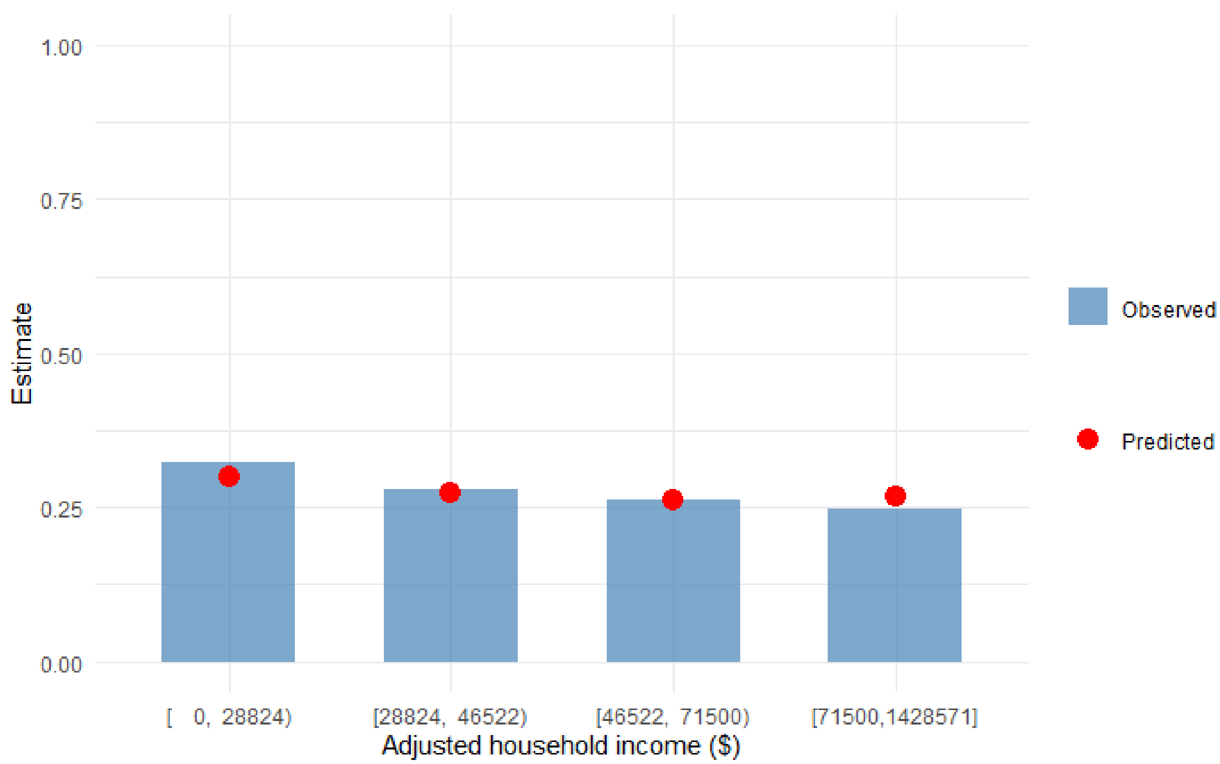


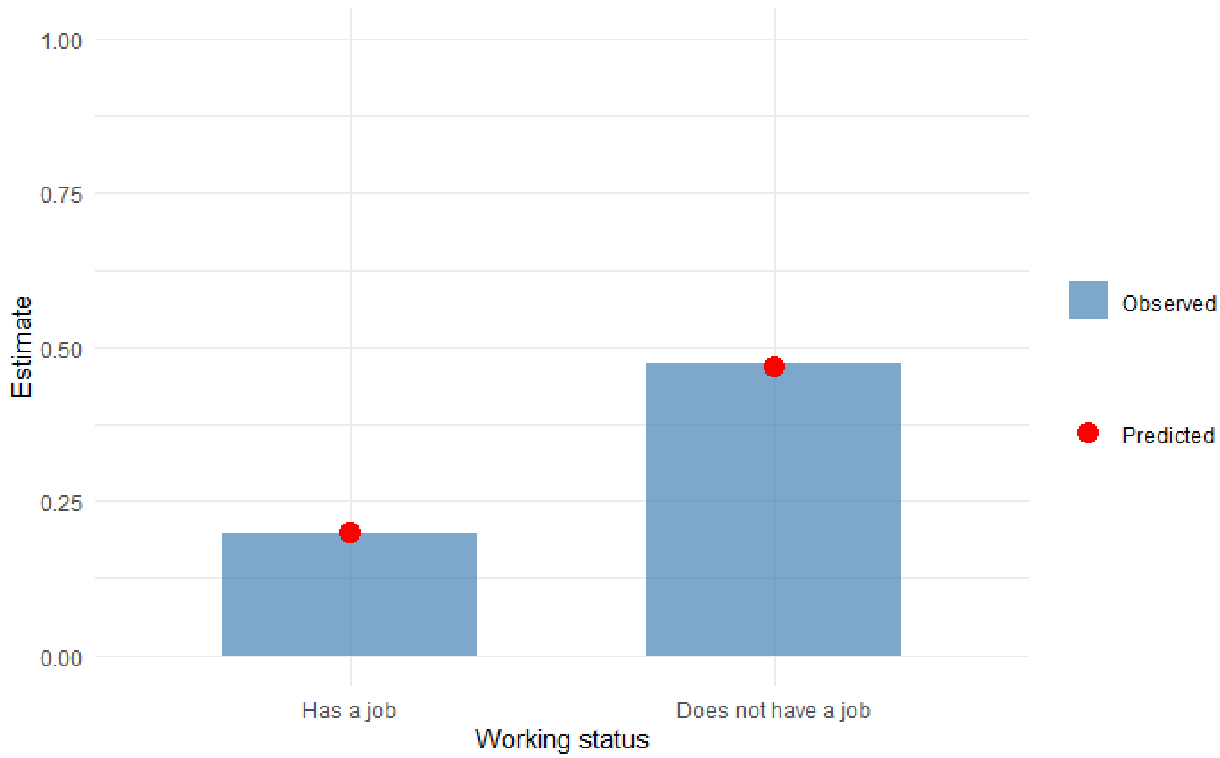
1.00
0.75
0.50
0.25
0.00
Estimate
Post-secondary school
Secondary school
Less than secondary school
Highest education level
Observed
Predicted



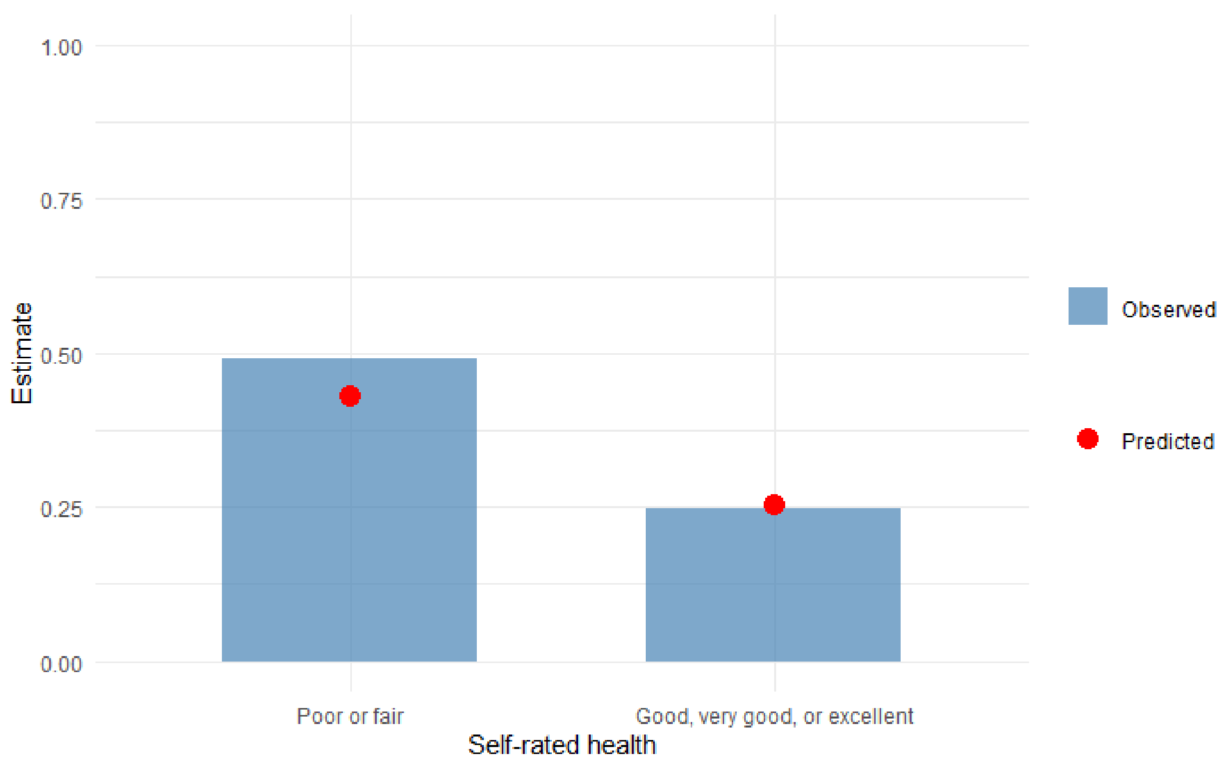
1.00
0.75
0.50
0.25
0.00
Estimate
White
Not white
Ethnicity
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
Immigrant
Observed
Predicted

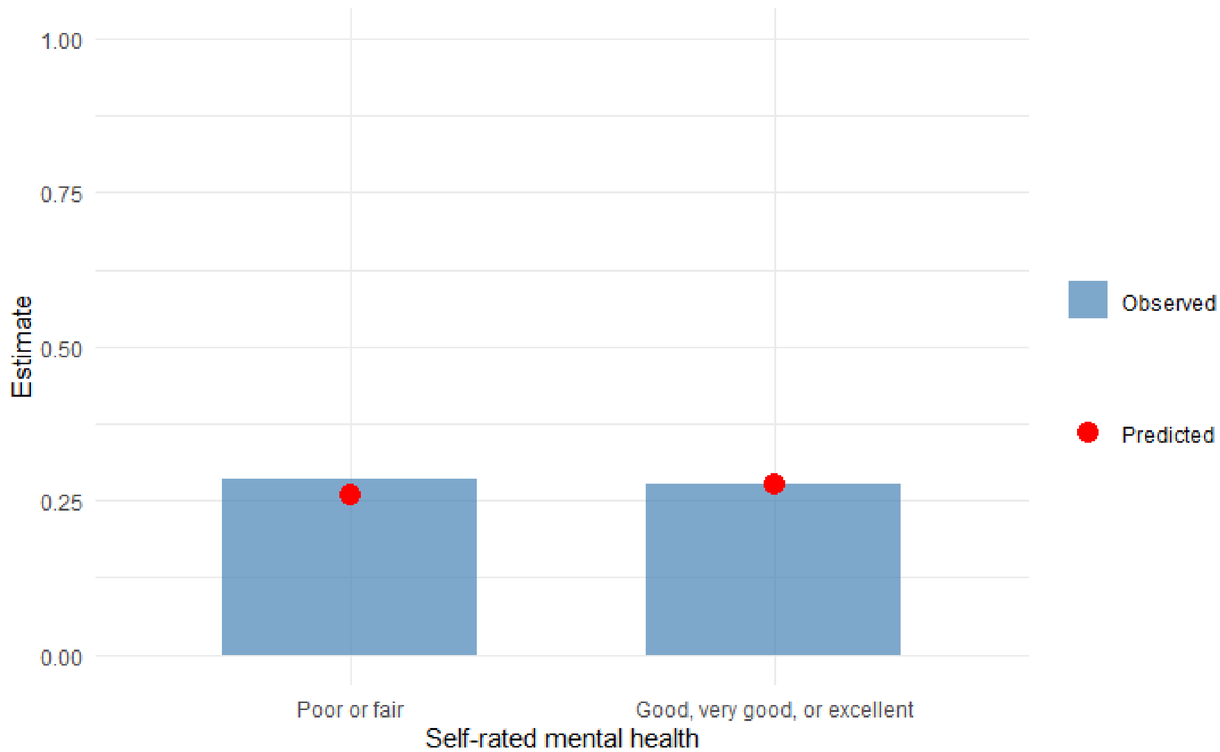

1.00
0.75
0.50
0.25
0.00
Estimate
[0, 28824)
[28824, 46522)
[46522, 71500)
[71500,1428571]
Adjusted household income ($)
Observed
Predicted



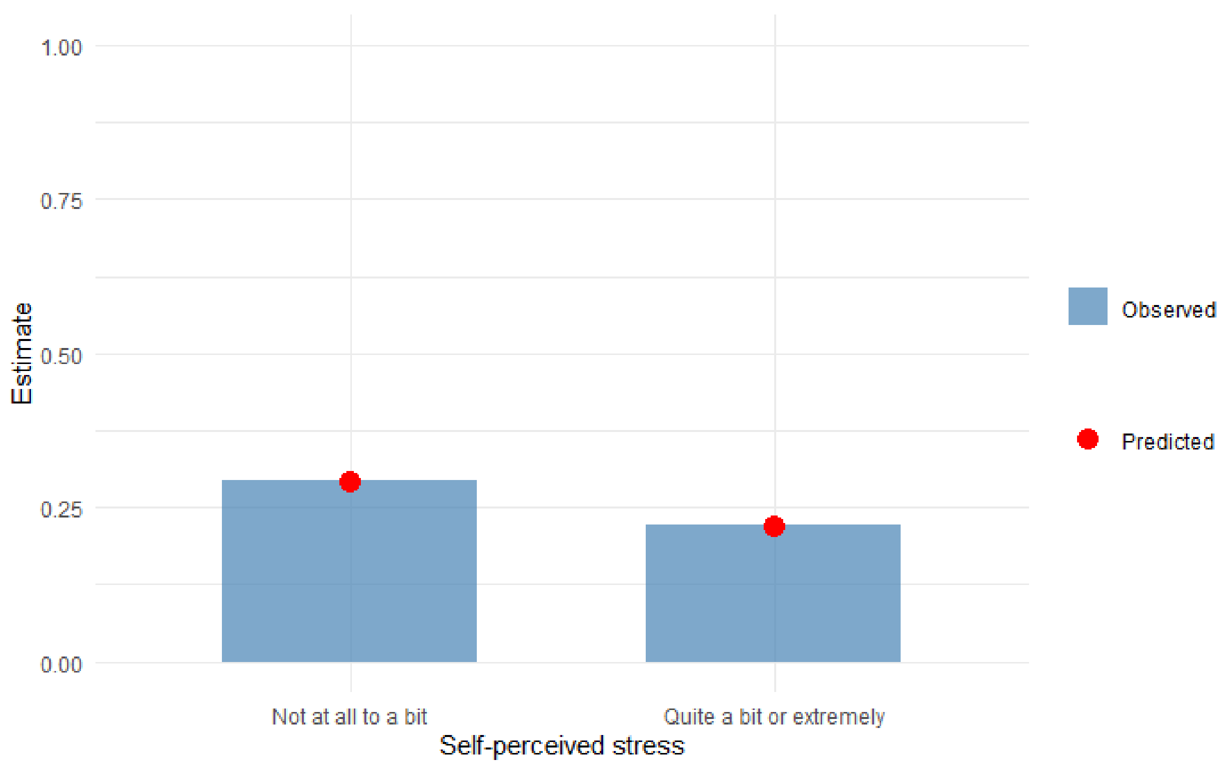
1.00
0.75
0.50
0.25
0.00
Estimate
Has a job
Does not have a job
Working status
Observed
Predicted



1.00
0.75
0.50
0.25
0.00
Estimate
Poor or fair
Good, very good, or excellent
Self-rated health
Observed
Predicted

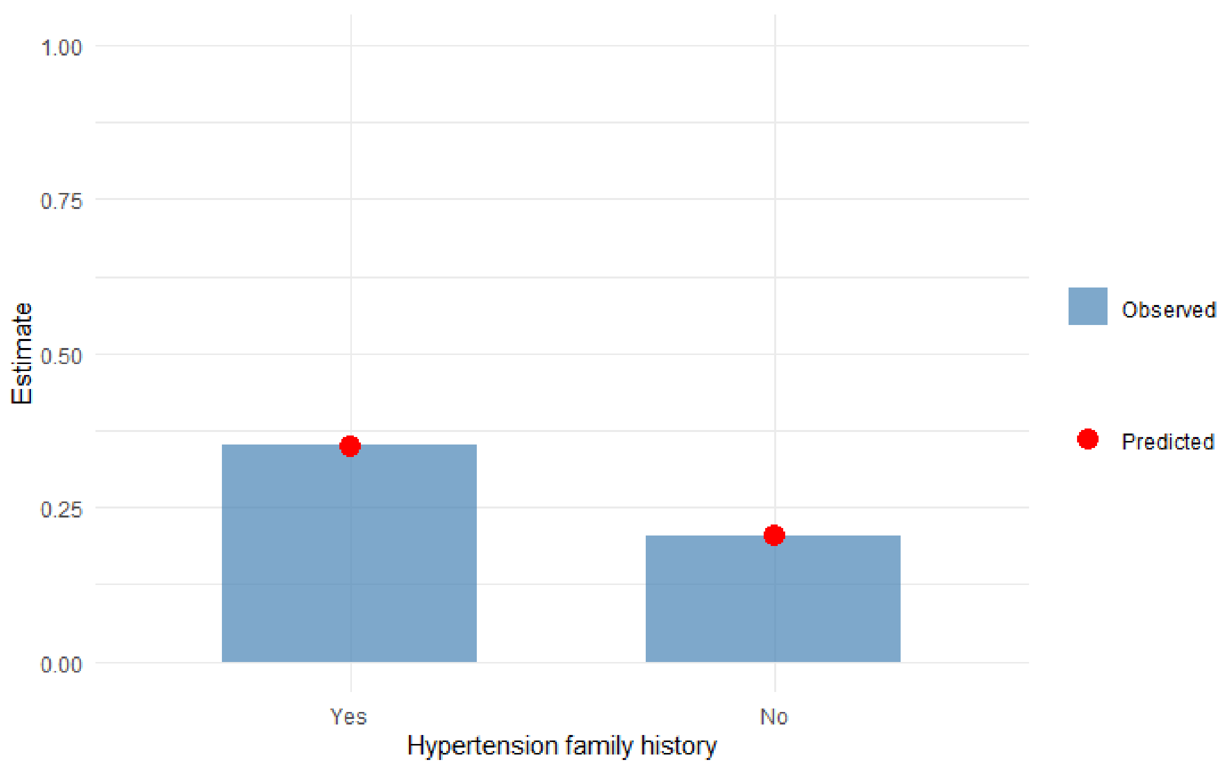


1.00
0.75
0.50
0.25
0.00
Estimate
Observed
Predicted
Poor or fair
Good, very good, or excellent
Self-rated mental health

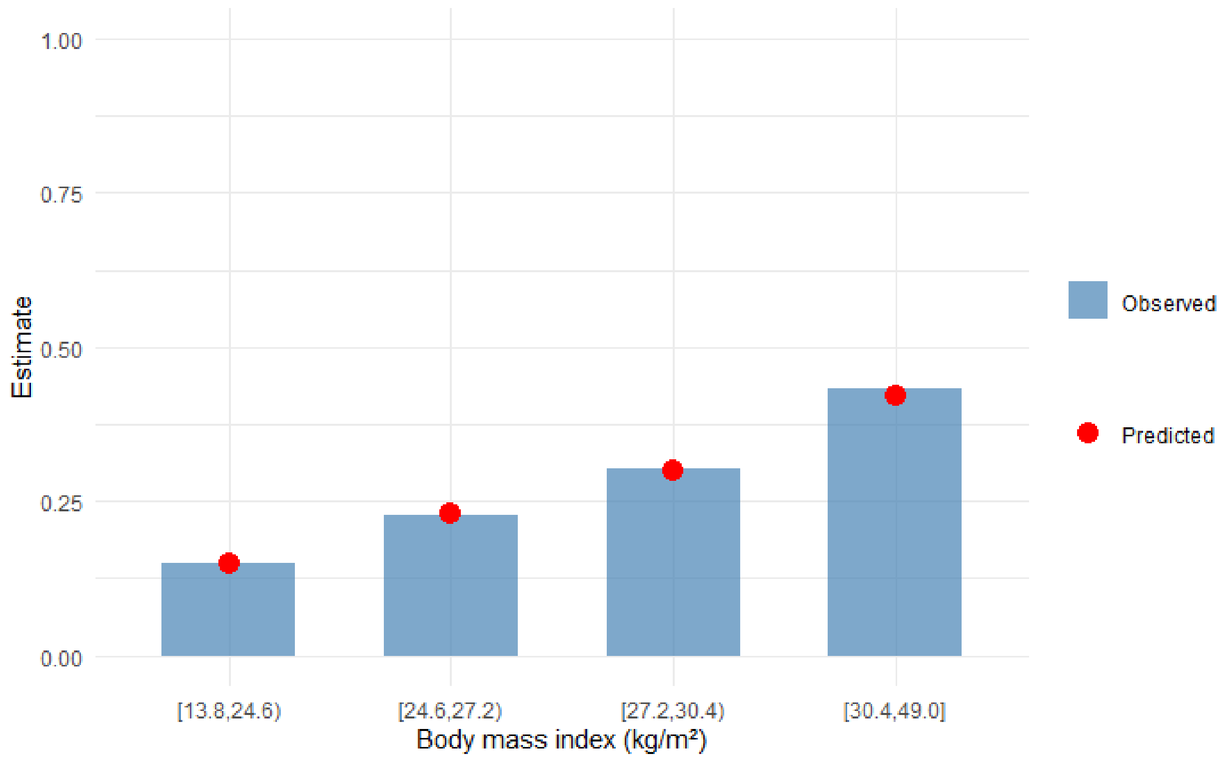


1.00
0.75
0.50
0.25
0.00
Estimate
Observed
Predicted
Not at all to a bit
Quite a bit or extremely
Self-perceived stress

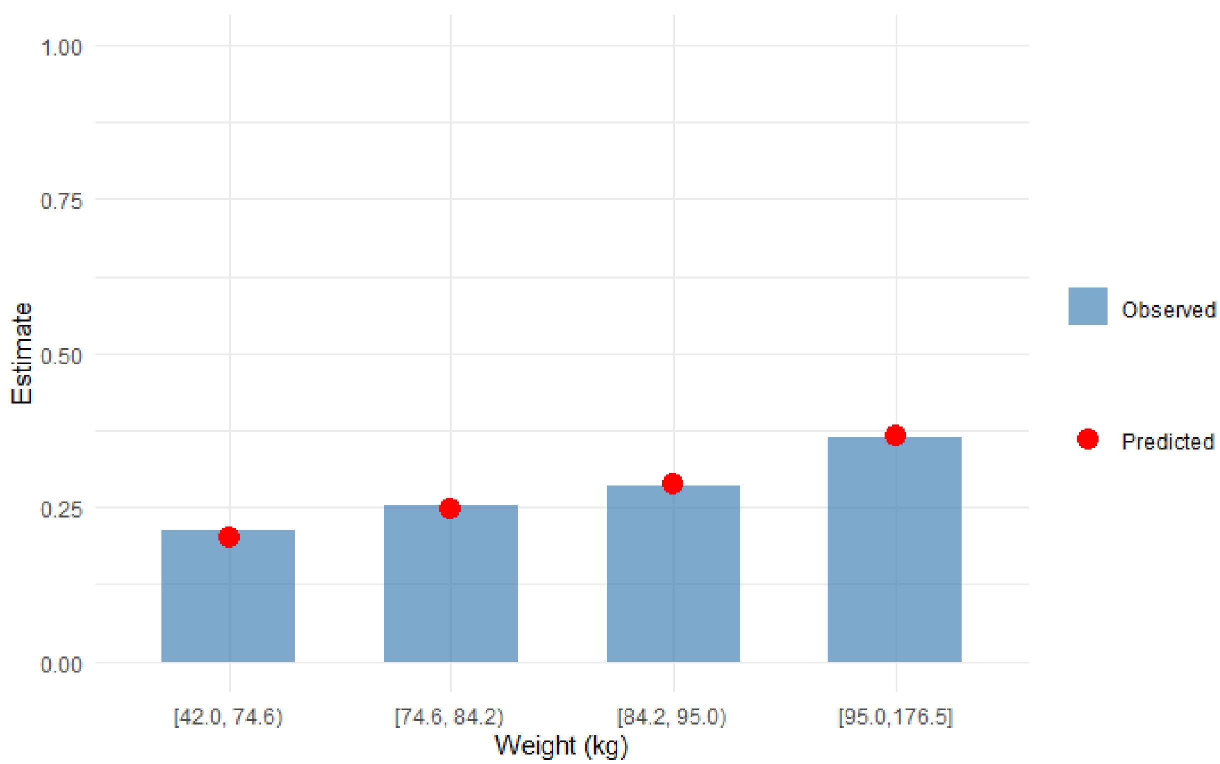
Estimate
1.00
0.75
0.50
0.25
0.00
Strong
Weak
Sense of belonging
Observed
Predicted



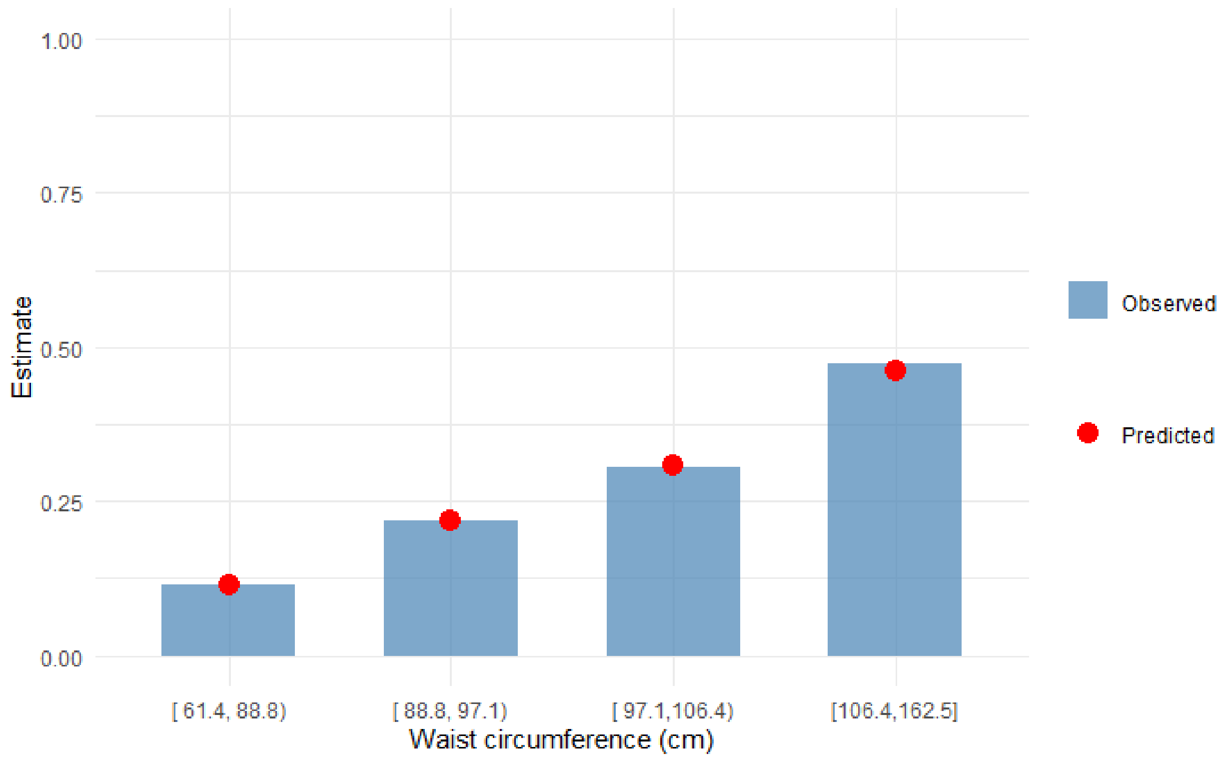
Estimate
1.00
0.75
0.50
0.25
0.00
Yes
No
Hypertension family history
Observed
Predicted

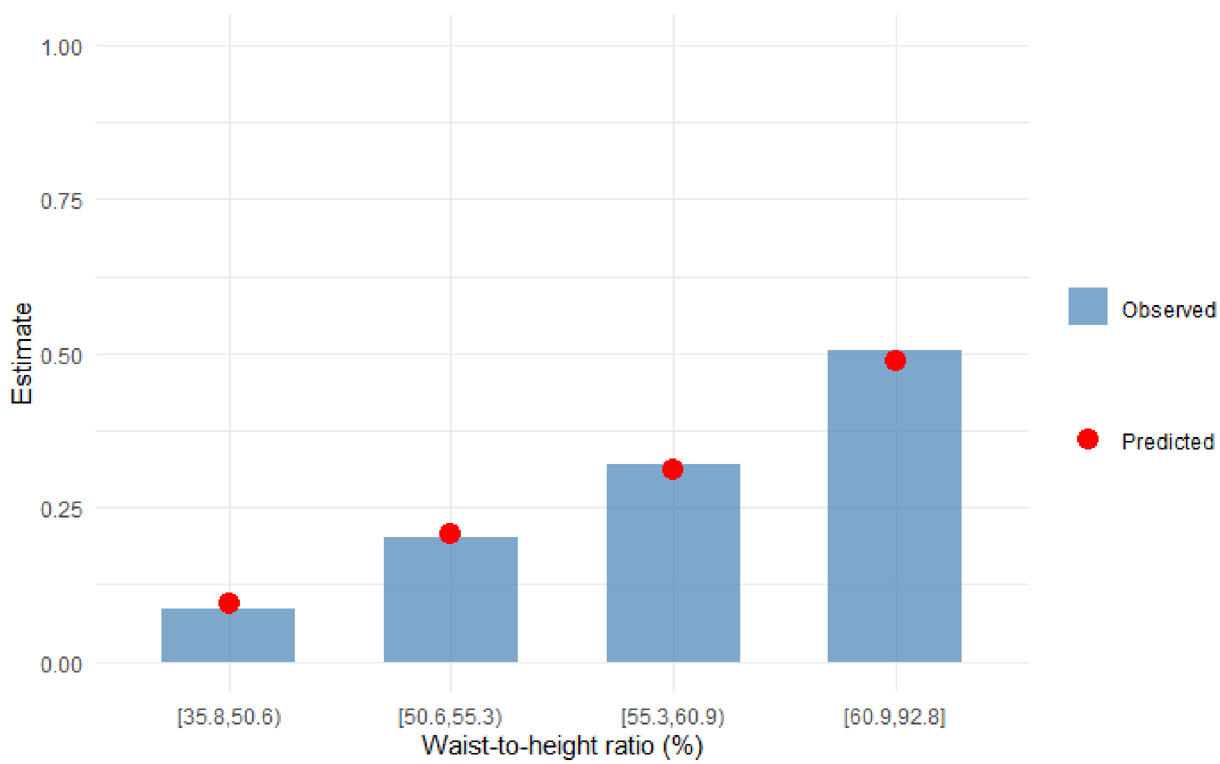


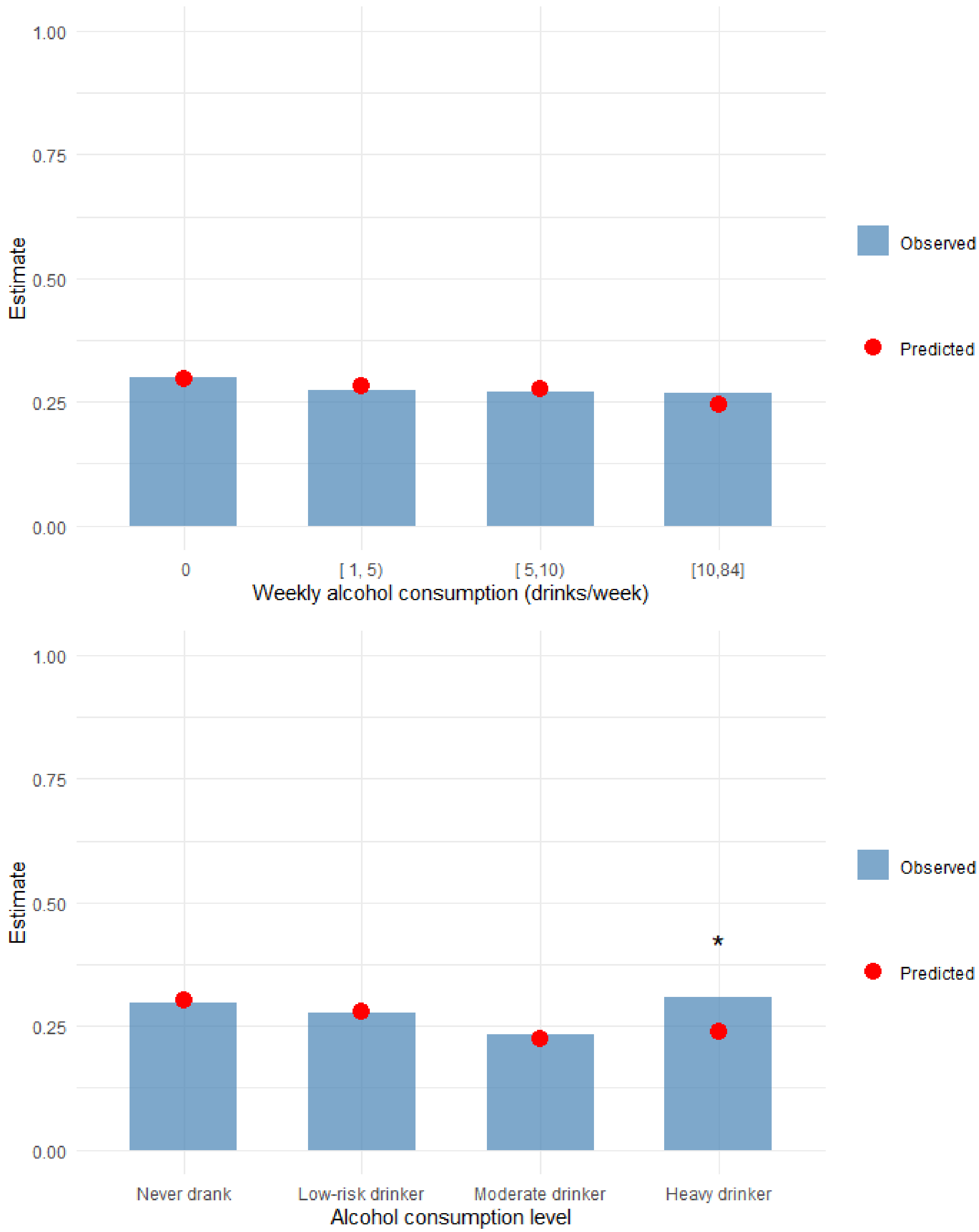
1.00
0.75
0.50
0.25
0.00
Estimate
Observed
Predicted
[13.8,24.6)
[24.6,27.2)
[27.2,30.4)
[30.4,49.0]
Body mass index (kg/m²)

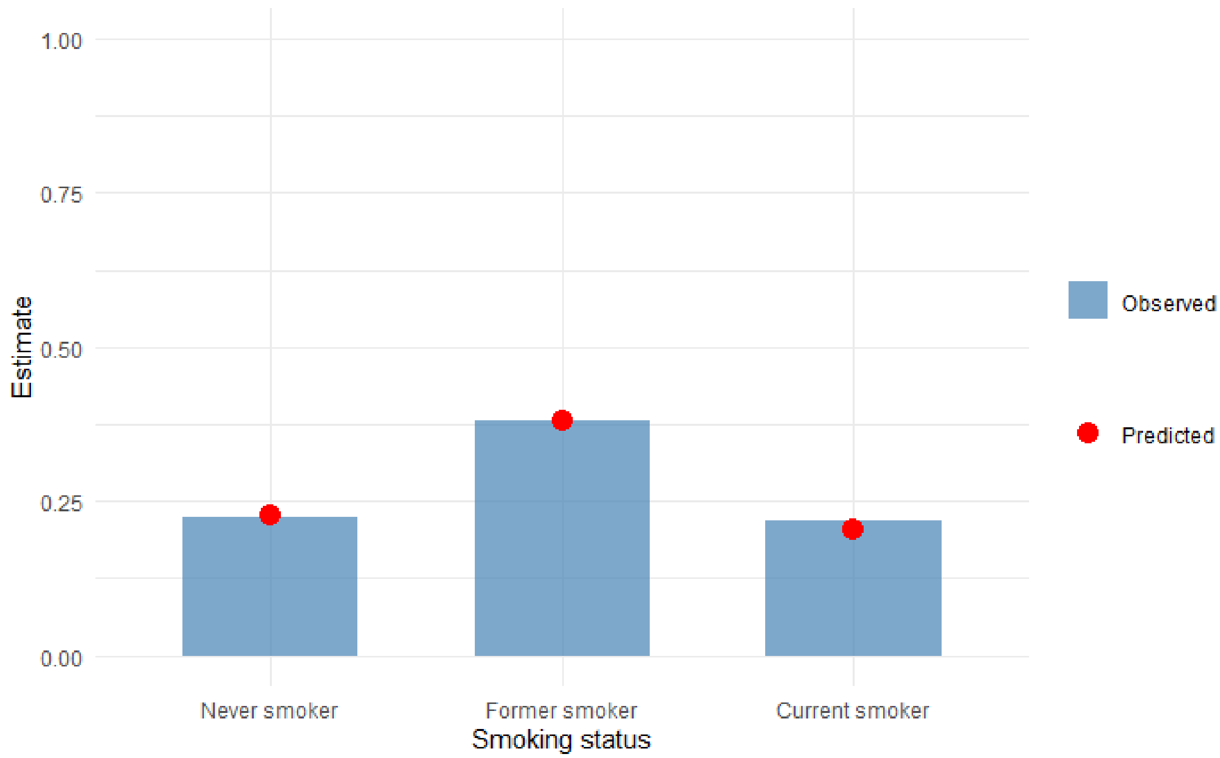


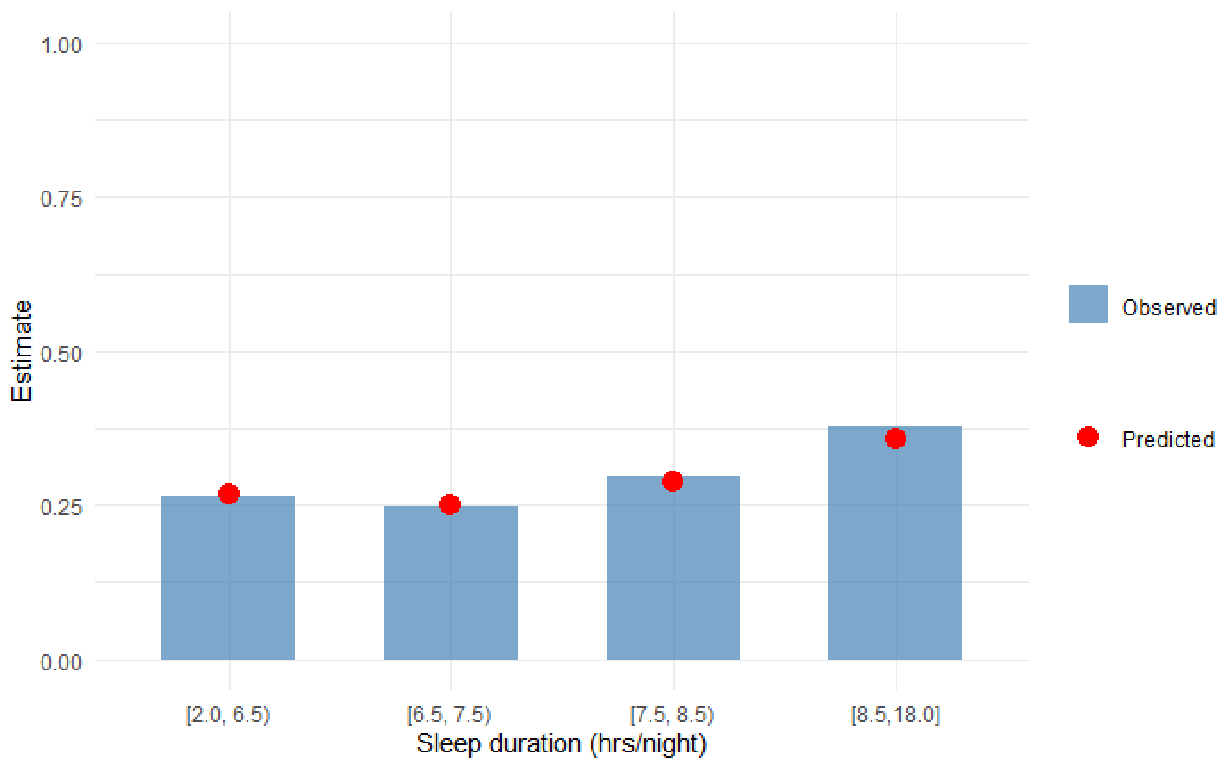
1.00
0.75
0.50
0.25
0.00
Estimate
Observed
Predicted
[42.0, 74.6)
[74.6, 84.2)
[84.2, 95.0)
[95.0,176.5]
Weight (kg)

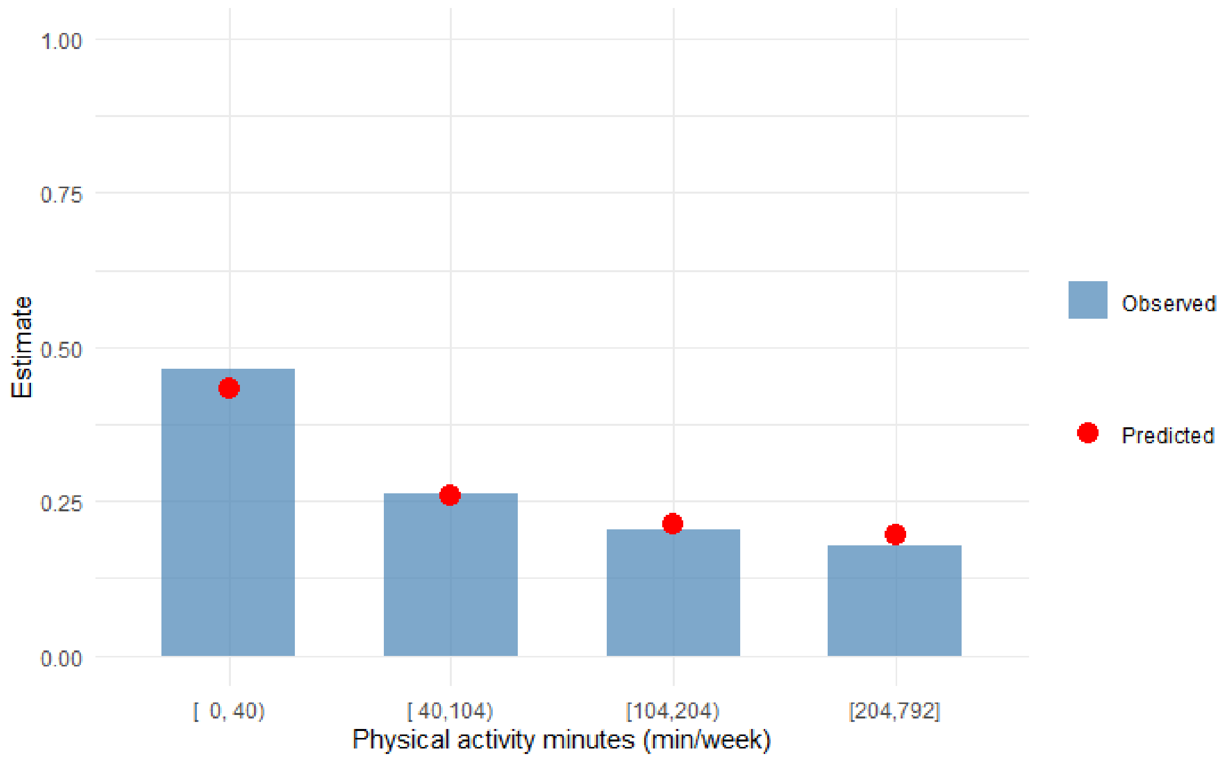

1.00
0.75
0.50
0.25
0.00
Estimate
[61.4, 88.8)
[88.8, 97.1)
[97.1,106.4)
[106.4,162.5]
Waist circumference (cm)
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
[35.8,50.6)
[50.6,55.3)
[55.3,60.9)
[60.9,92.8]
Waist-to-height ratio (%)
Observed
Predicted

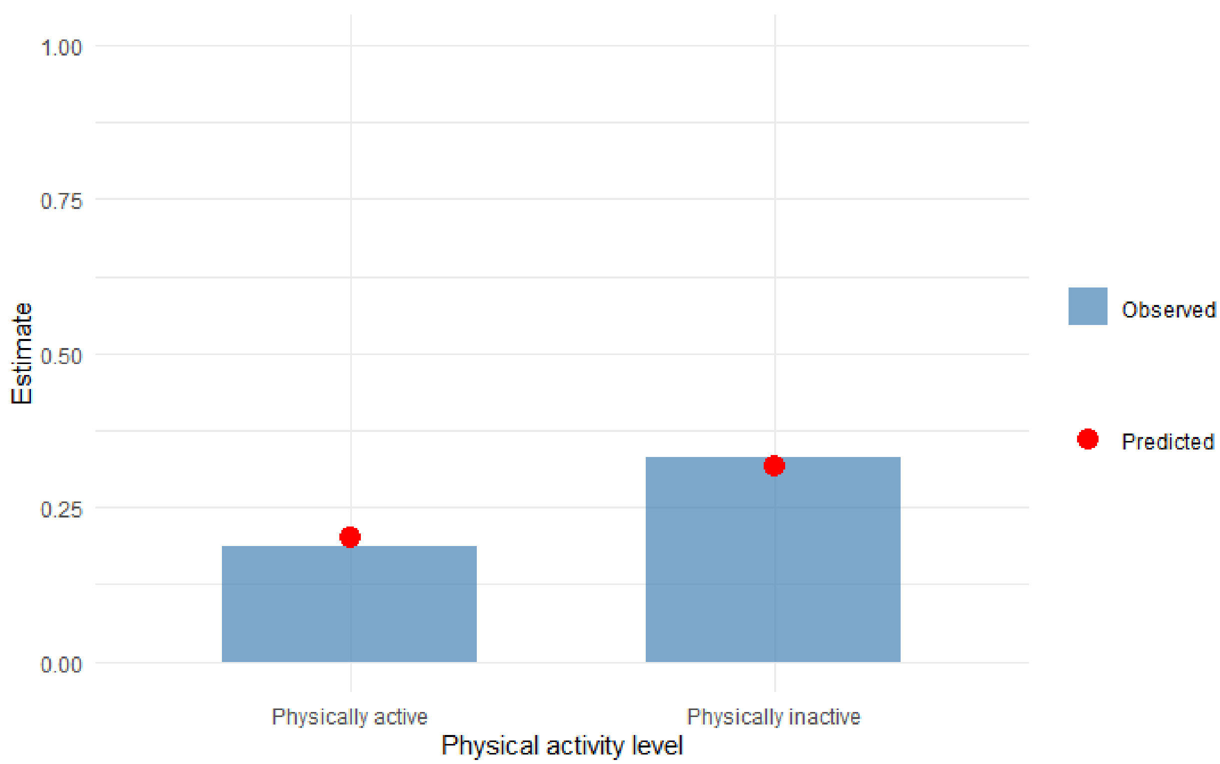

1.00
0.75
0.50
0.25
0.00
Estimate
0
[1, 5)
[5,10)
[10,84]
Weekly alcohol consumption (drinks/week)
Observed
Predicted
1.00
0.75
0.50
0.25
0.00
Estimate
*
Never drank
Low-risk drinker
Moderate drinker
Heavy drinker
Alcohol consumption level
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
Observed
Predicted
Never smoker
Former smoker
Current smoker
Smoking status

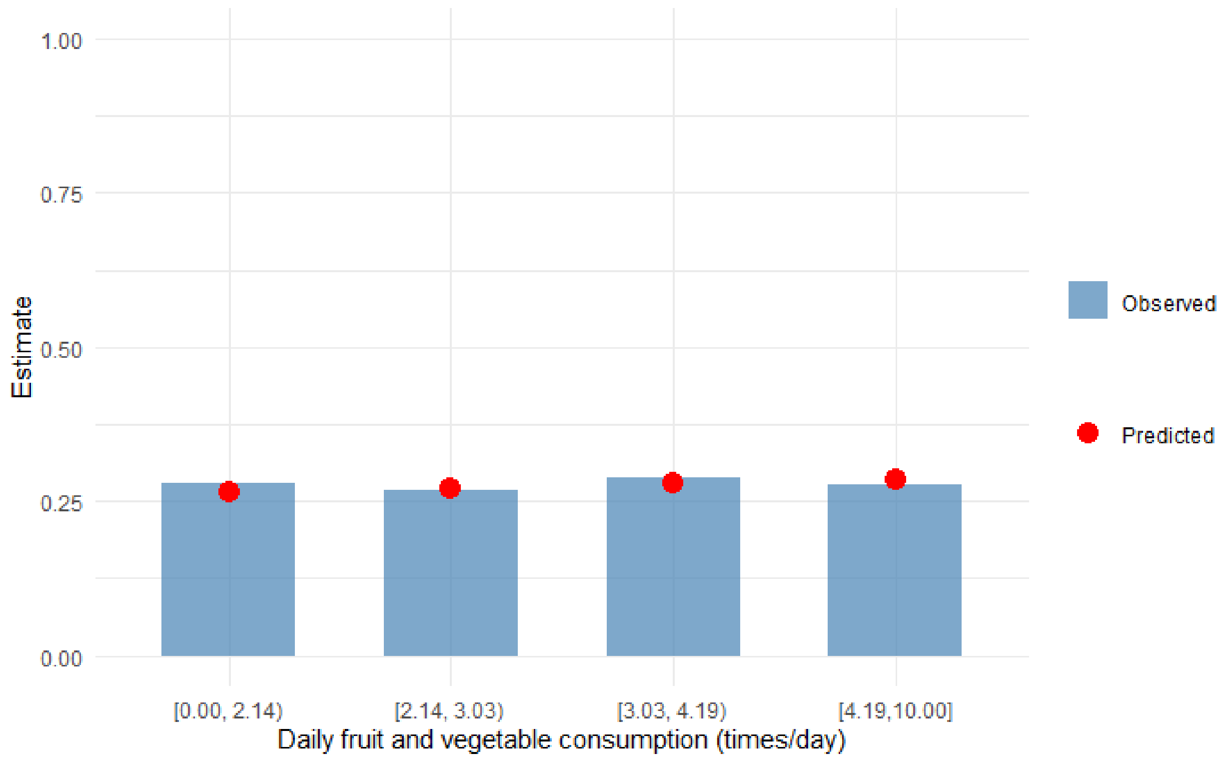

1.00
0.75
0.50
0.25
0.00
Estimate
Observed
Predicted
[2.0, 6.5)
[6.5, 7.5)
[7.5, 8.5)
[8.5,18.0]
Sleep duration (hrs/night)

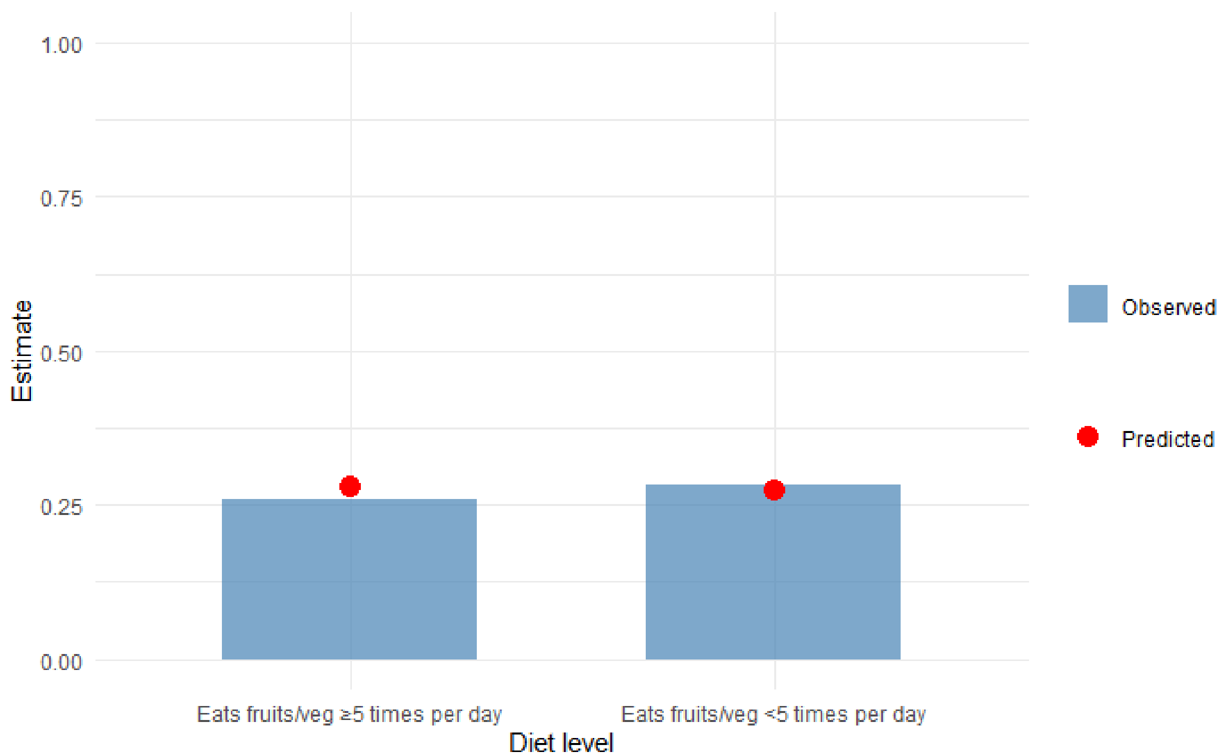


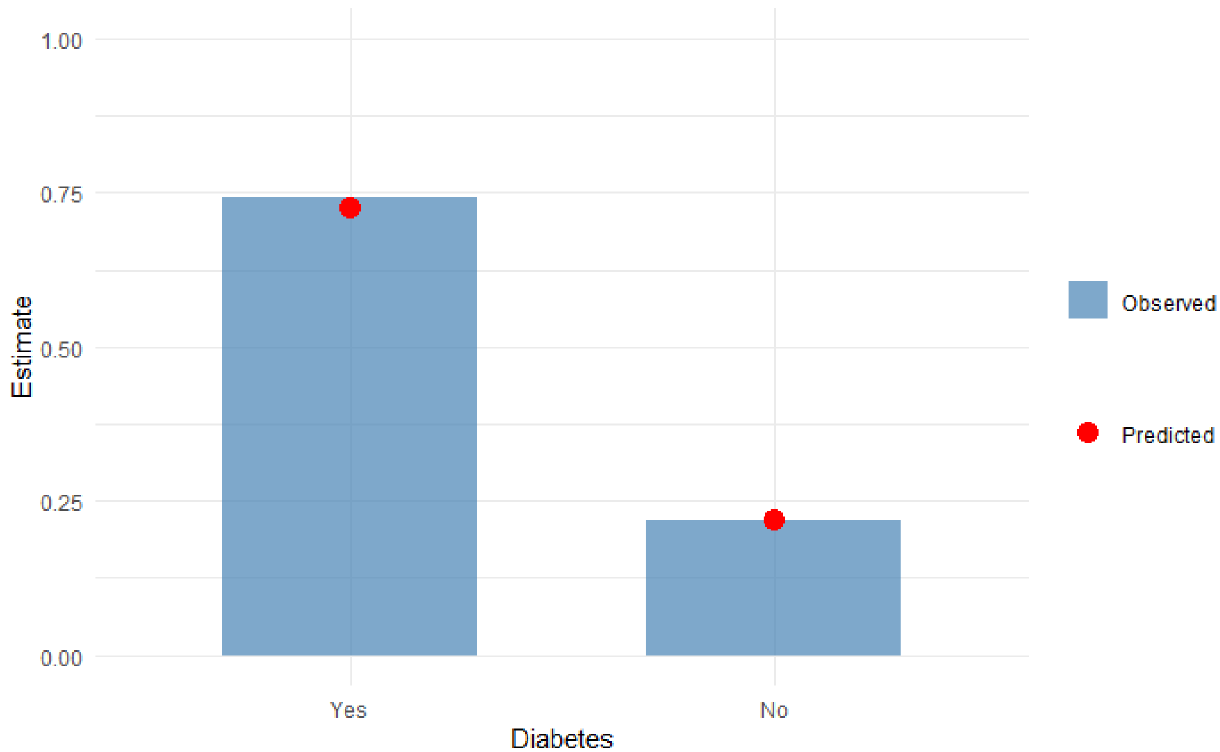
1.00
0.75
0.50
0.25
0.00
Estimate
[0, 40)
[40,104)
[104,204)
[204,792]
Physical activity minutes (min/week)
Observed
Predicted



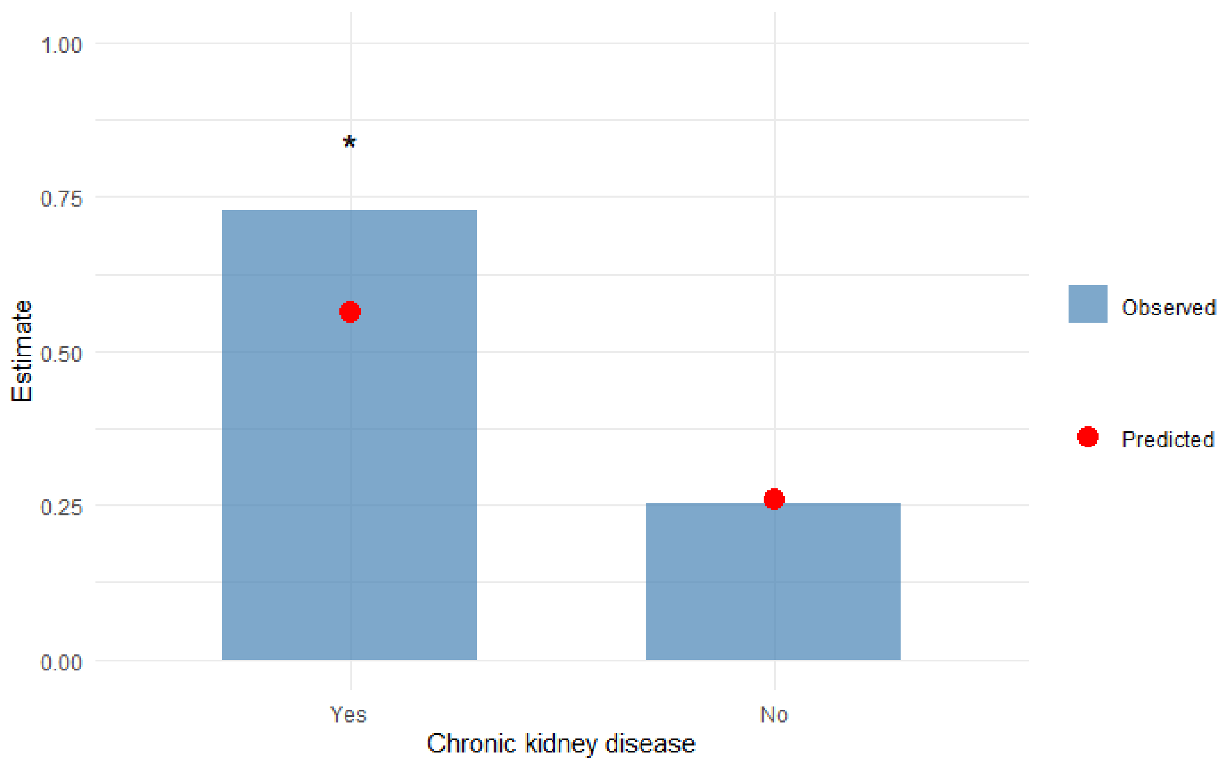
1.00
0.75
0.50
0.25
0.00
Estimate
Physically active
Physically inactive
Physical activity level
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
[0.00, 2.14)
[2.14, 3.03)
[3.03, 4.19)
[4.19,10.00]
Daily fruit and vegetable consumption (times/day)
Observed
Predicted

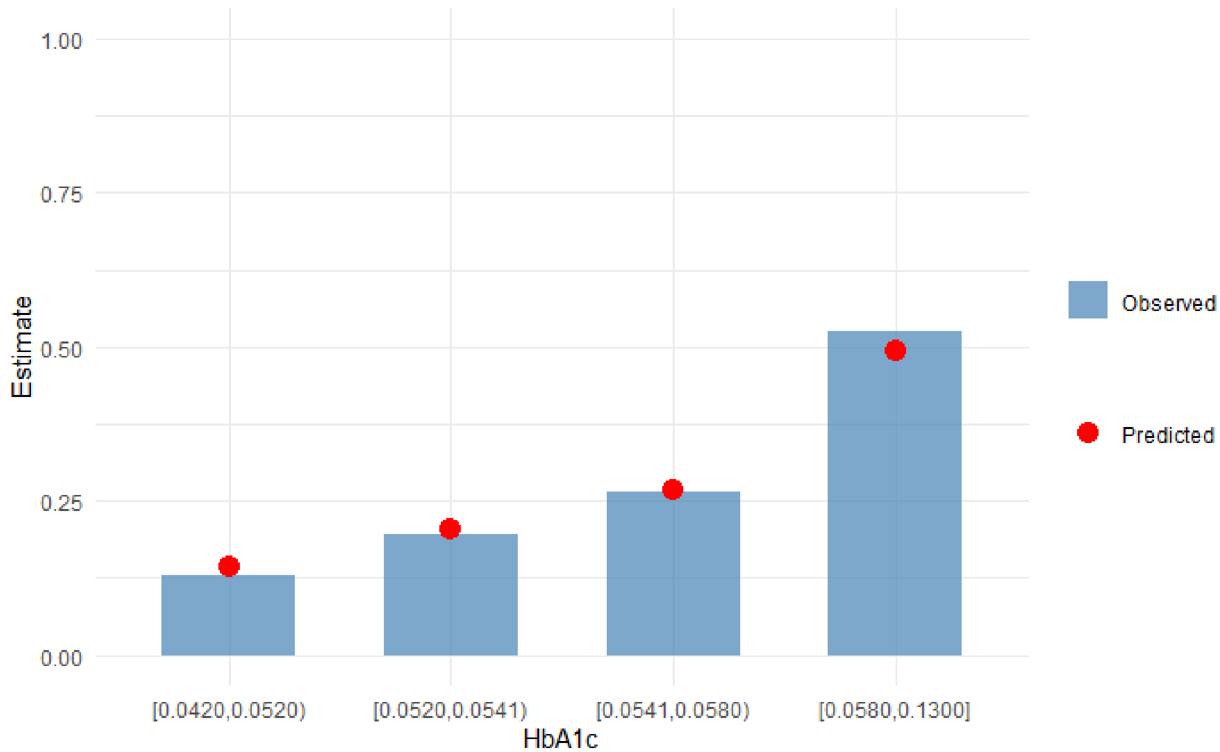

1.00
0.75
0.50
0.25
0.00
Estimate
Eats fruits/veg ≥5 times per day
Eats fruits/veg <5 times per day
Diet level
Observed
Predicted



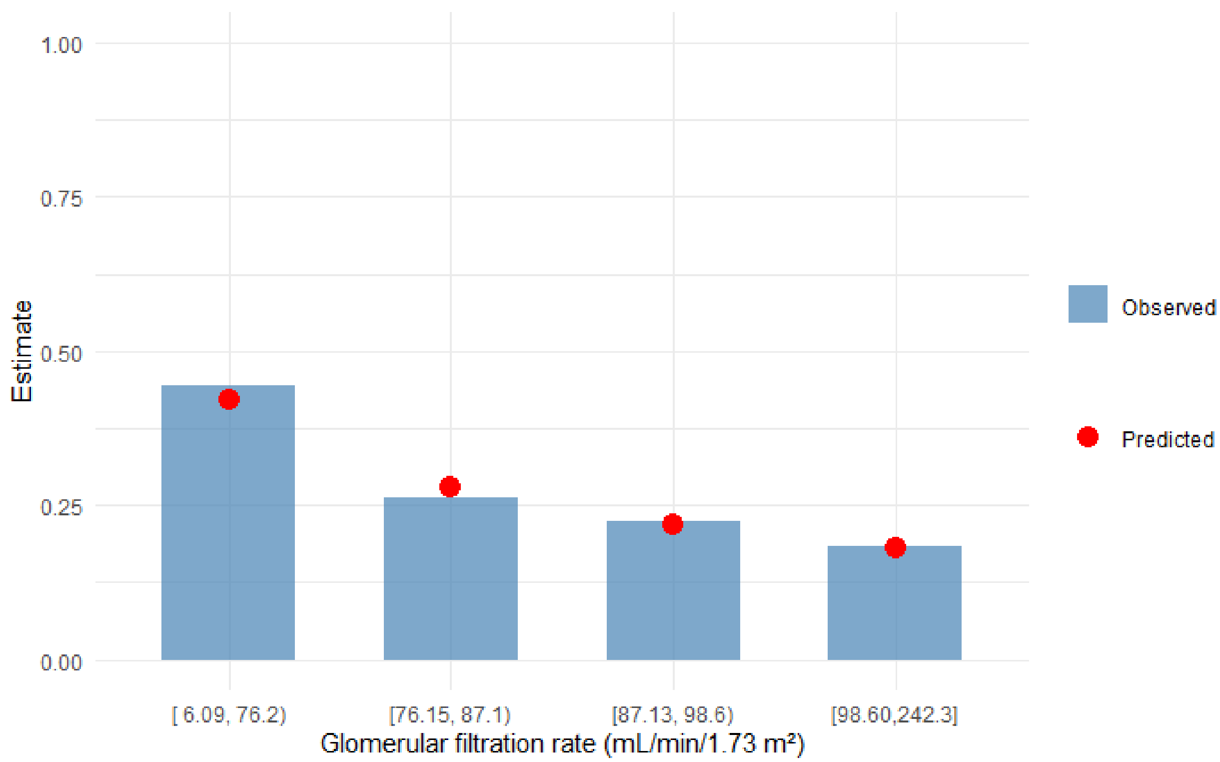
1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
Diabetes
Observed
Predicted



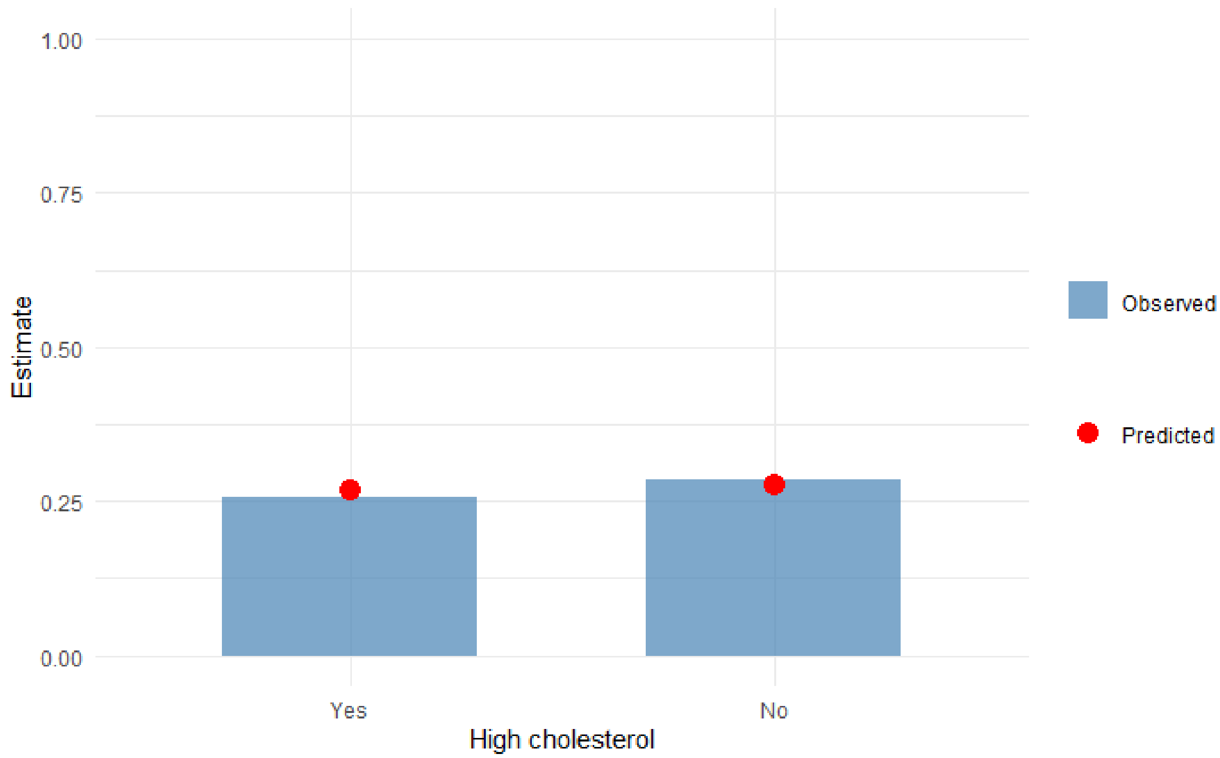
1.00
0.75
0.50
0.25
0.00
Estimate
*
Yes
No
Chronic kidney disease
Observed
Predicted

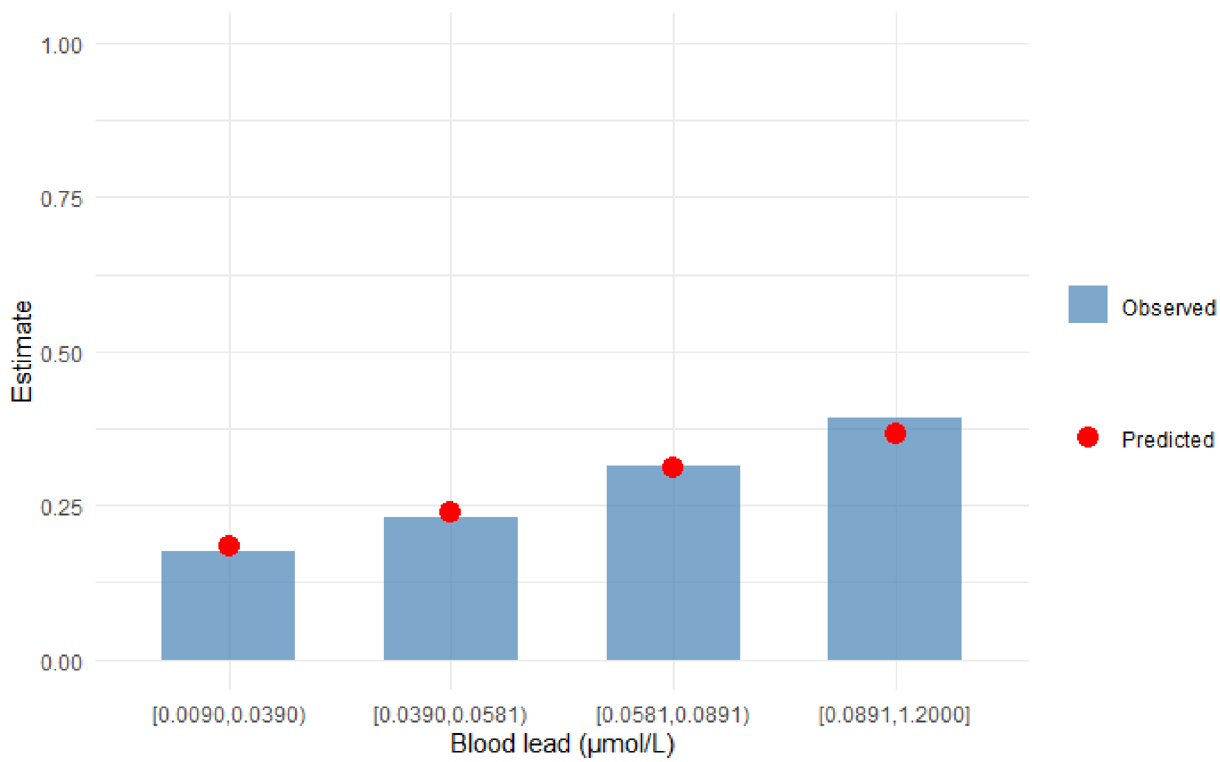


1.00
0.75
0.50
0.25
0.00
Estimate
[0.0420,0.0520)
[0.0520,0.0541)
[0.0541,0.0580)
[0.0580,0.1300]
HbA1c
Observed
Predicted

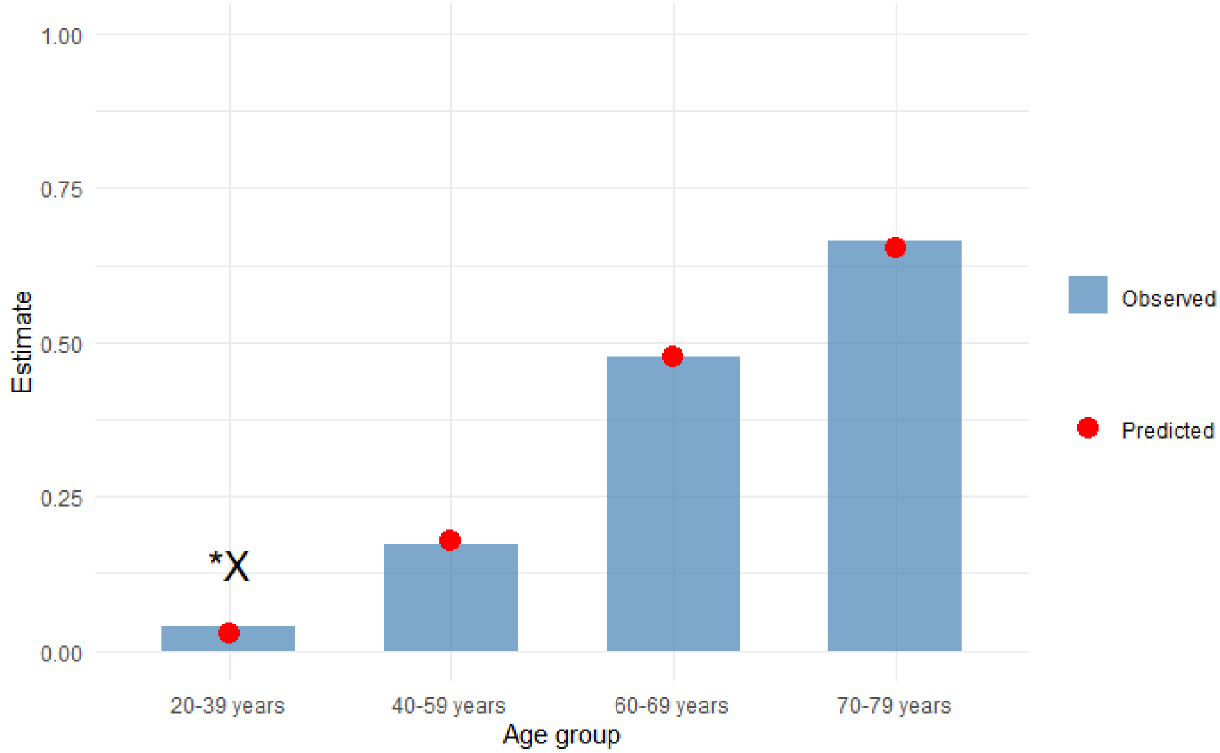


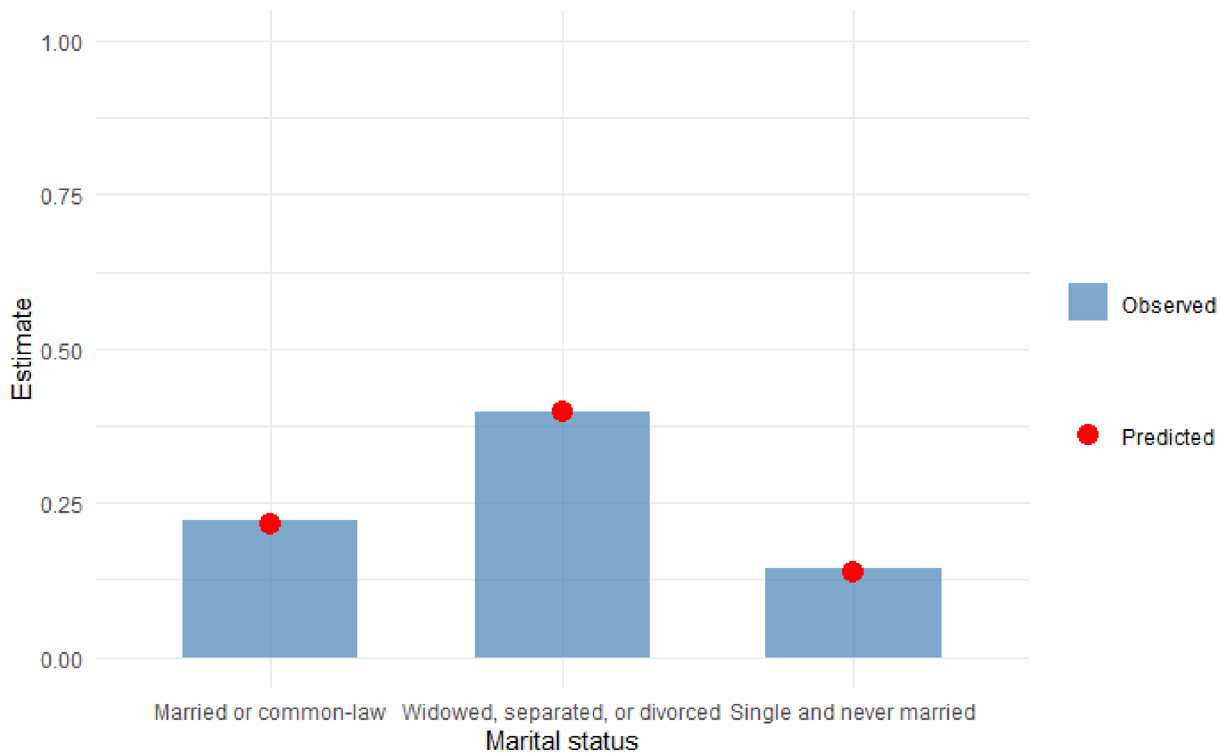
1.00
0.75
0.50
0.25
0.00
Estimate
[6.09, 76.2)
[76.15, 87.1)
[87.13, 98.6)
[98.60,242.3]
Glomerular filtration rate (mL/min/1.73 m²)
Observed
Predicted

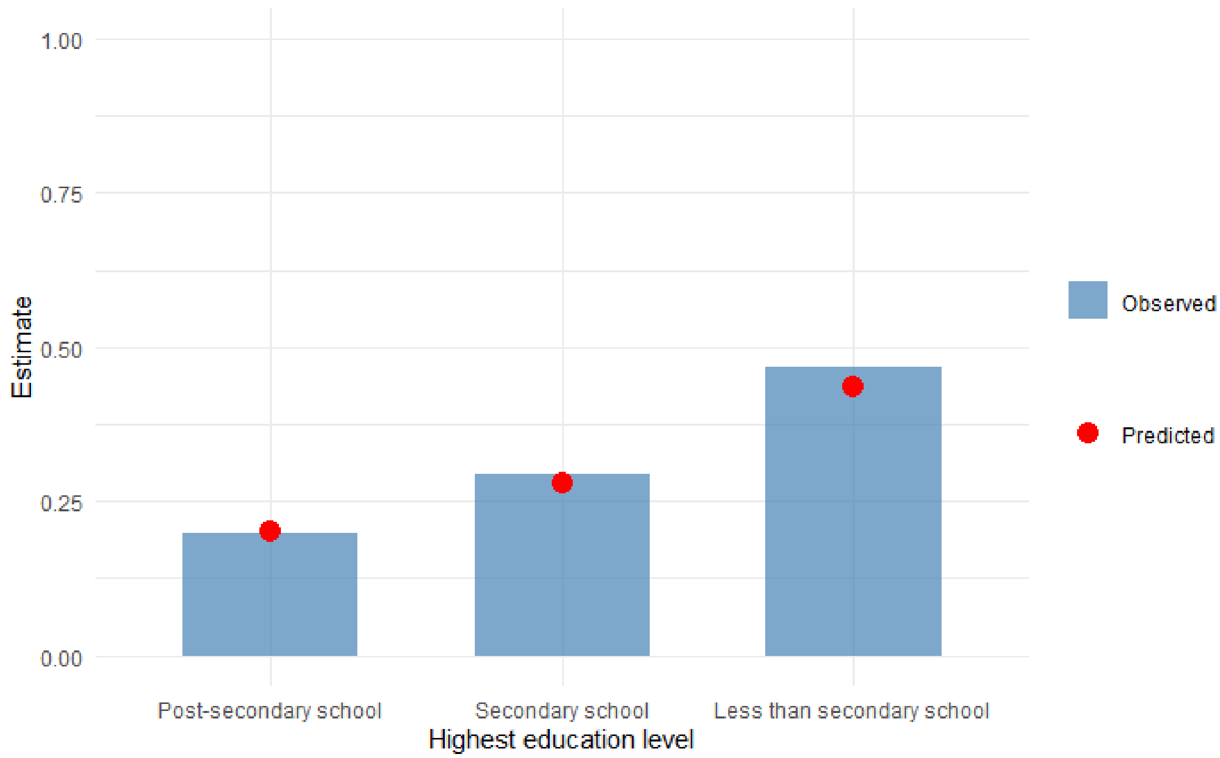

1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
High cholesterol
Observed
Predicted

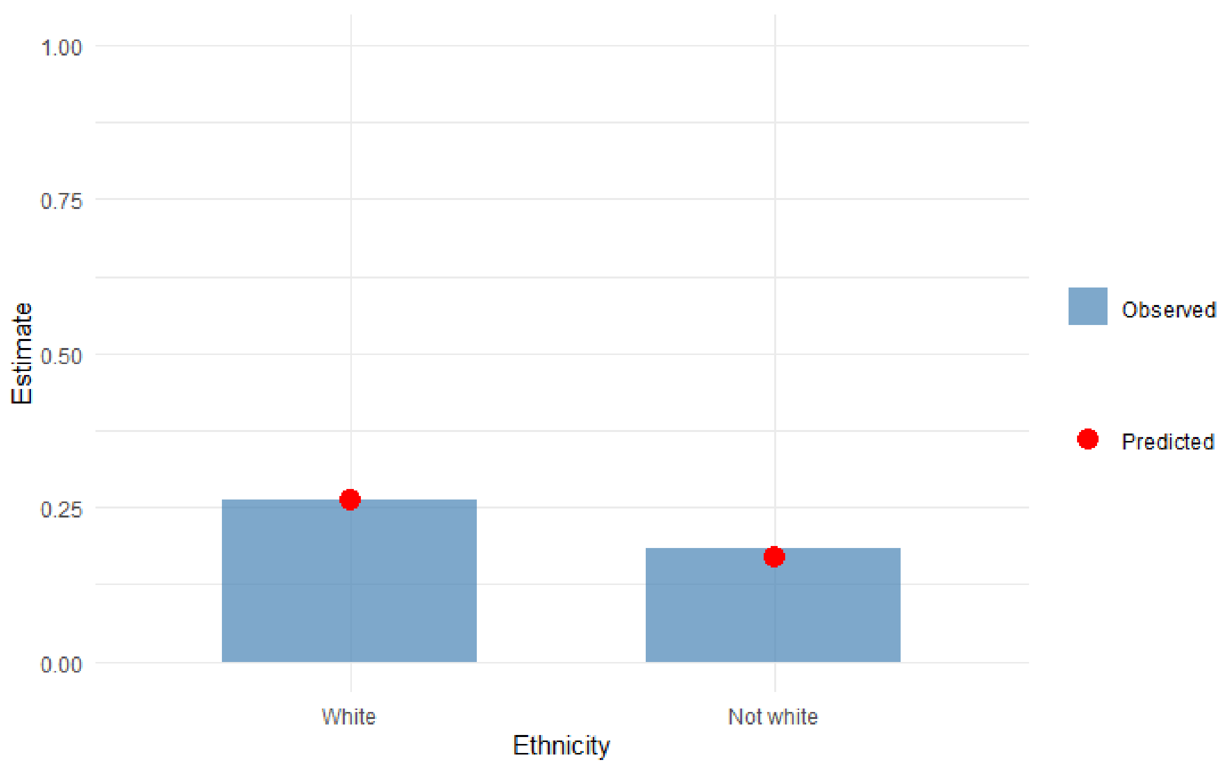

1.00
0.75
0.50
0.25
0.00
Estimate
[0.0090,0.0390)
[0.0390,0.0581)
[0.0581,0.0891)
[0.0891,1.2000]
Blood lead (μmol/L)
Observed
Predicted

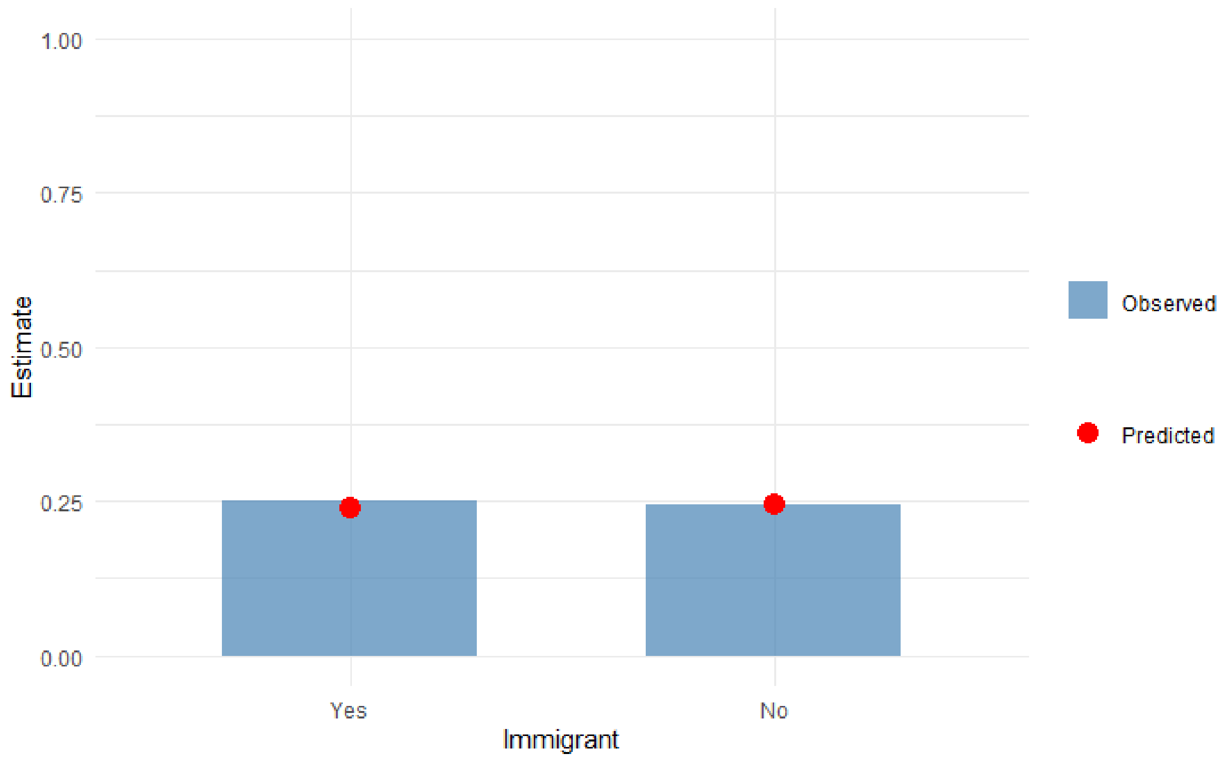
Female Reduced Model:
X – excluded subgroup with observed estimate less than 5%
*** – subgroup with difference between observed and predicted estimates over 20%**

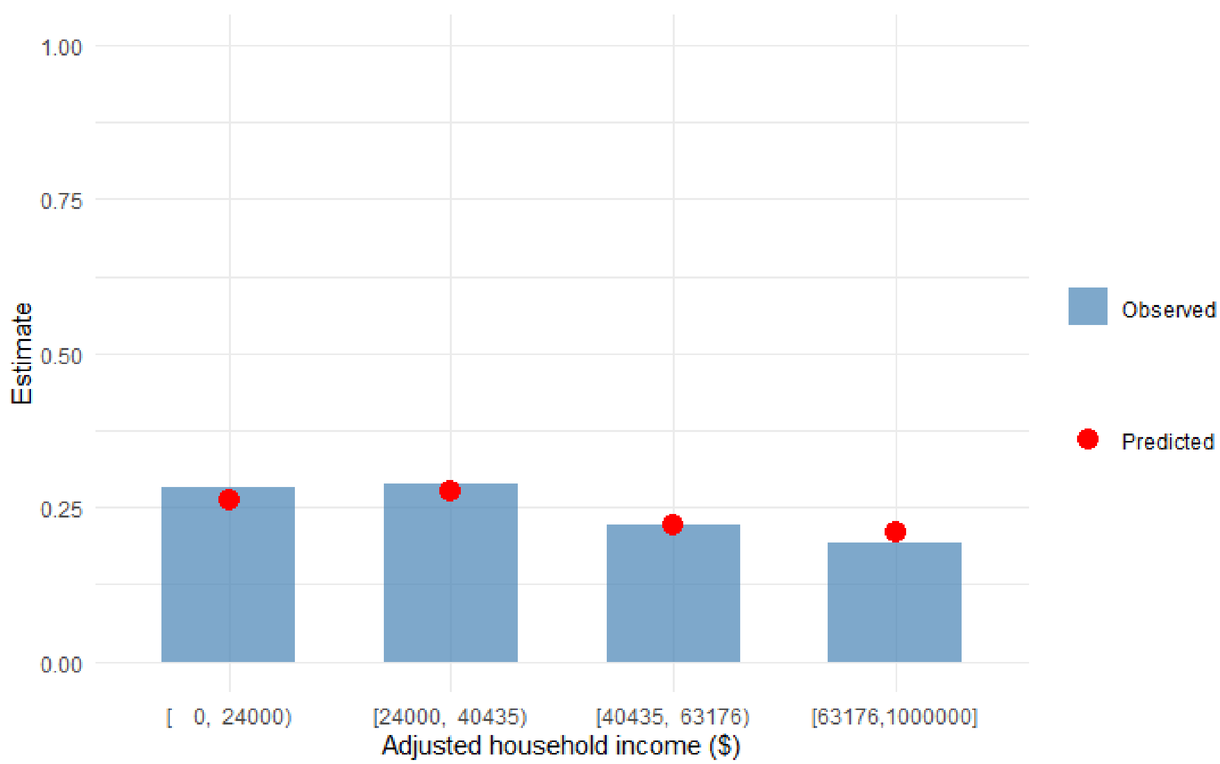


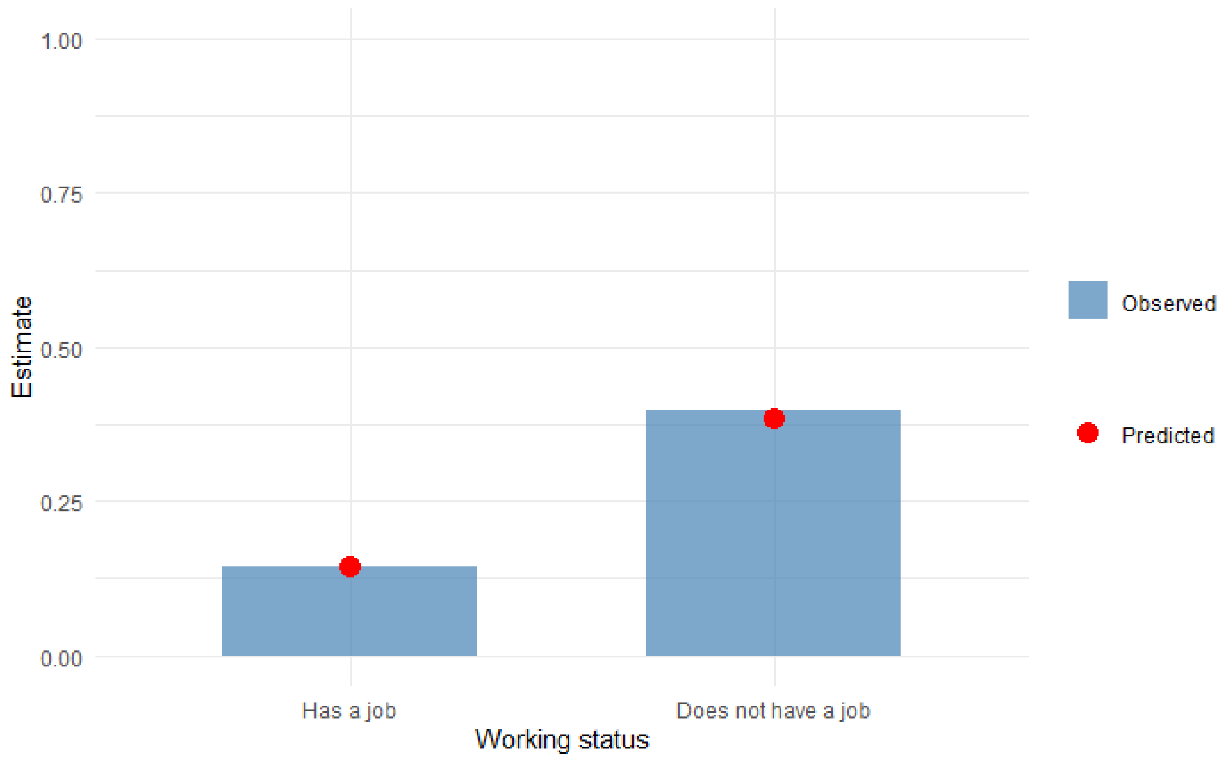



1.00
0.75
0.50
0.25
0.00
Estimate
Post-secondary school
Secondary school
Less than secondary school
Highest education level
Observed
Predicted

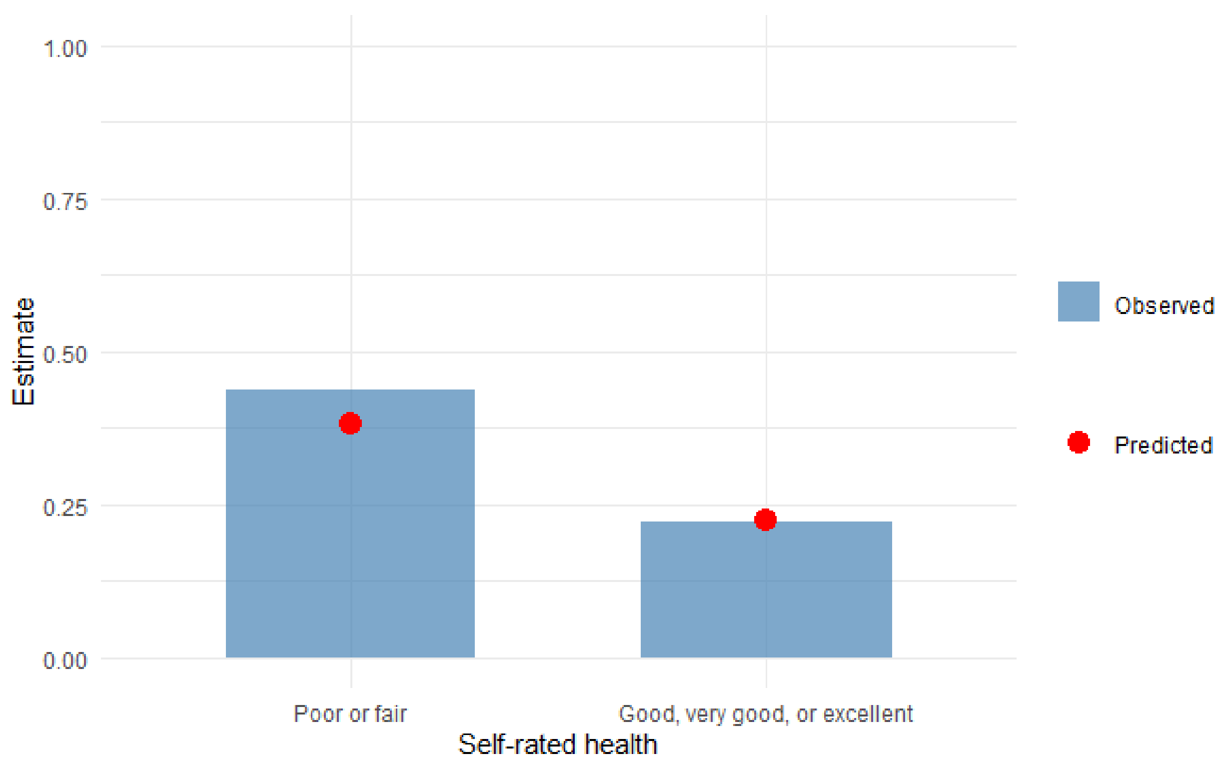

1.00
0.75
0.50
0.25
0.00
Estimate
White
Not white
Ethnicity
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
Immigrant
Observed
Predicted

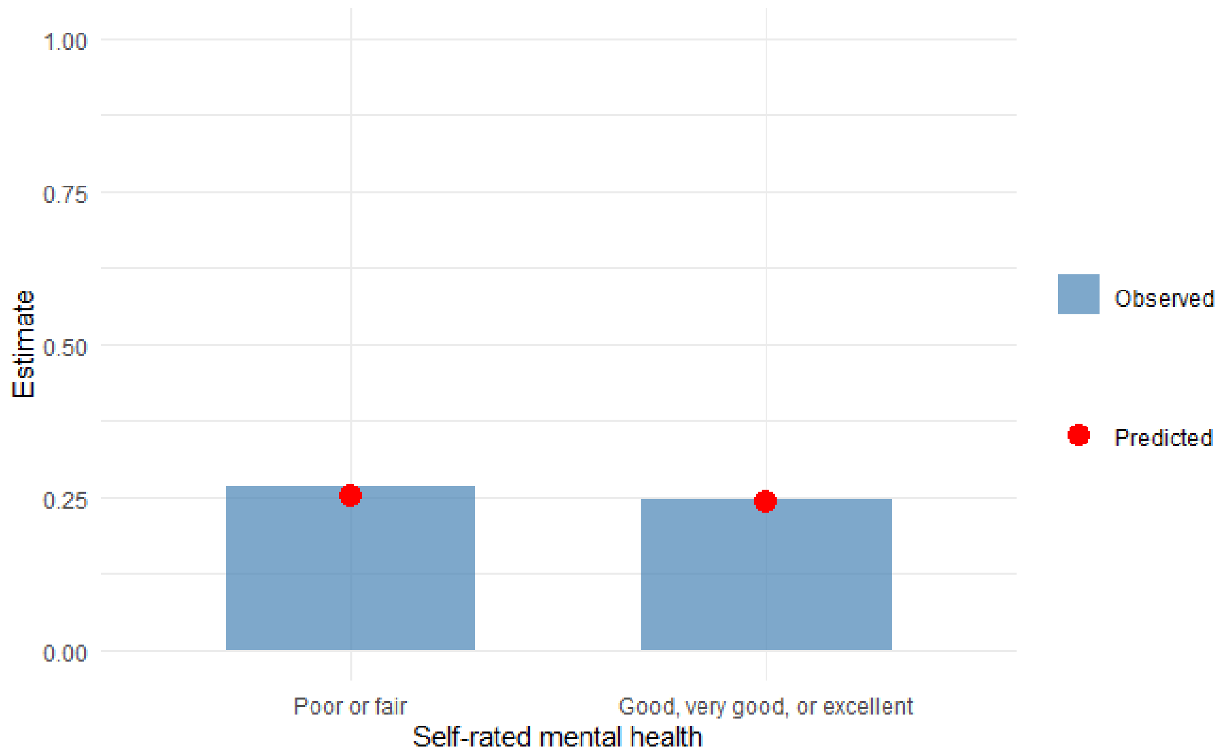

1.00
0.75
0.50
0.25
0.00
Estimate
[0, 24000)
[24000, 40435)
[40435, 63176)
[63176,1000000]
Adjusted household income ($)
Observed
Predicted

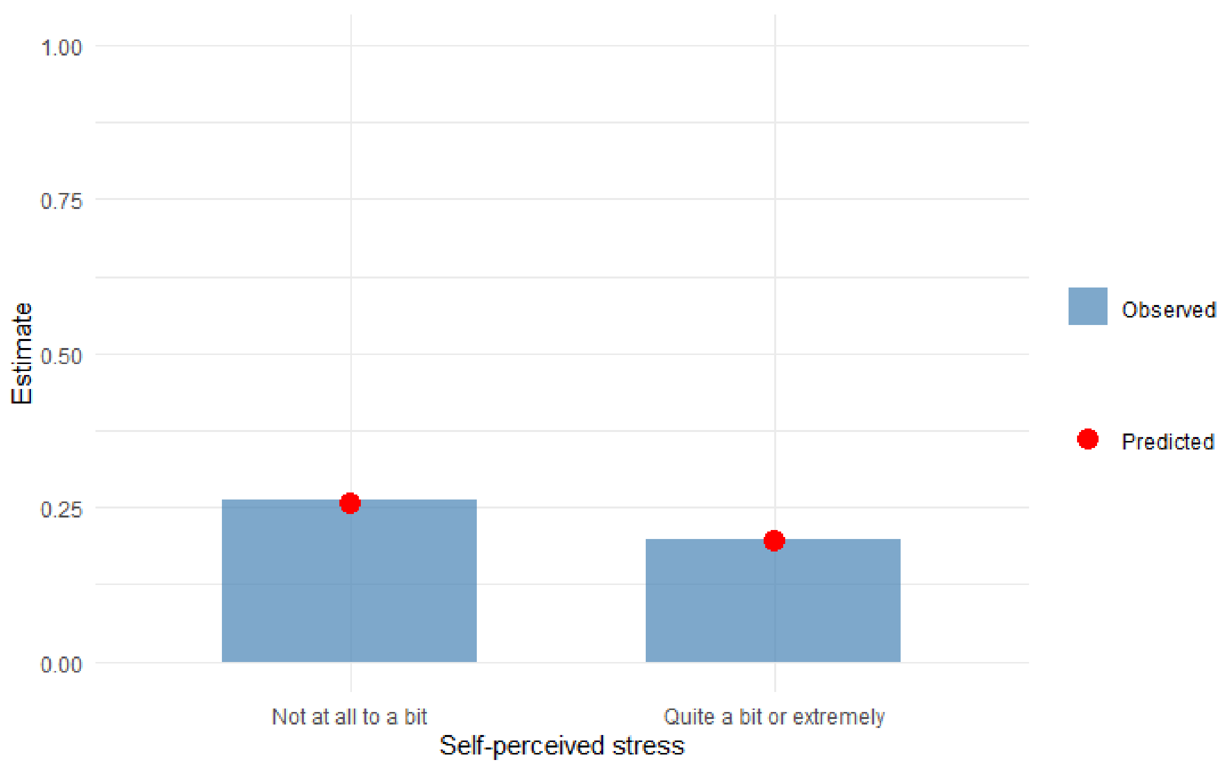


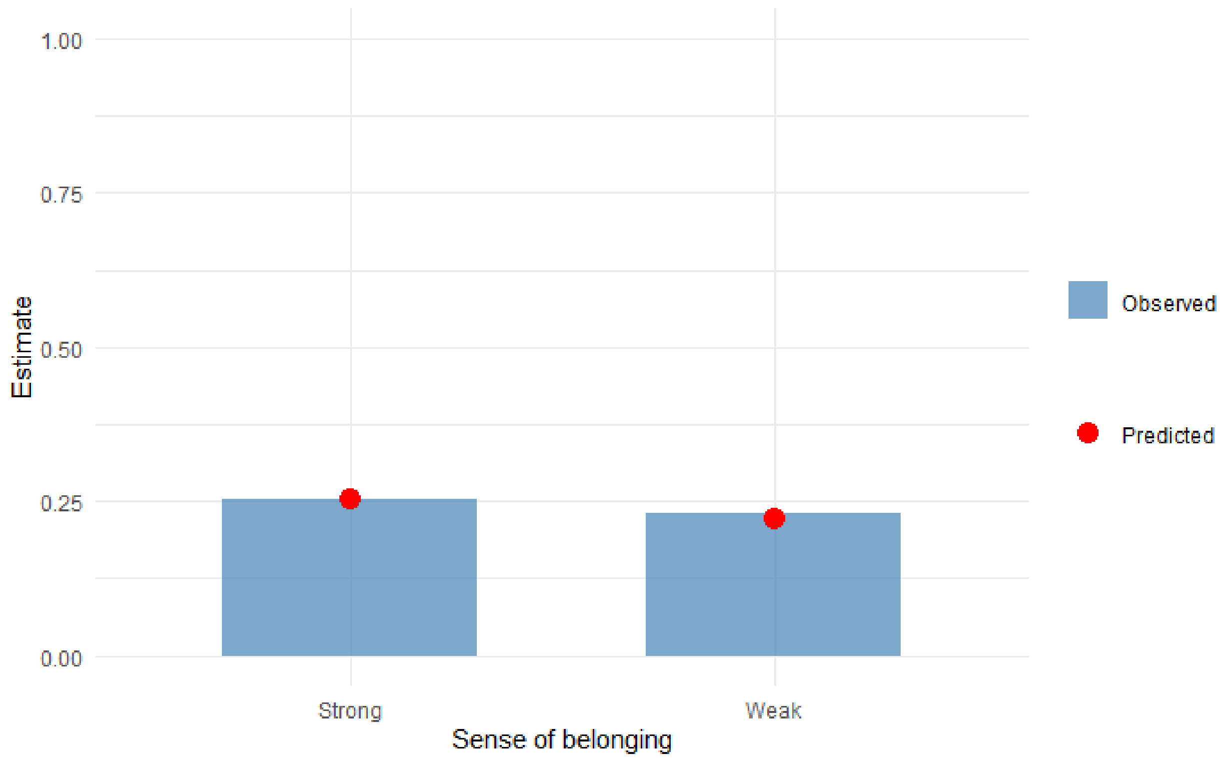
1.00
0.75
0.50
0.25
0.00
Estimate
Has a job
Does not have a job
Working status
Observed
Predicted

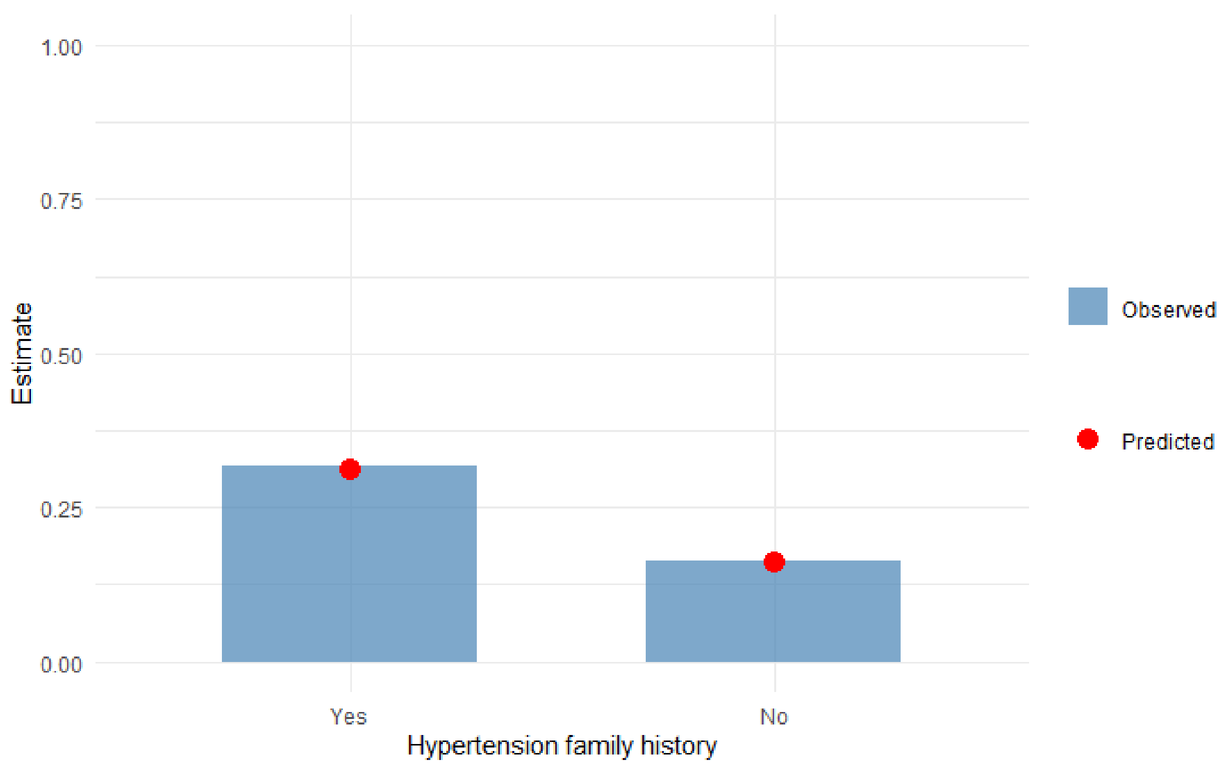


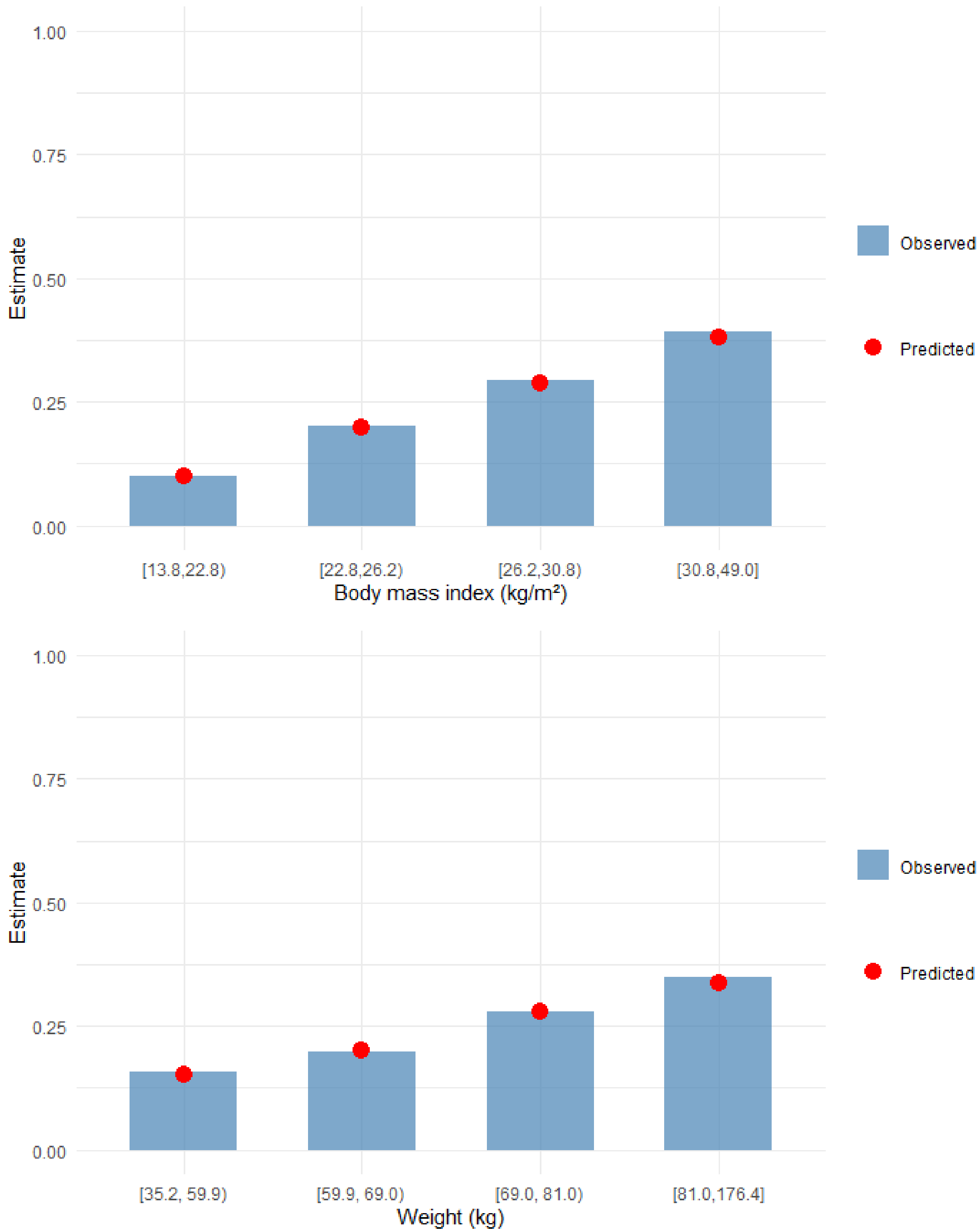
1.00
0.75
0.50
0.25
0.00
Estimate
Poor or fair
Good, very good, or excellent
Self-rated health
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
Observed
Predicted
Poor or fair
Good, very good, or excellent
Self-rated mental health

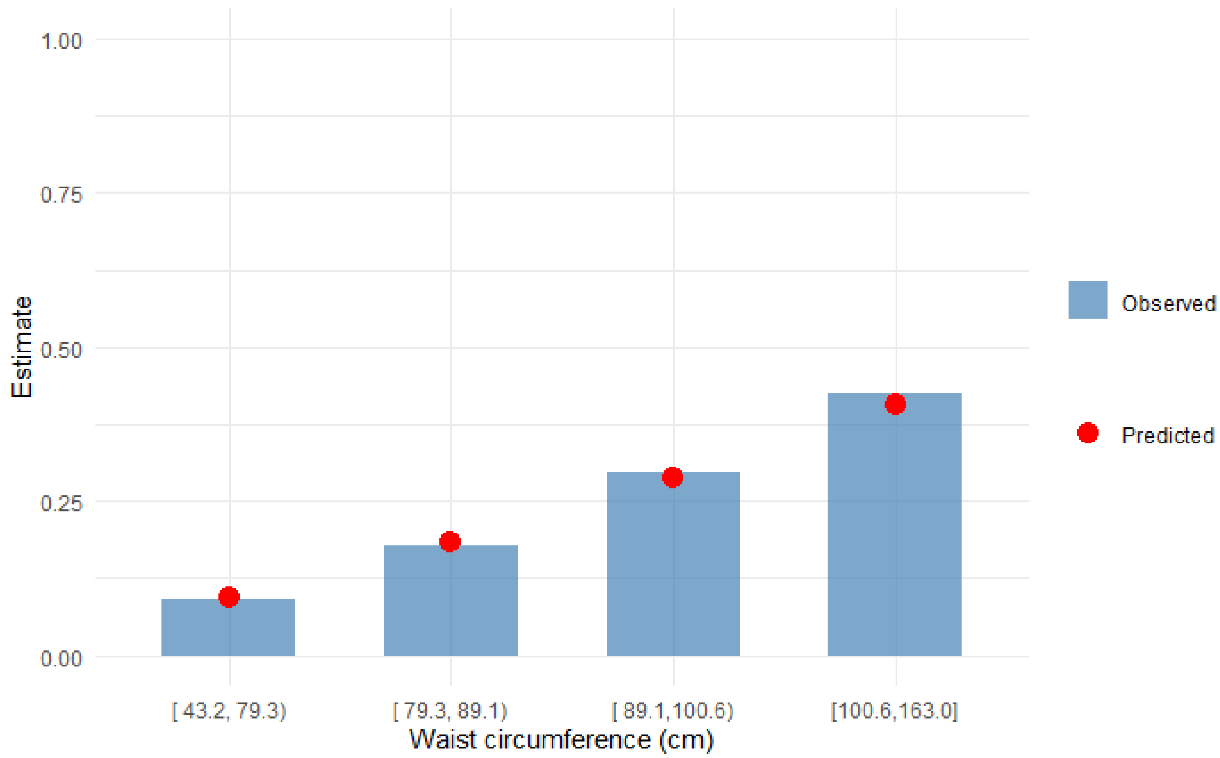

1.00
0.75
0.50
0.25
0.00
Estimate
Observed
Predicted
Not at all to a bit
Quite a bit or extremely
Self-perceived stress

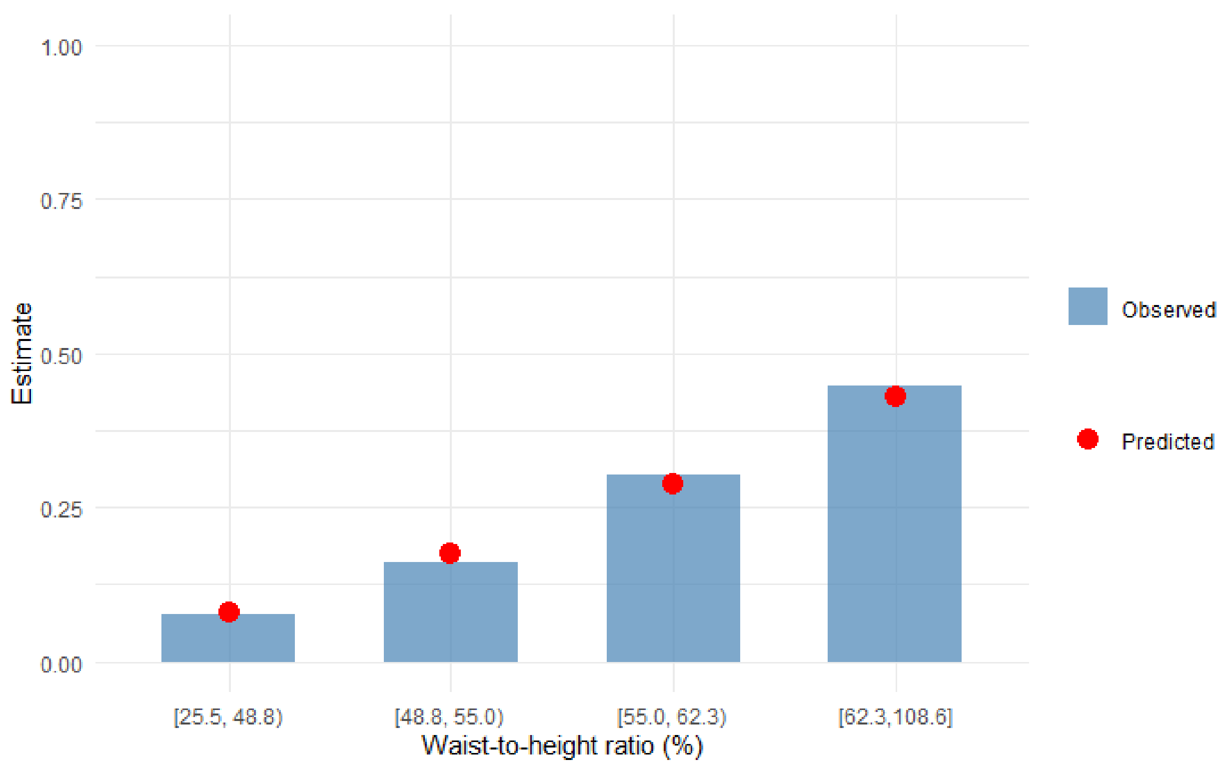

1.00
0.75
0.50
0.25
0.00
Estimate
Strong
Weak
Sense of belonging
Observed
Predicted

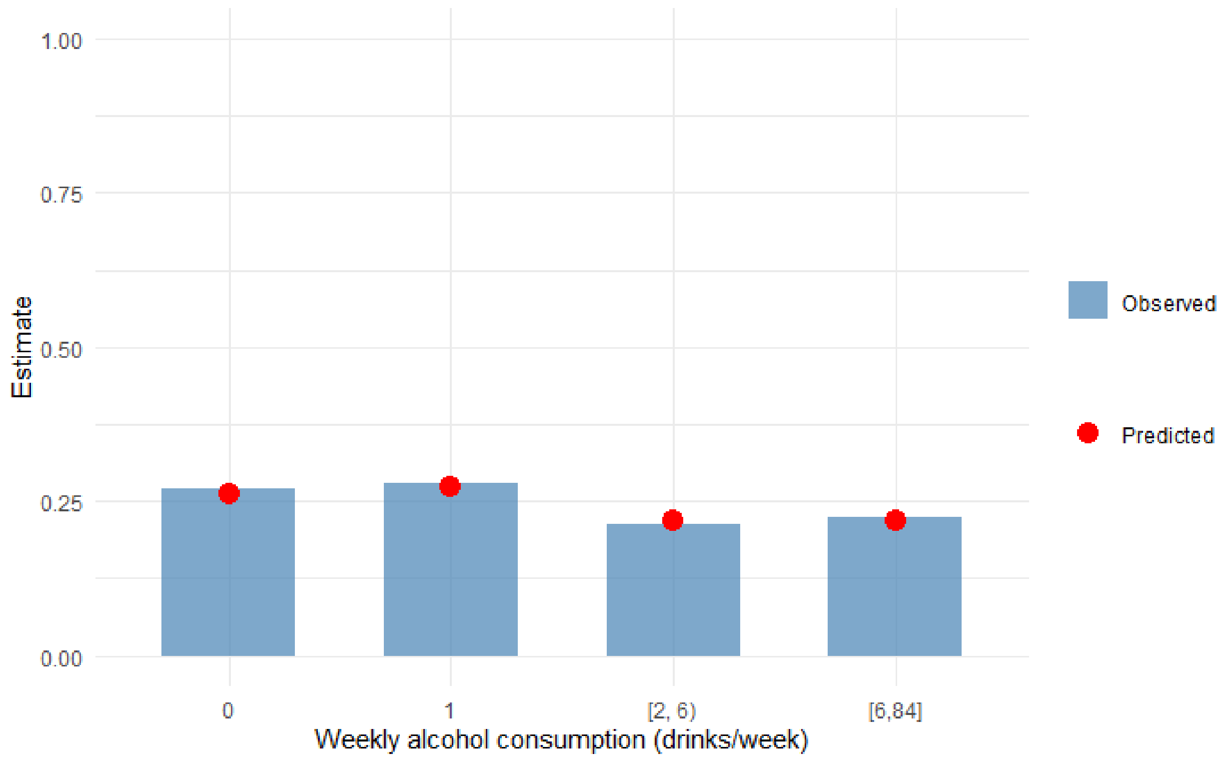

1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
Hypertension family history
Observed
Predicted

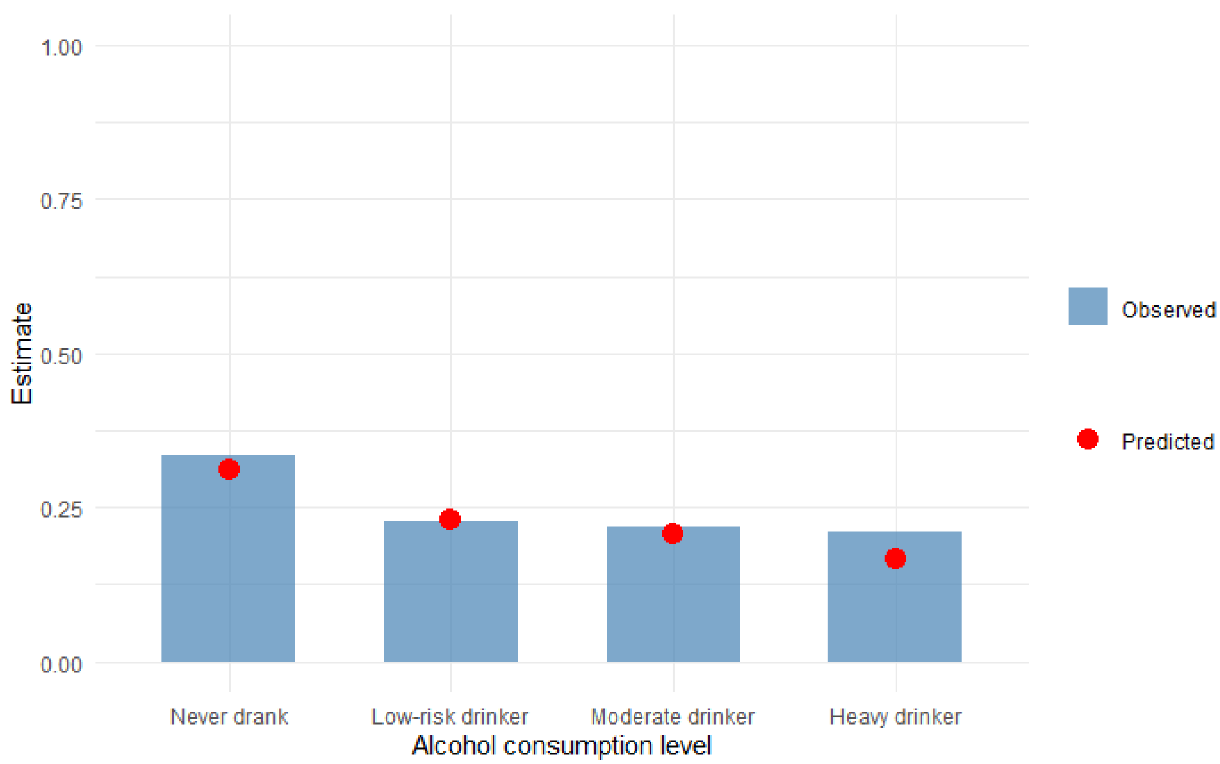


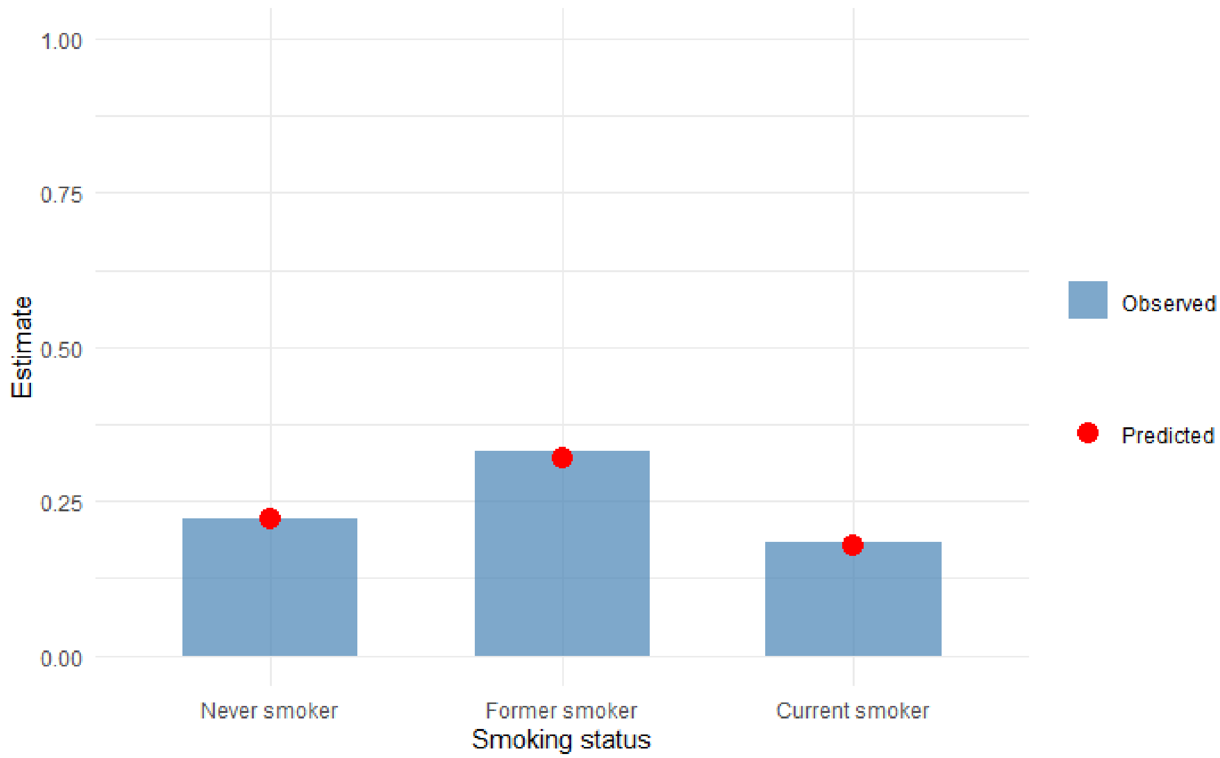
1.00
0.75
0.50
0.25
0.00
Estimate
[13.8,22.8)
[22.8,26.2)
[26.2,30.8)
[30.8,49.0]
Body mass index (kg/m²)
Observed
Predicted
1.00
0.75
0.50
0.25
0.00
Estimate
[35.2, 59.9)
[59.9, 69.0)
[69.0, 81.0)
[81.0,176.4]
Weight (kg)
Observed
Predicted

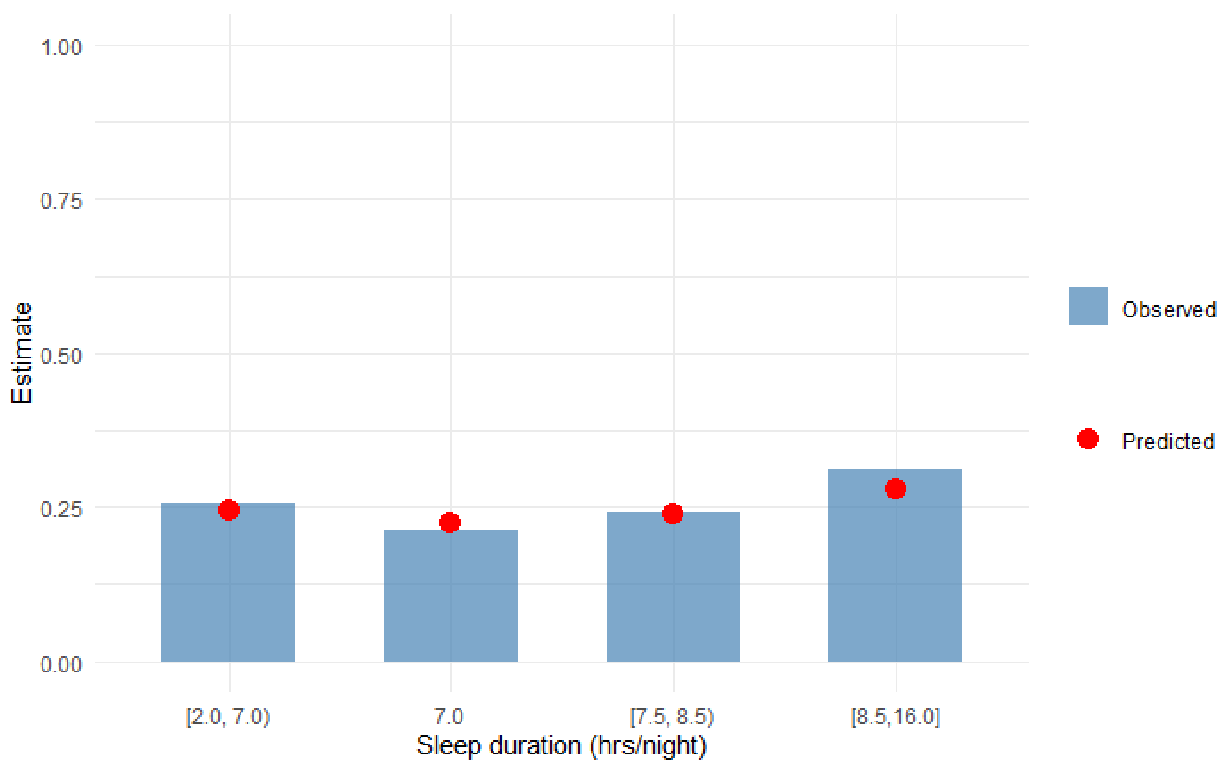

1.00
0.75
0.50
0.25
0.00
Estimate
[43.2, 79.3)
[79.3, 89.1)
[89.1,100.6)
[100.6,163.0]
Waist circumference (cm)
Observed
Predicted

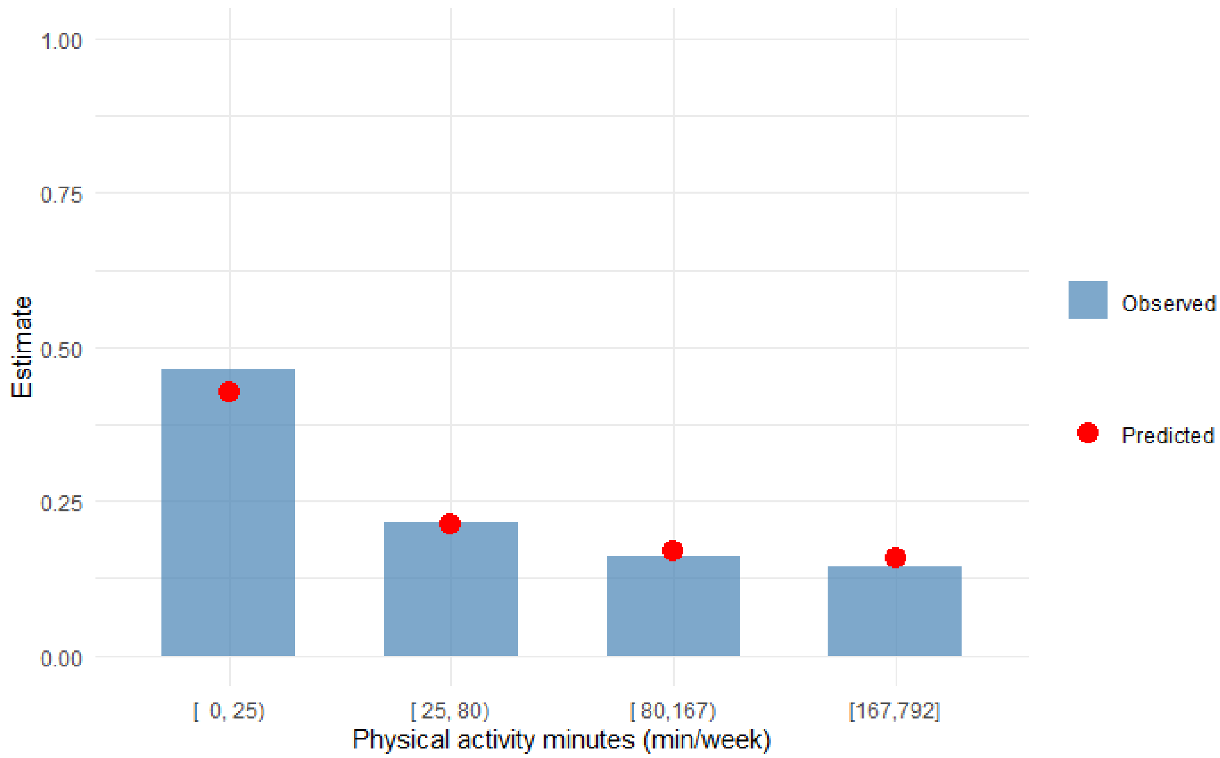

1.00
0.75
0.50
0.25
0.00
Estimate
[25.5, 48.8)
[48.8, 55.0)
[55.0, 62.3)
[62.3,108.6]
Waist-to-height ratio (%)
Observed
Predicted

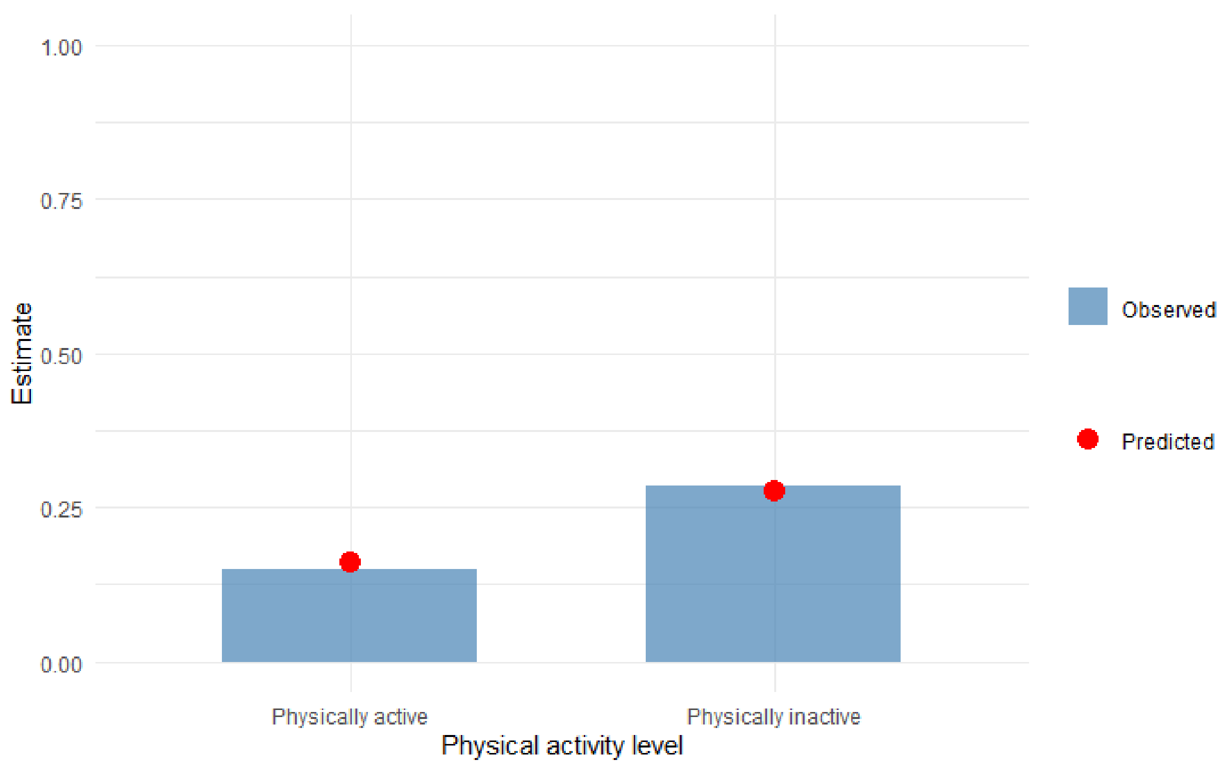

1.00
0.75
0.50
0.25
0.00
Estimate
0
1
[2, 6)
[6,84]
Weekly alcohol consumption (drinks/week)
Observed
Predicted

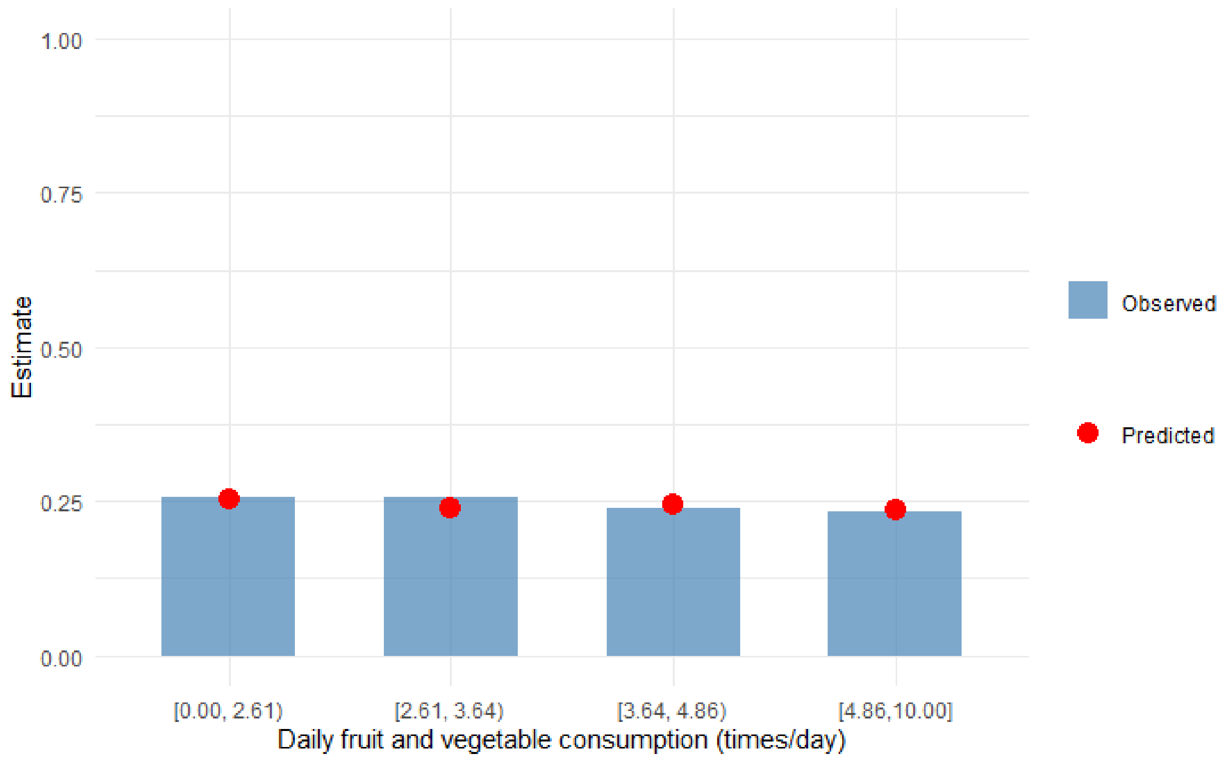

1.00
0.75
0.50
0.25
0.00
Estimate
Never drank
Low-risk drinker
Moderate drinker
Heavy drinker
Alcohol consumption level
Observed
Predicted

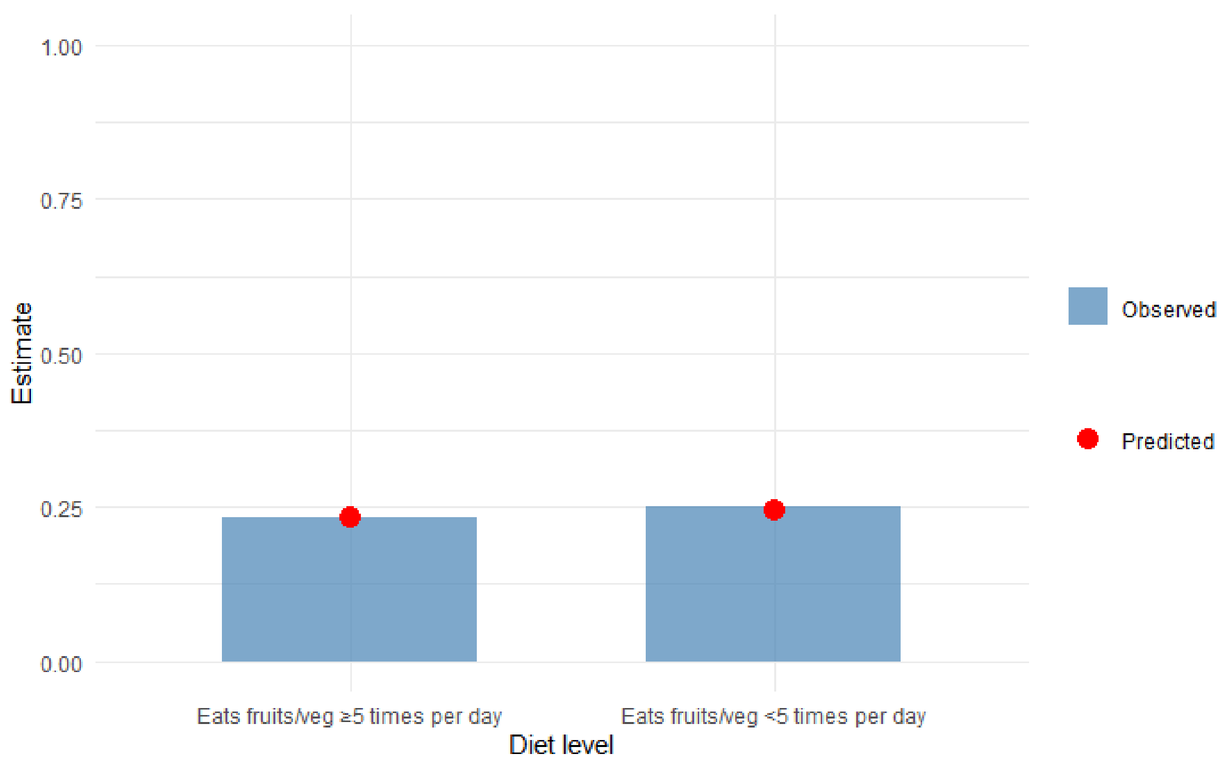

Estimate
1.00
0.75
0.50
0.25
0.00
Never smoker
Former smoker
Current smoker
Smoking status
Observed
Predicted

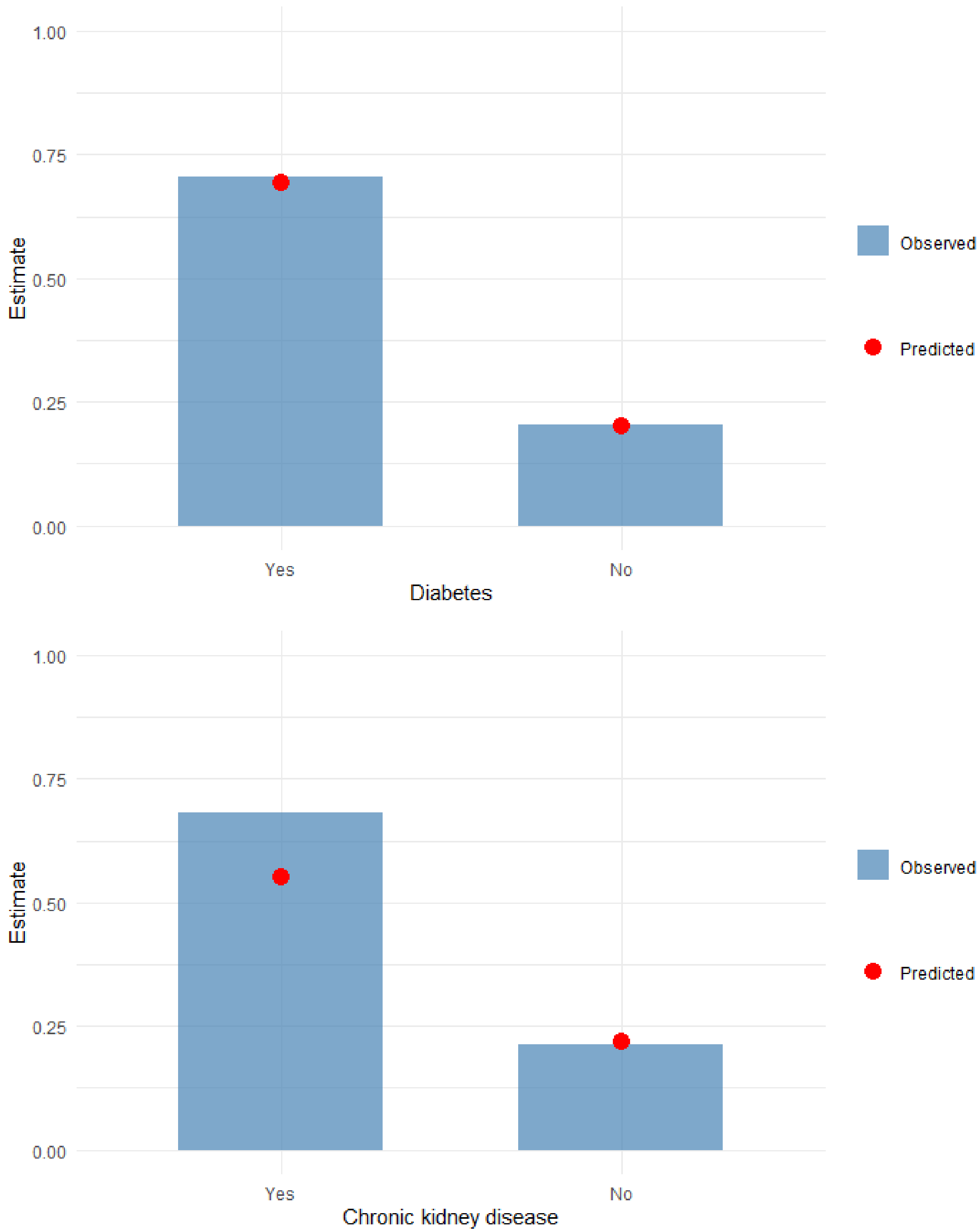

Estimate
1.00
0.75
0.50
0.25
0.00
[2.0, 7.0)
7.0
[7.5, 8.5)
[8.5,16.0]
Sleep duration (hrs/night)
Observed
Predicted

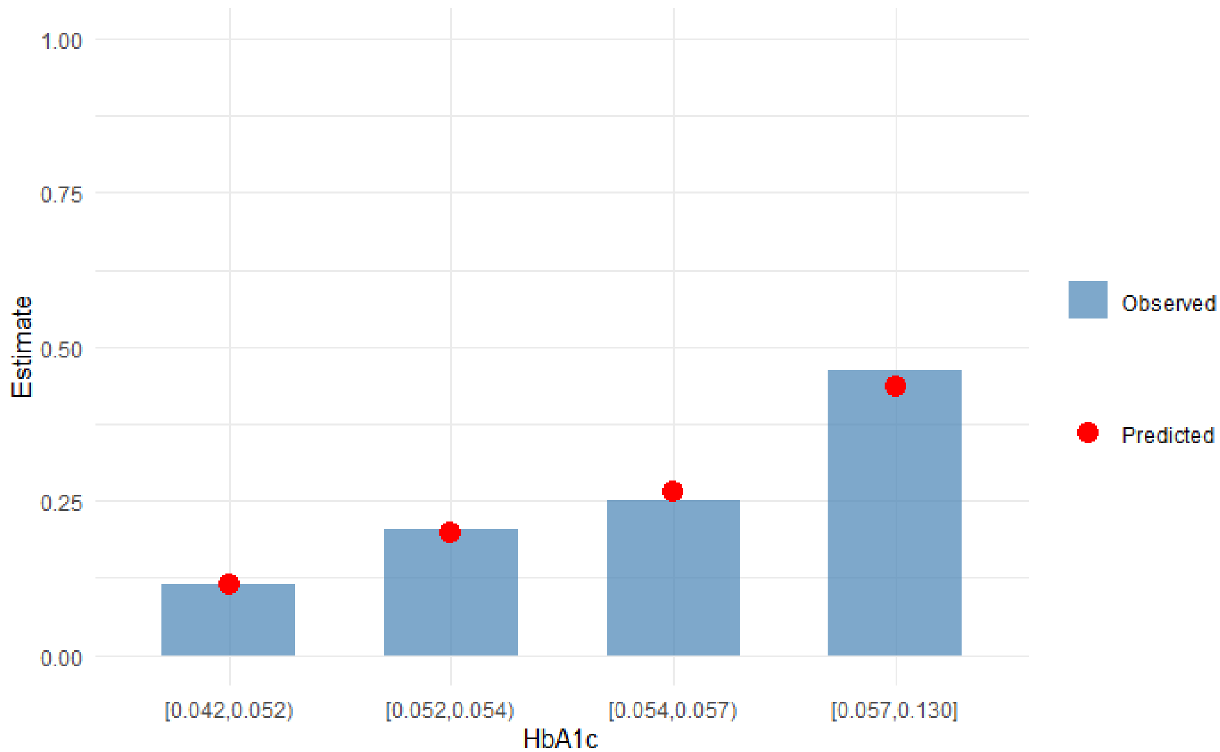

1.00
0.75
0.50
0.25
0.00
Estimate
[0, 25)
[25, 80)
[80,167)
[167,792]
Physical activity minutes (min/week)
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
Physically active
Physically inactive
Physical activity level
Observed
Predicted

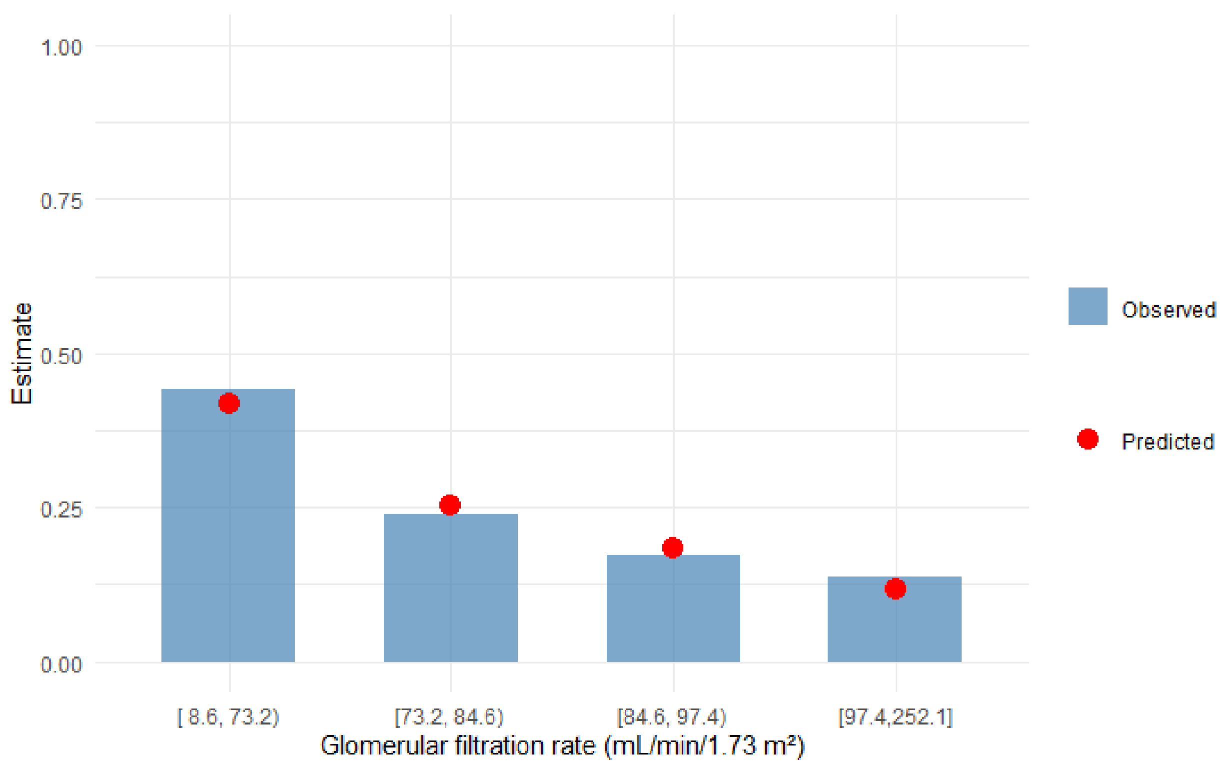

1.00
0.75
0.50
0.25
0.00
Estimate
[0.00, 2.61)
[2.61, 3.64)
[3.64, 4.86)
[4.86,10.00]
Daily fruit and vegetable consumption (times/day)
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
Eats fruits/veg ≥5 times per day
Eats fruits/veg <5 times per day
Diet level
Observed
Predicted

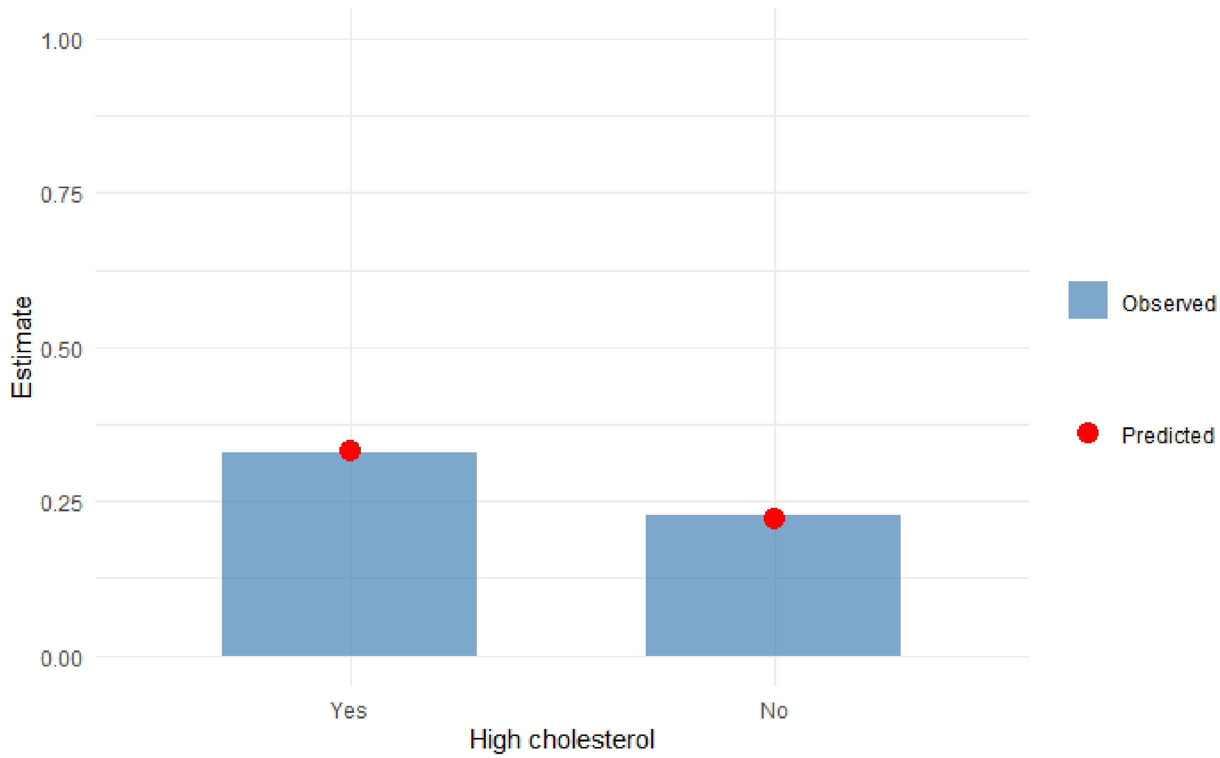

1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
Diabetes
Observed
Predicted
1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
Chronic kidney disease
Observed
Predicted

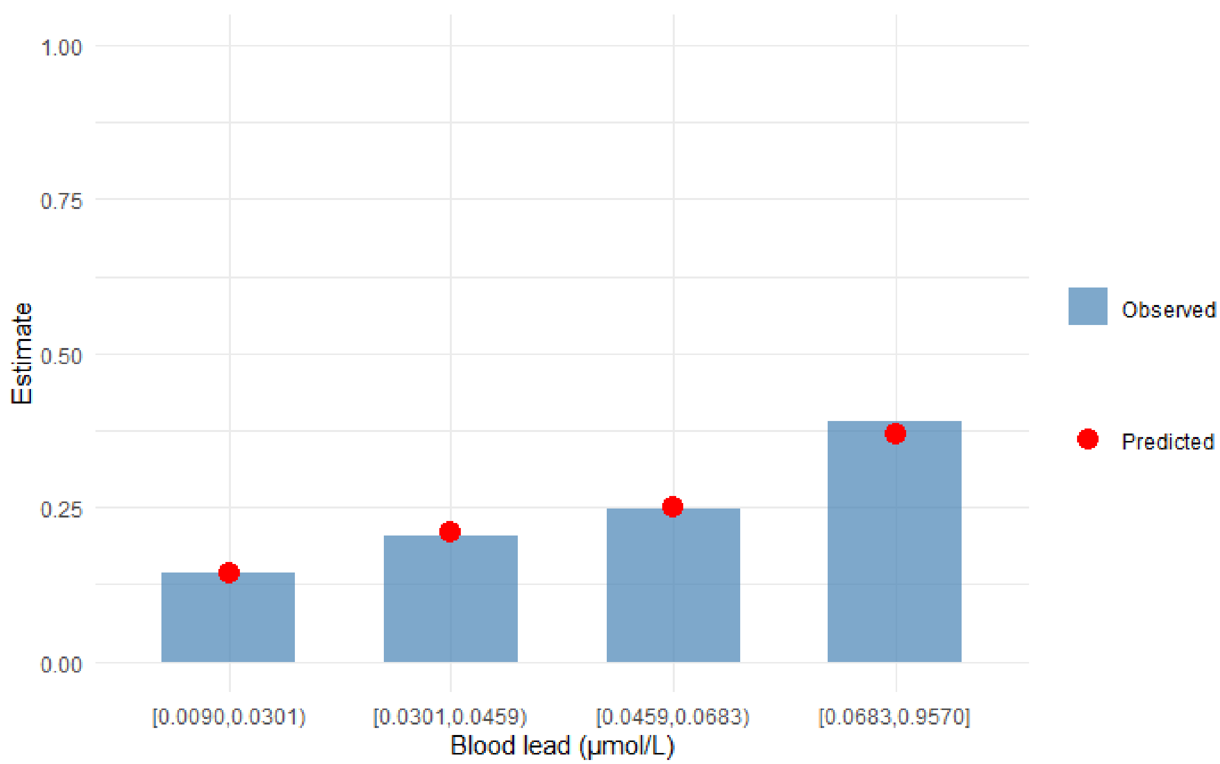


1.00
0.75
0.50
0.25
0.00
Estimate
[0.042,0.052)
[0.052,0.054)
[0.054,0.057)
[0.057,0.130]
HbA1c
Observed
Predicted



1.00
0.75
0.50
0.25
0.00
Estimate
[8.6, 73.2)
[73.2, 84.6)
[84.6, 97.4)
[97.4,252.1]
Glomerular filtration rate (mL/min/1.73 m²)
Observed
Predicted

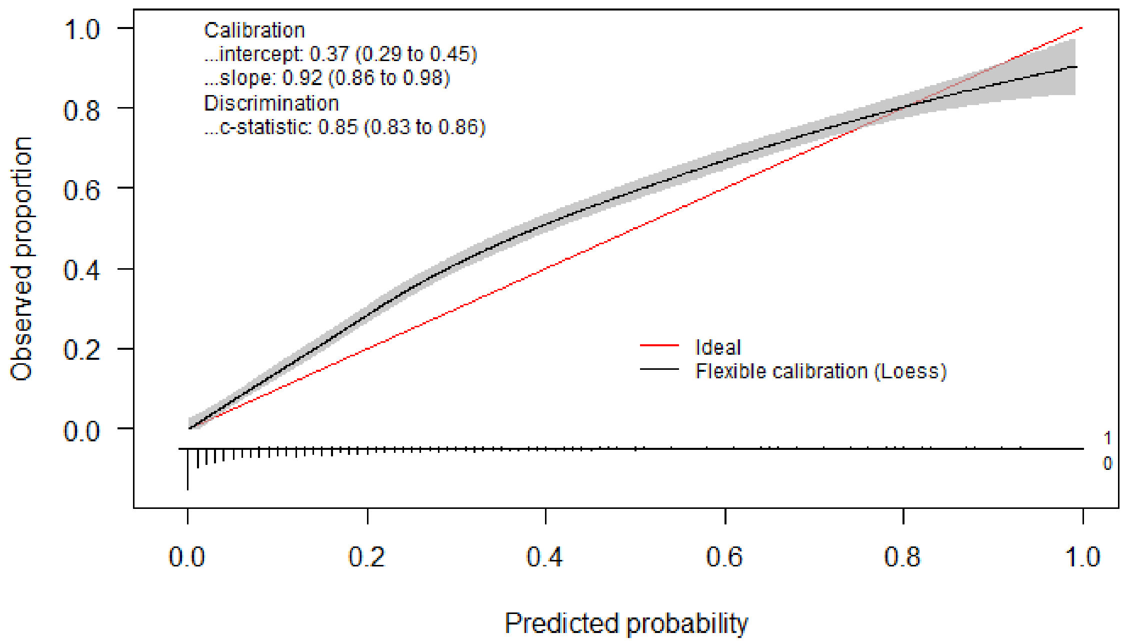

1.00
0.75
0.50
0.25
0.00
Estimate
Yes
No
High cholesterol
Observed
Predicted


1.00
0.75
0.50
0.25
0.00
Estimate
[0.0090,0.0301)
[0.0301,0.0459)
[0.0459,0.0683)
[0.0683,0.9570]
Blood lead (μmol/L)
Observed
Predicted

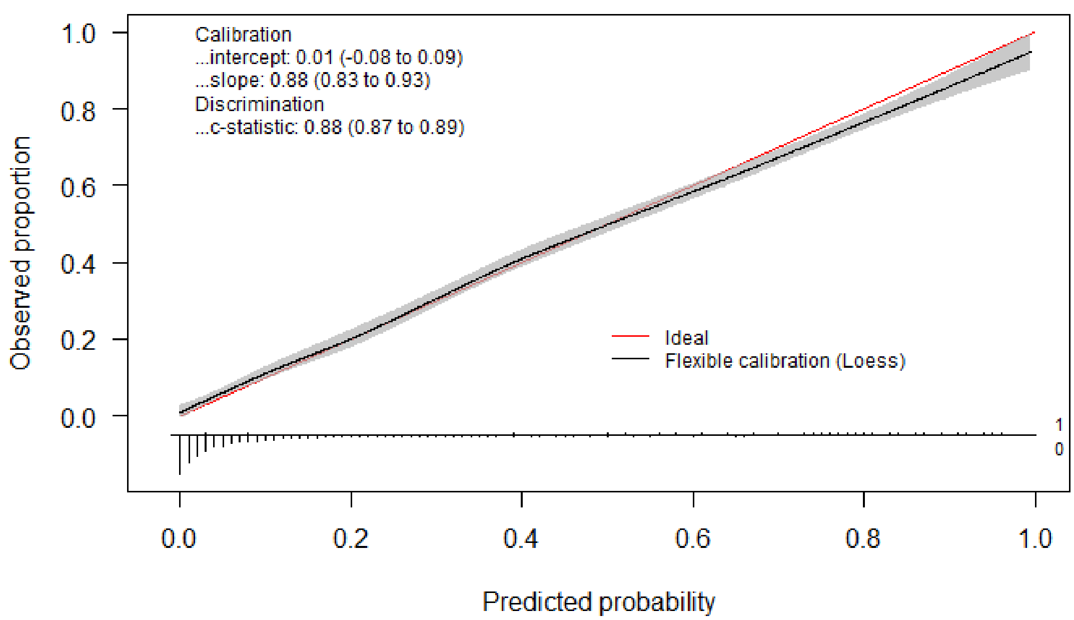
Appendix 9 – Sensitivity analyses

Calibration plots of models dropping observations with missing data:

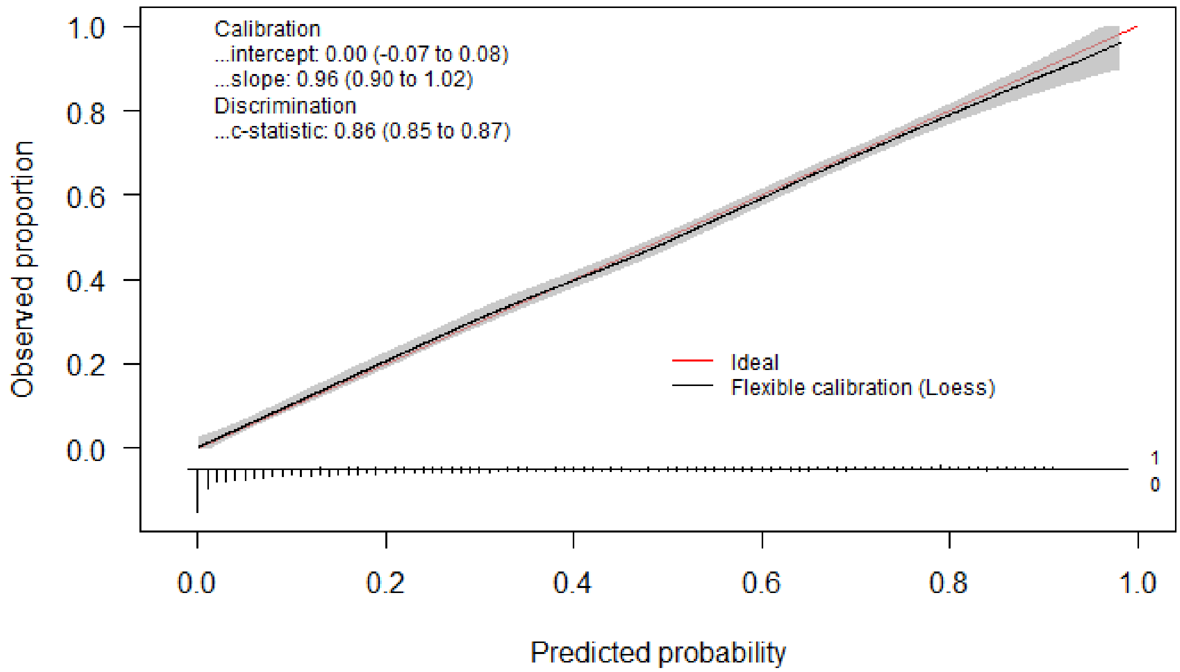
Male full model:



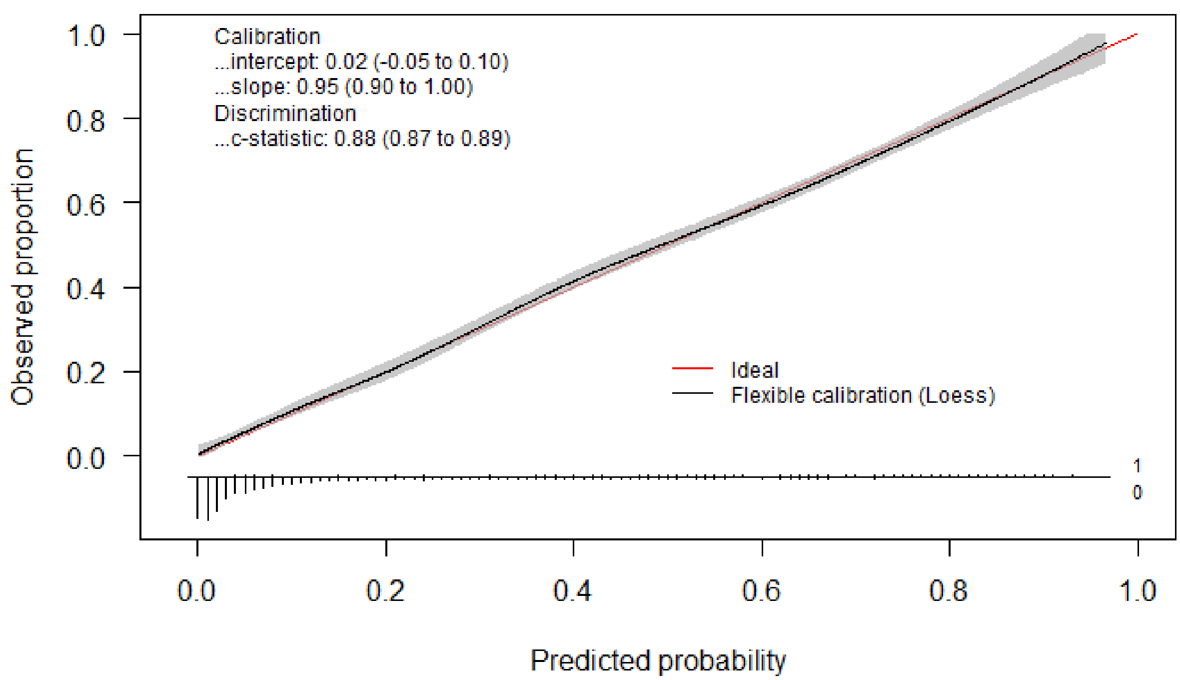
Female full model:



Male reduced model:

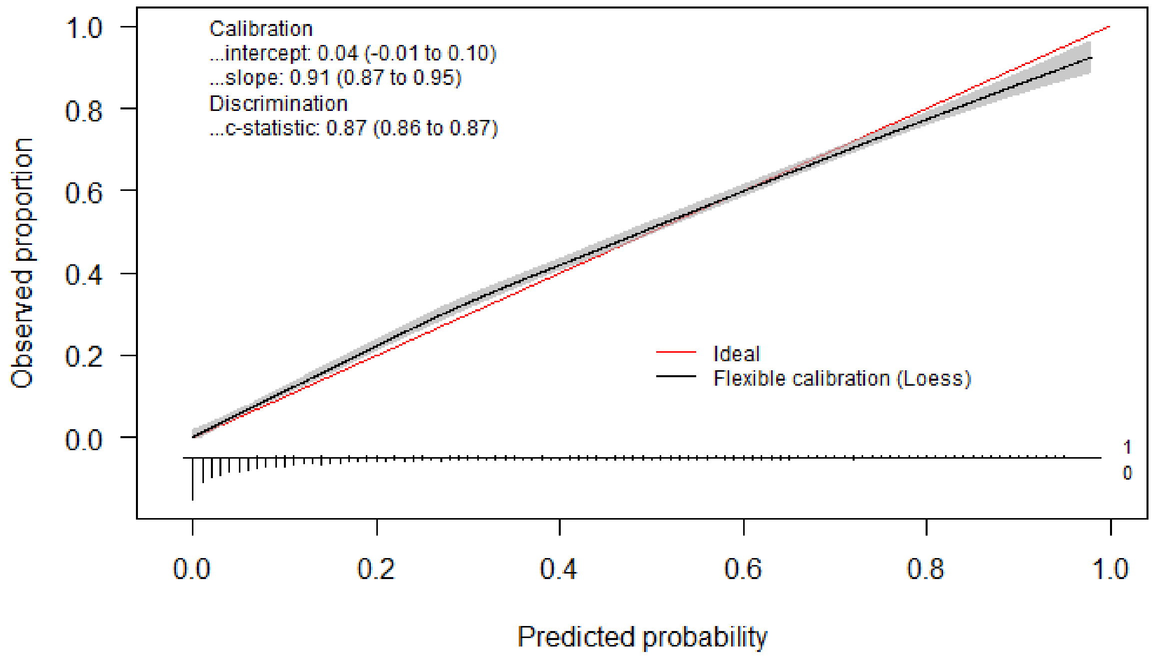


Female reduced model:

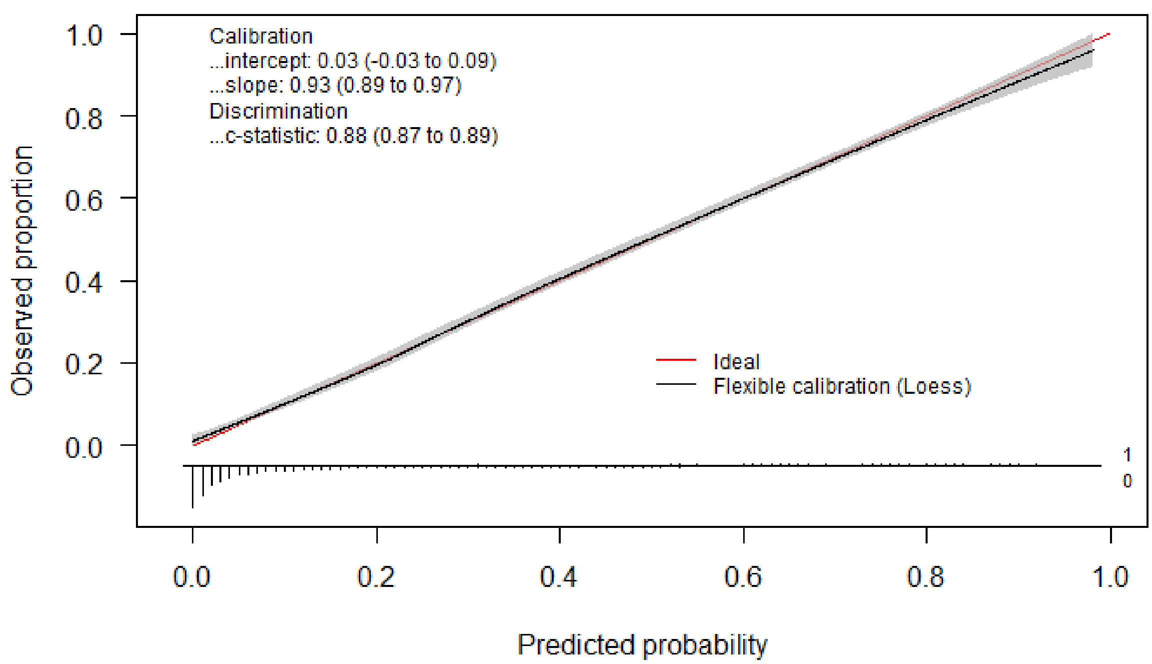


Calibration plots of models derived from four other imputed datasets:

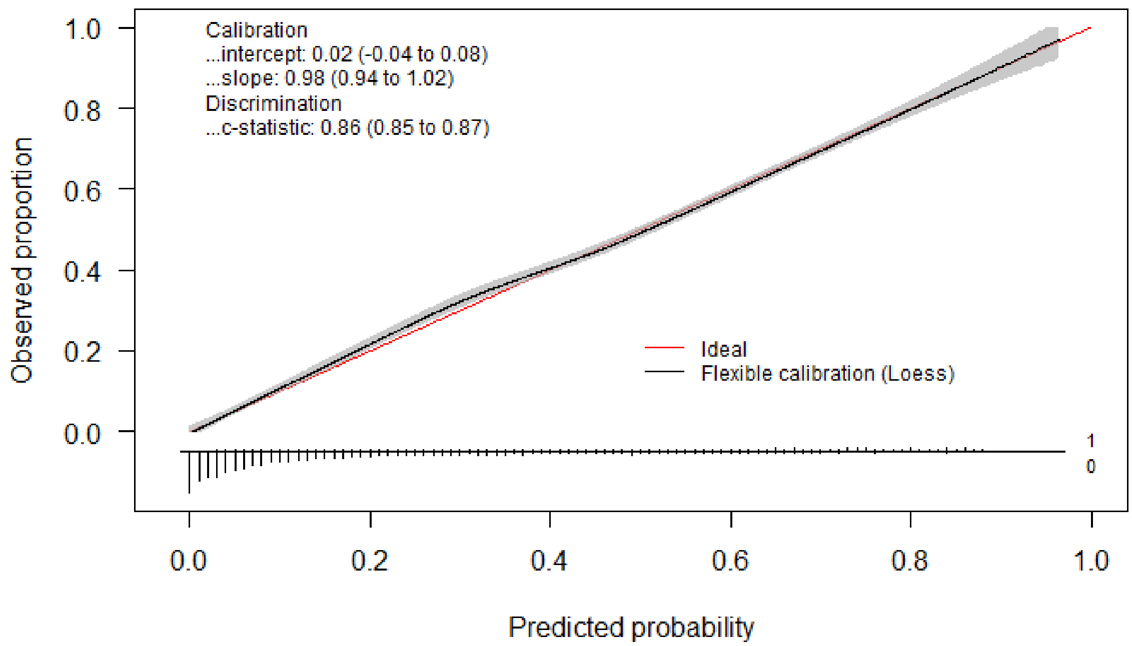
Male full model:



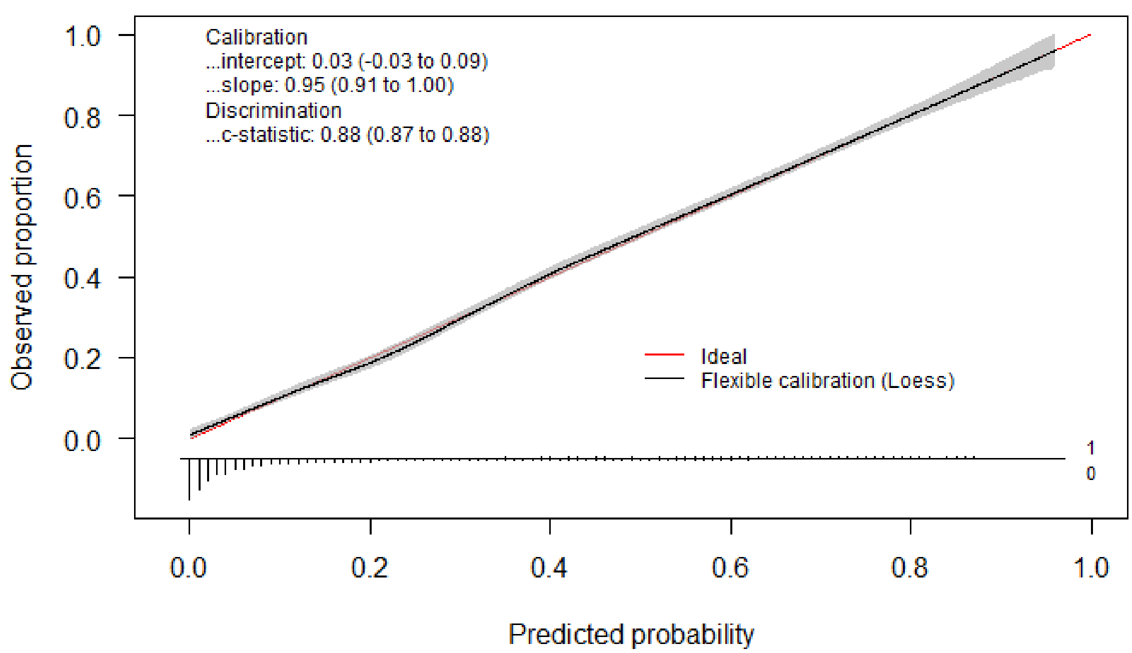
Female full model:



Male reduced model:

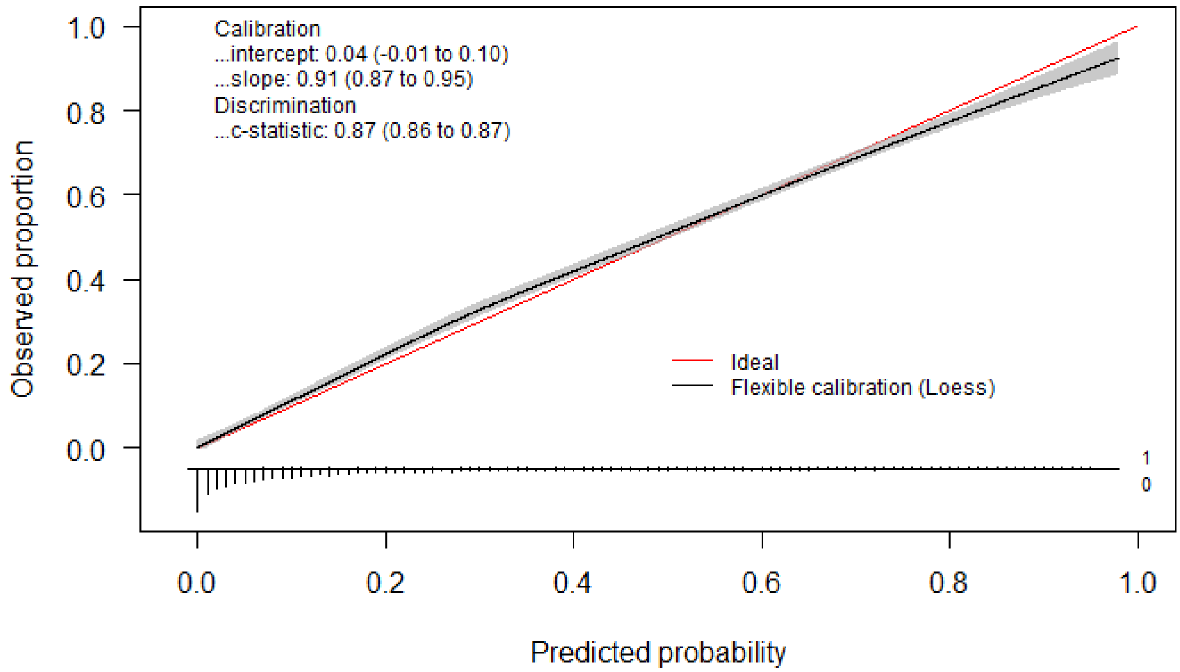


Female reduced model:

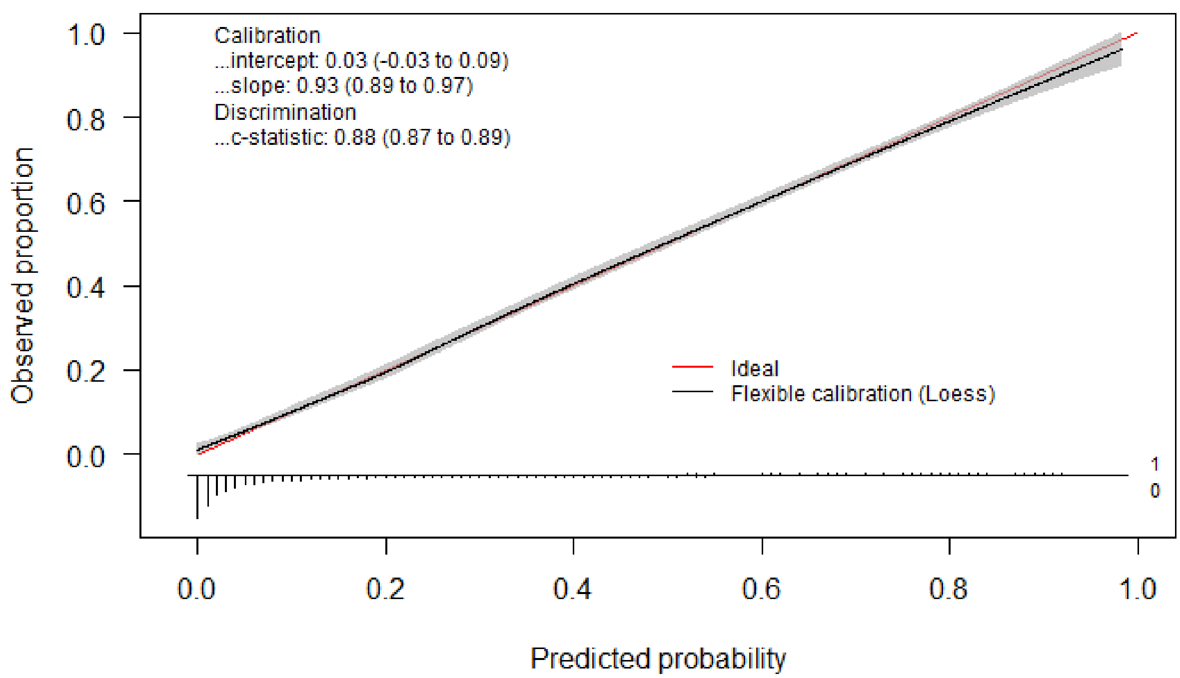


Calibration plots of models leaving skewness:

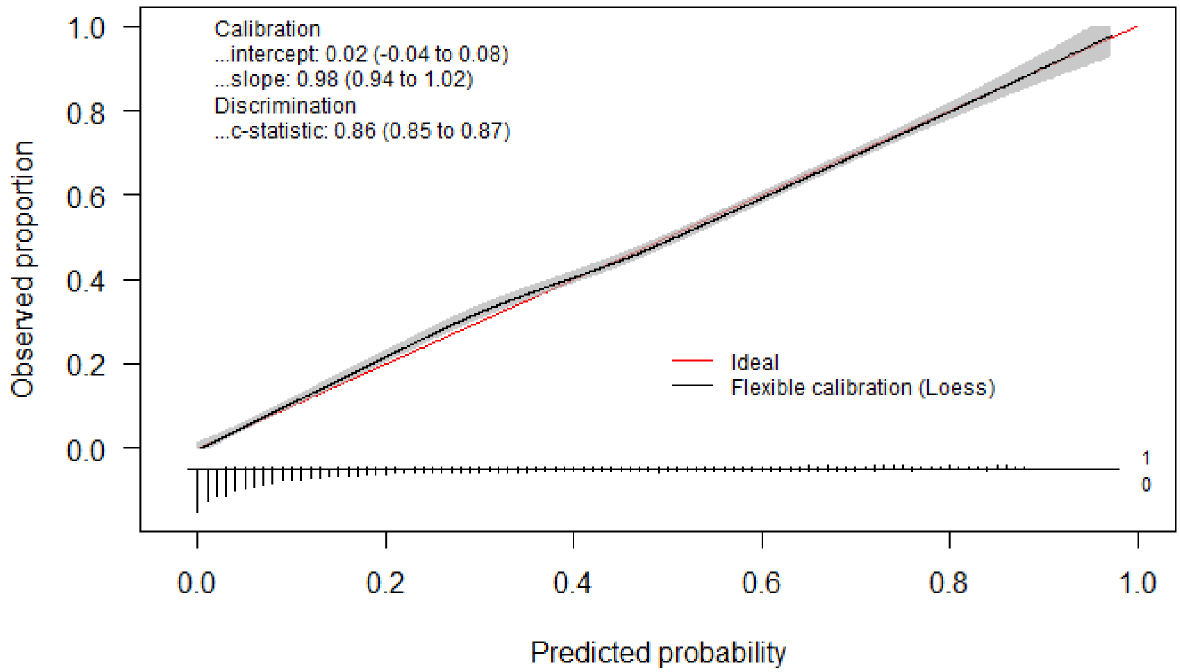
Male full model:



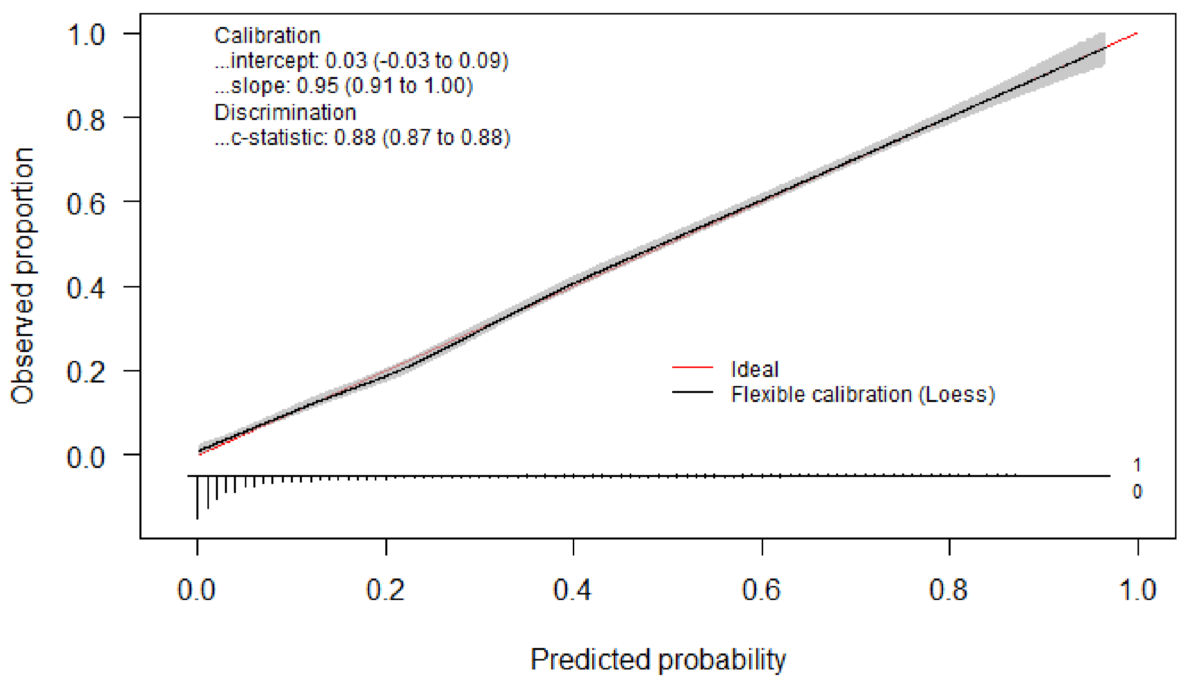
Female full model:



Male reduced model:

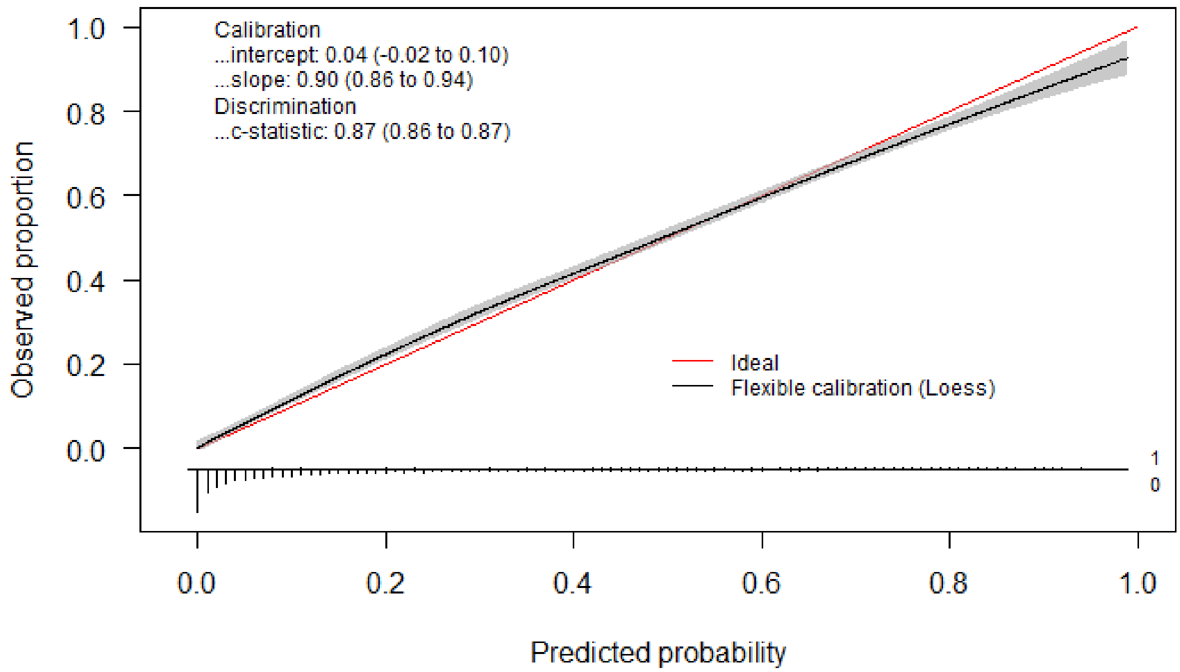


Female reduced model:

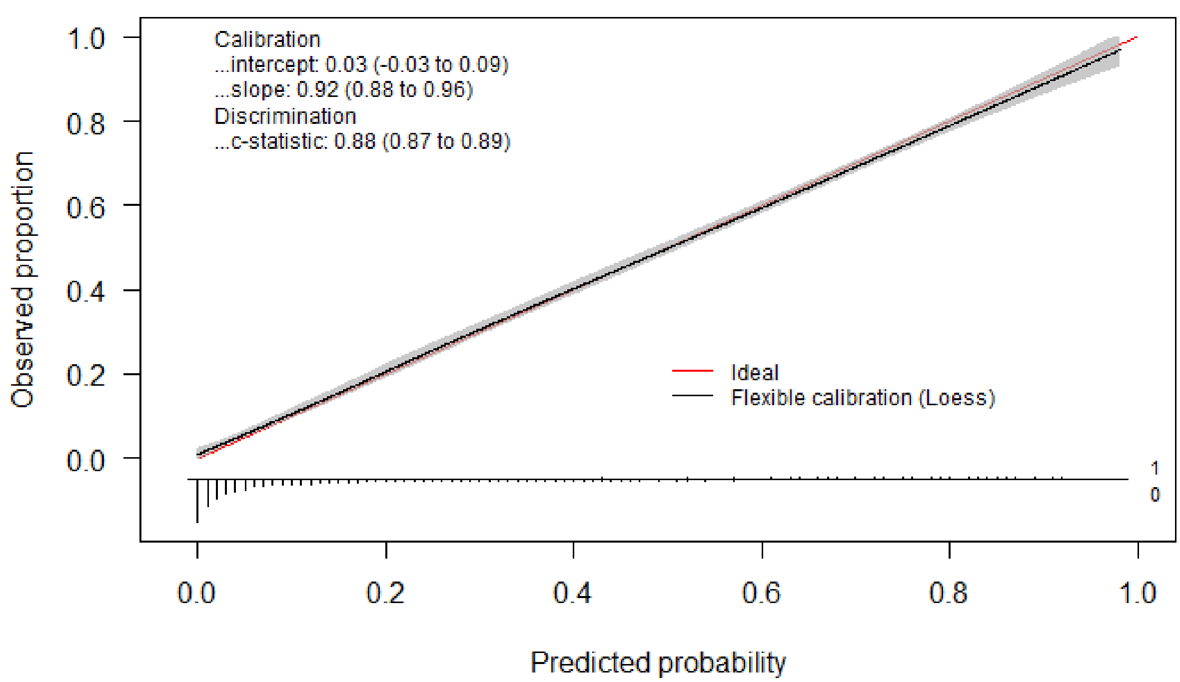


Calibration plots of models with waist-to-height ratio and its interactions re-included:

Male full model:

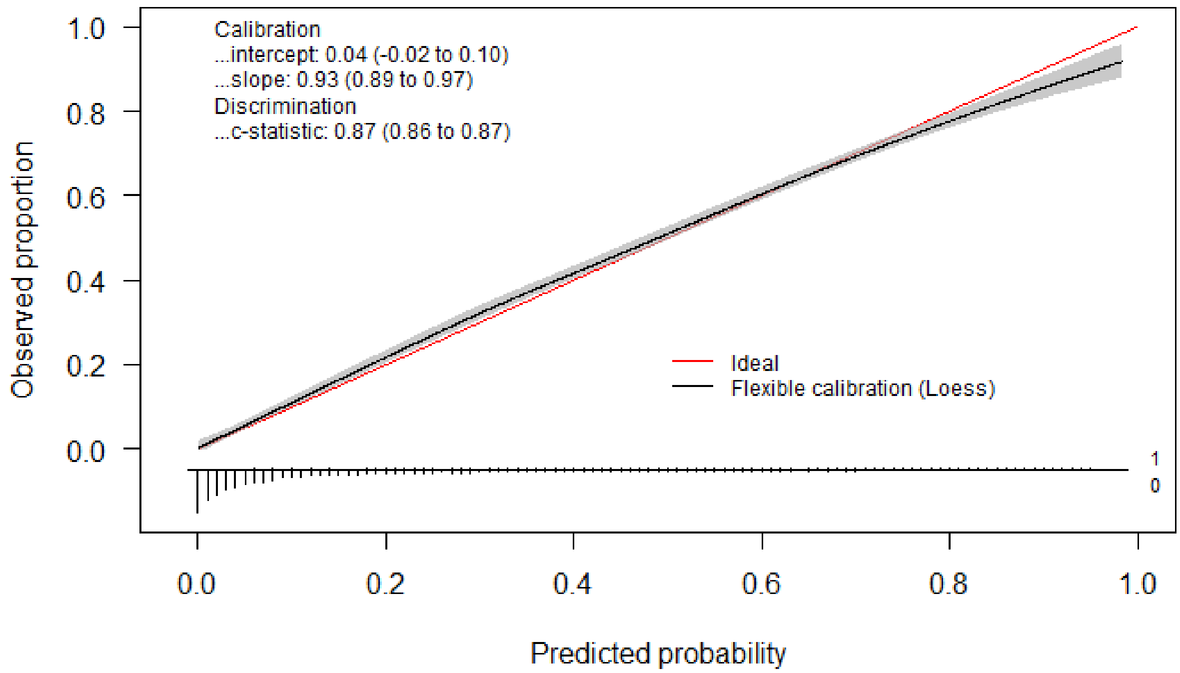


Female full model:

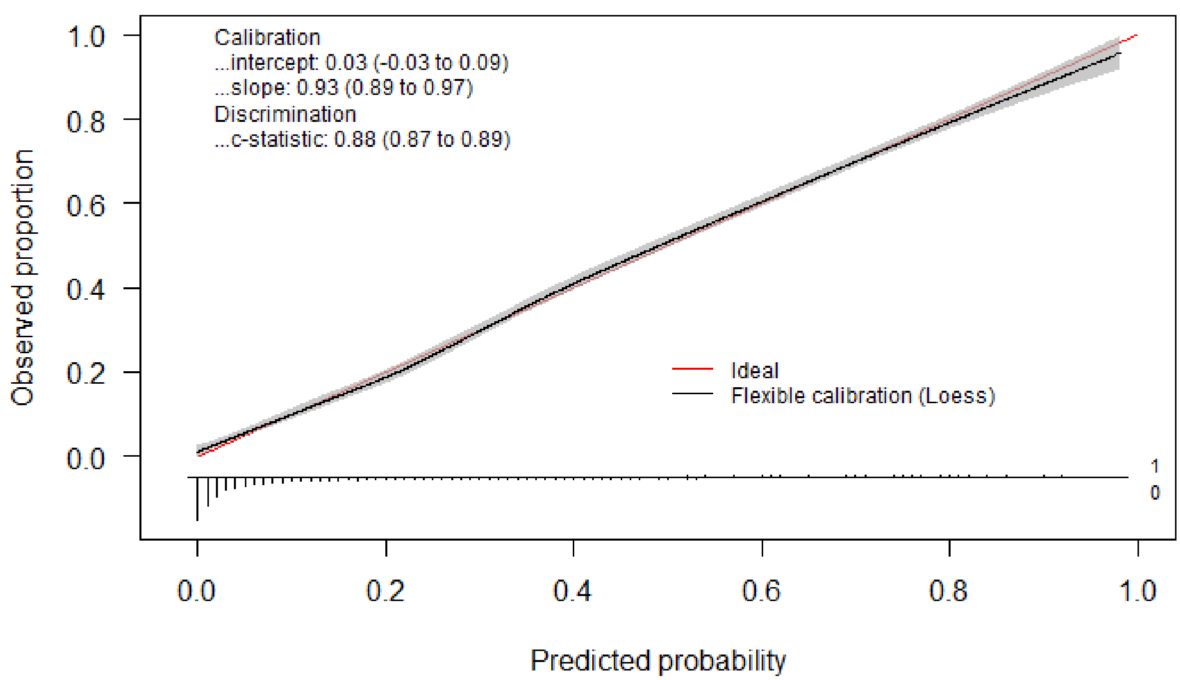


Calibration plots of models with linear interactions:

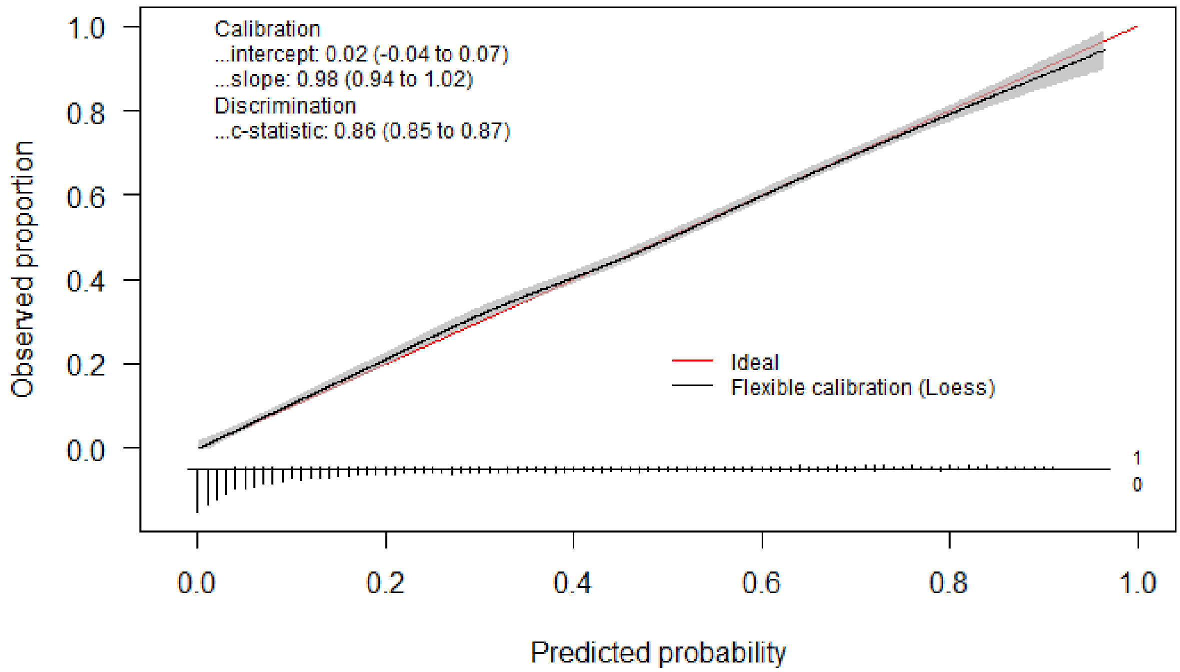
Male full model:



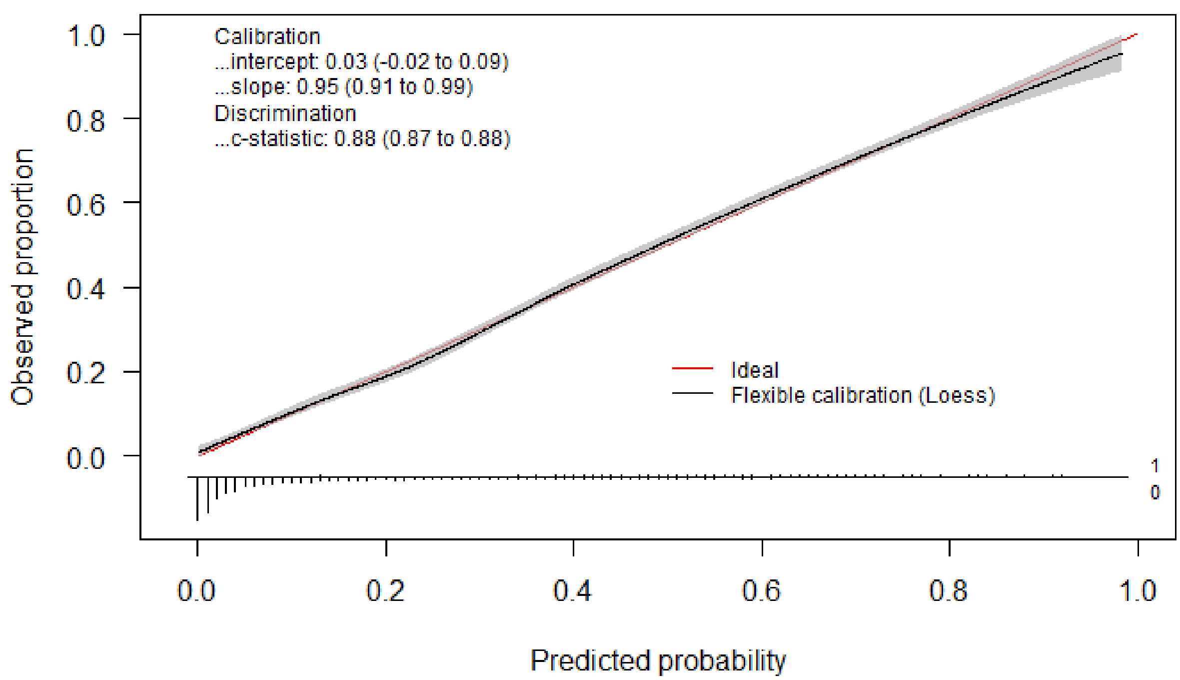
Female full model:



Male reduced model:

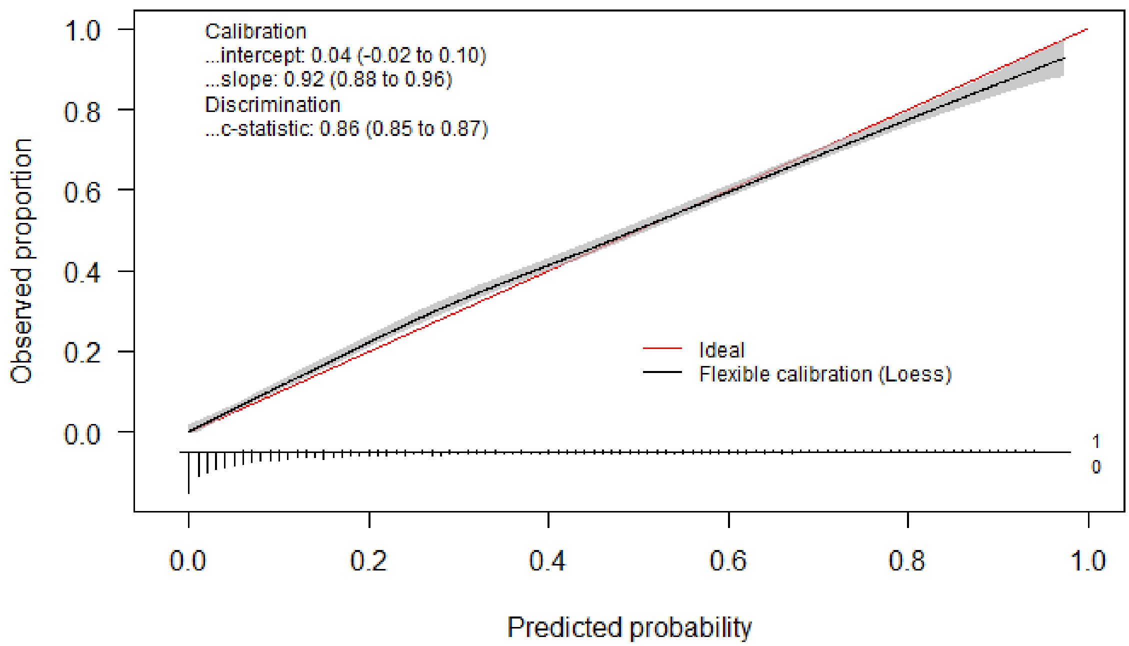


Female reduced model:

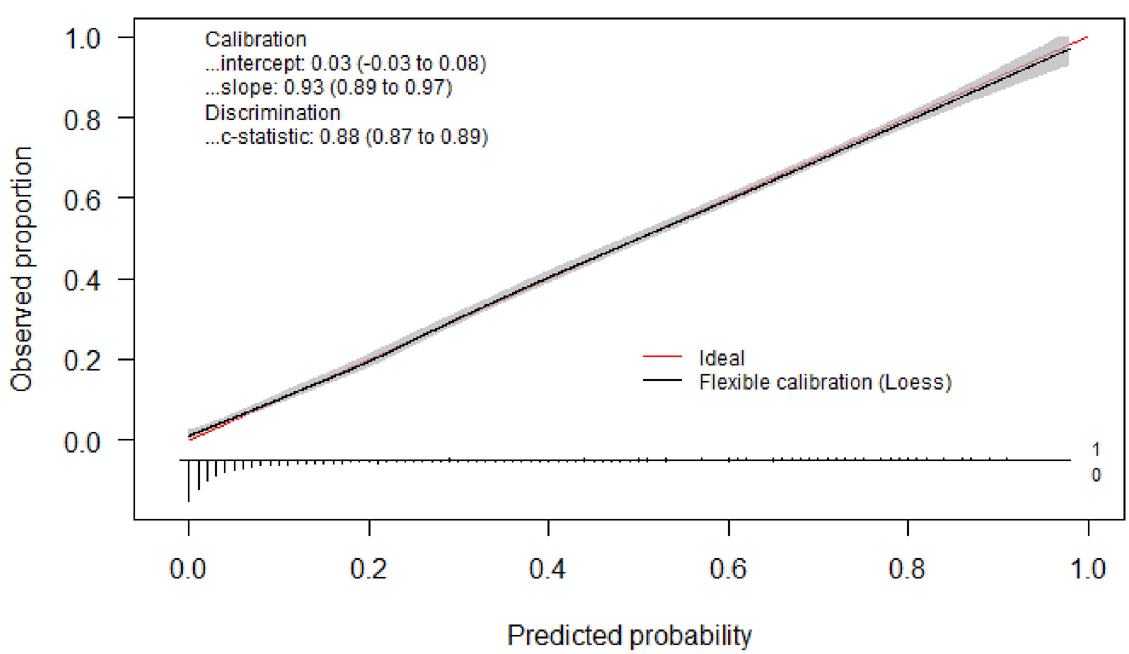


Calibration plots of models for hypertension ascertained with unadjusted blood pressures:

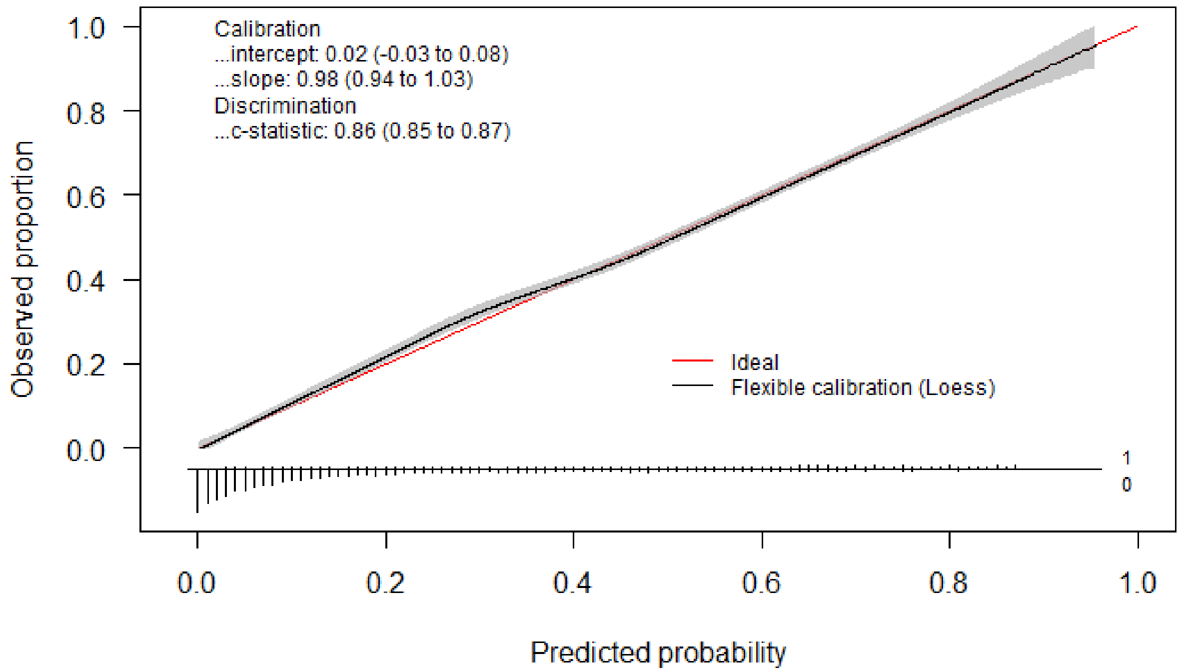
Male full model:



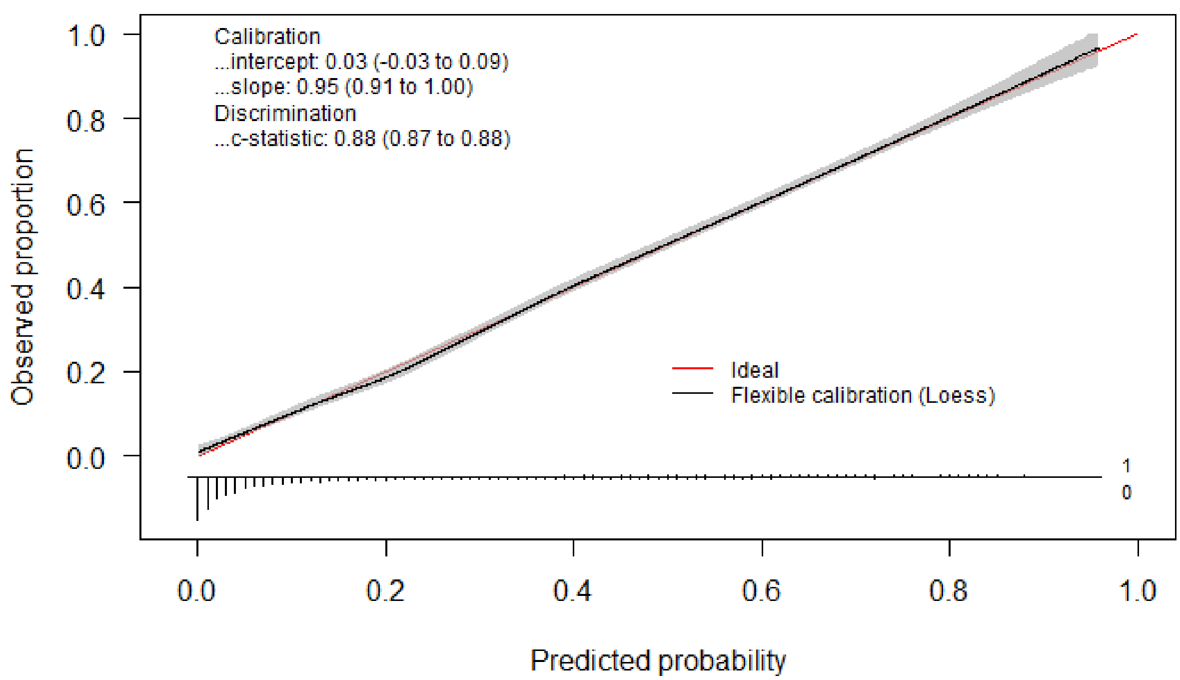
Female full model:



Male reduced model:

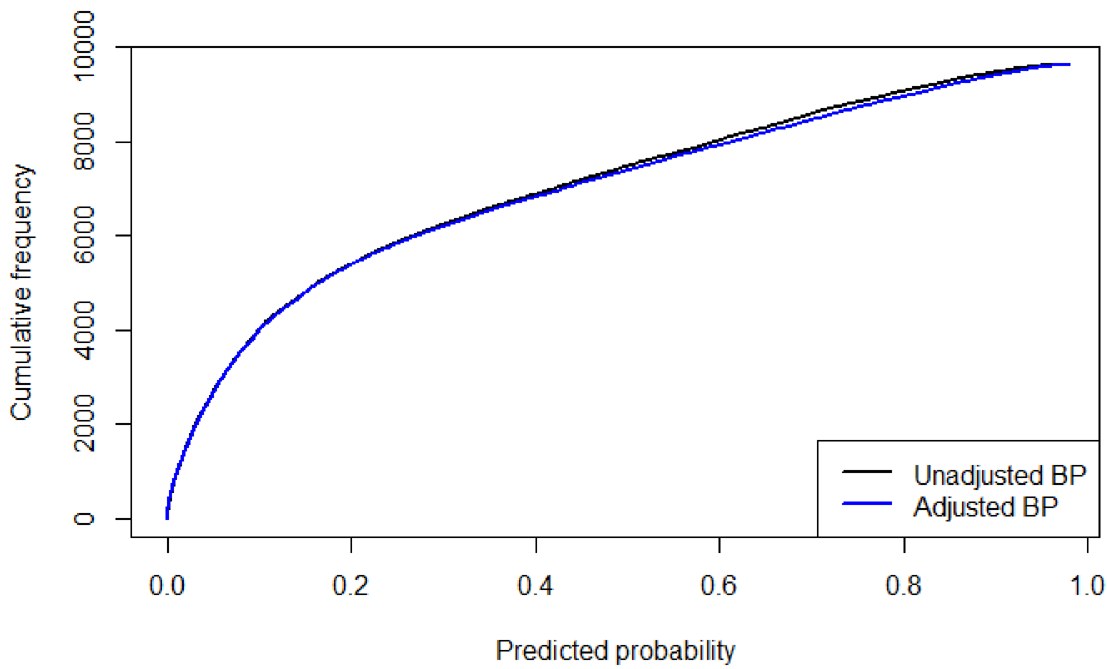


Female reduced model:

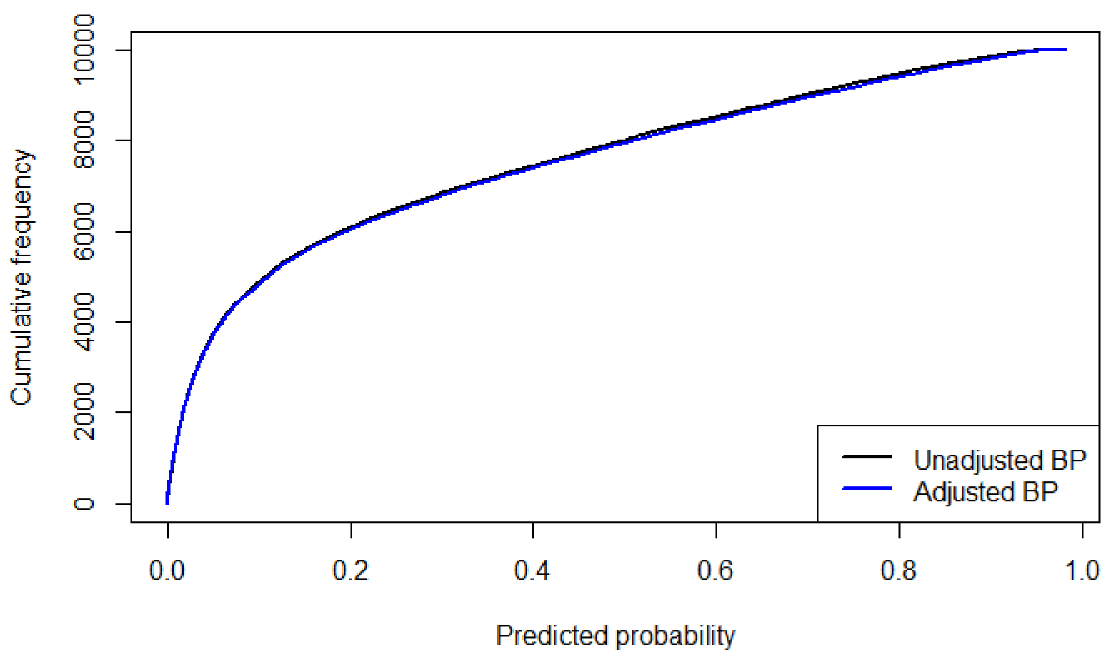


Cumulative predicted probability curves of models for hypertension ascertained with unadjusted blood pressures:

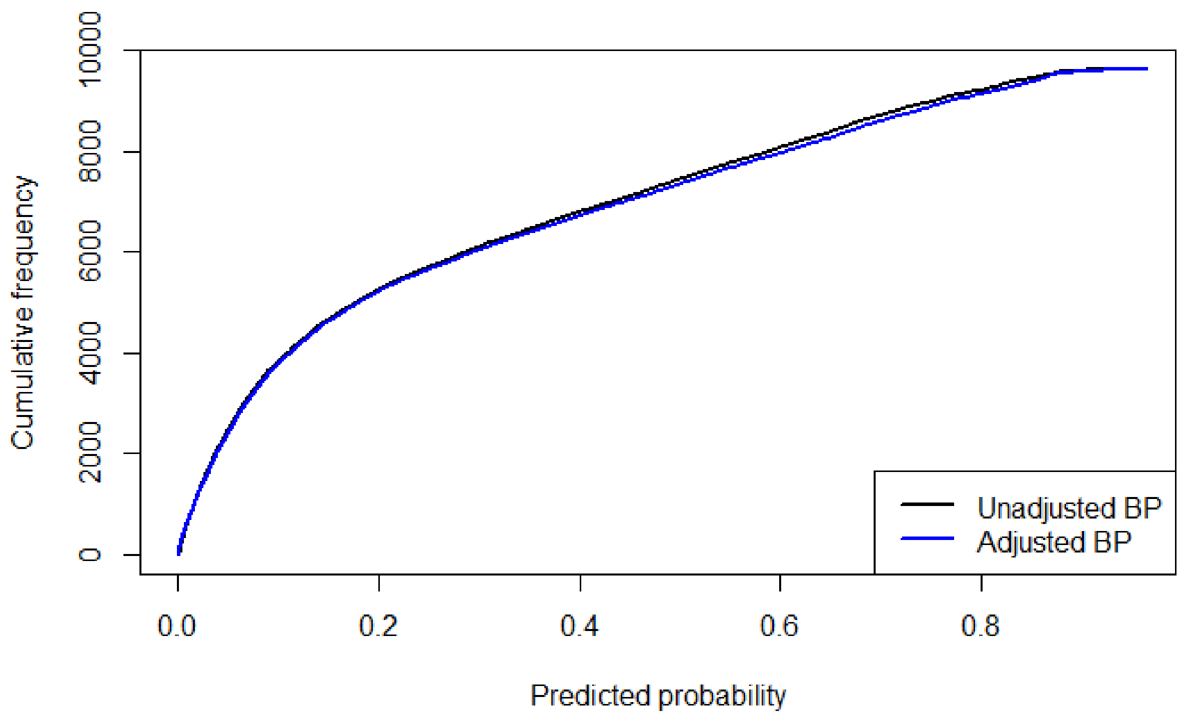
Male full model:



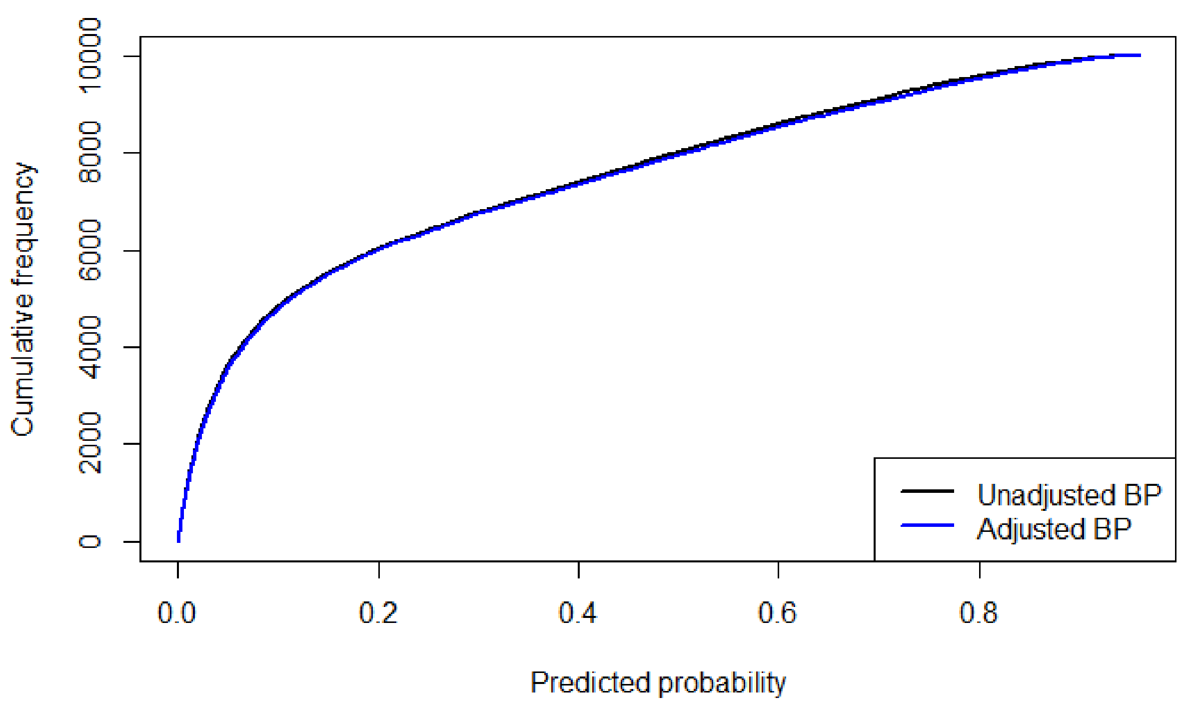
Female full model:



Male reduced model:

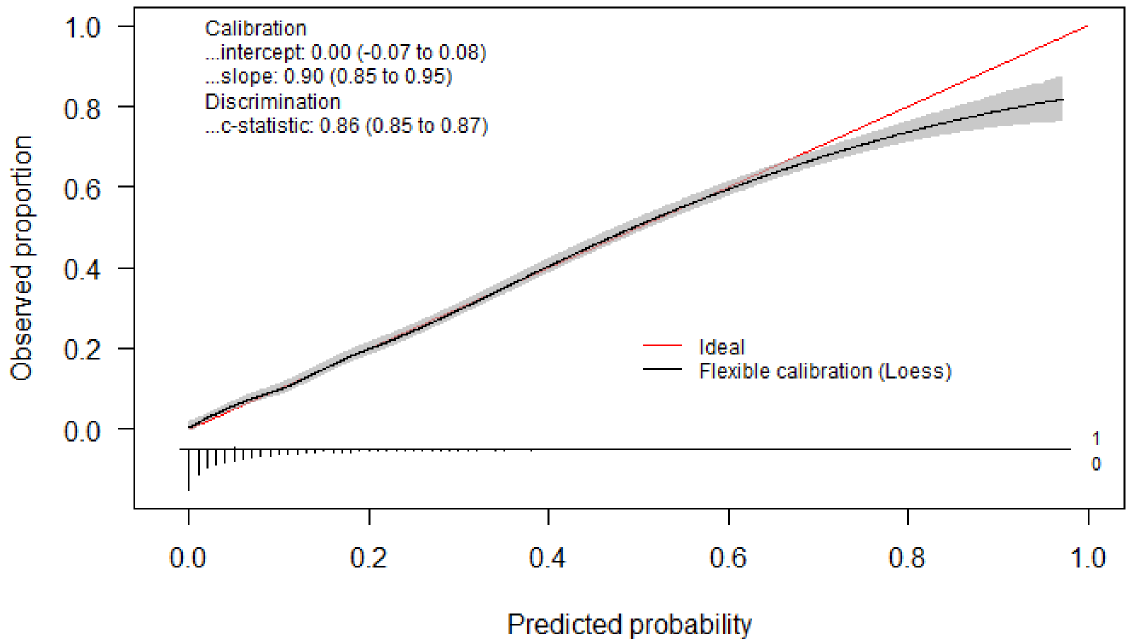


Female reduced model:

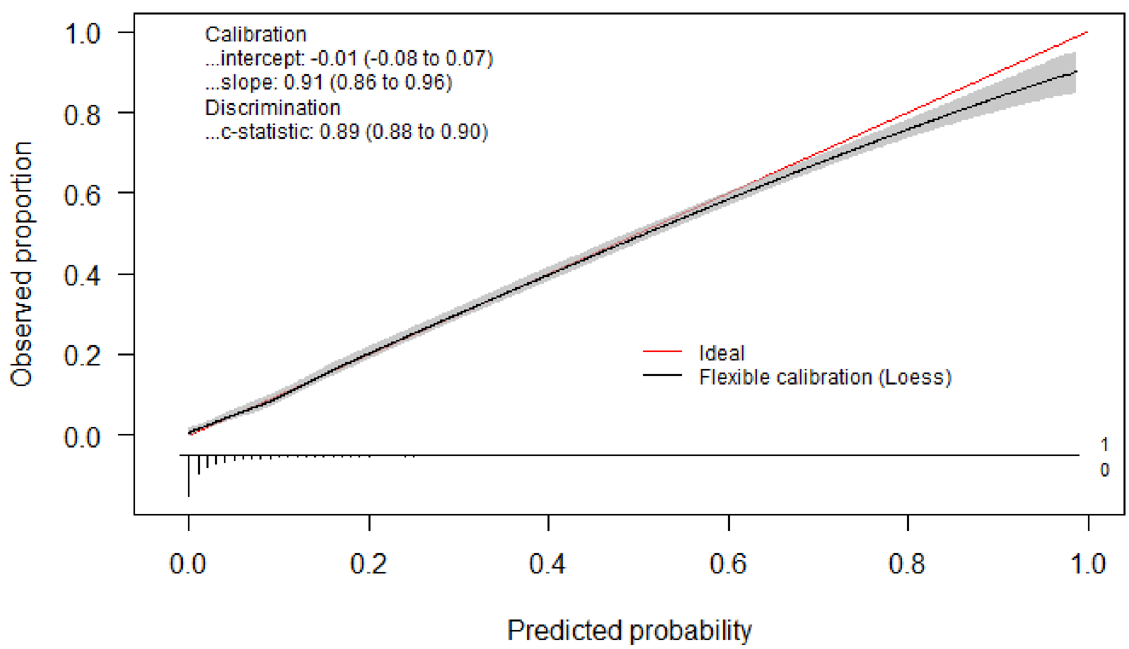


Calibration plots of models excluding respondents with controlled hypertension:

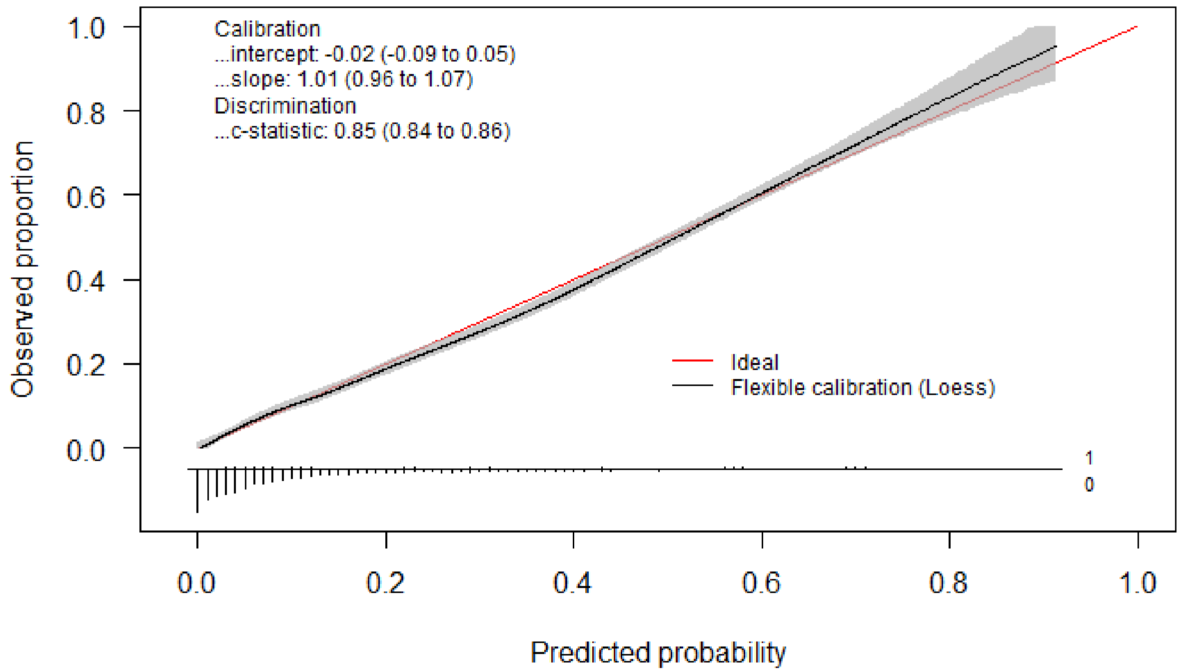
Male full model:



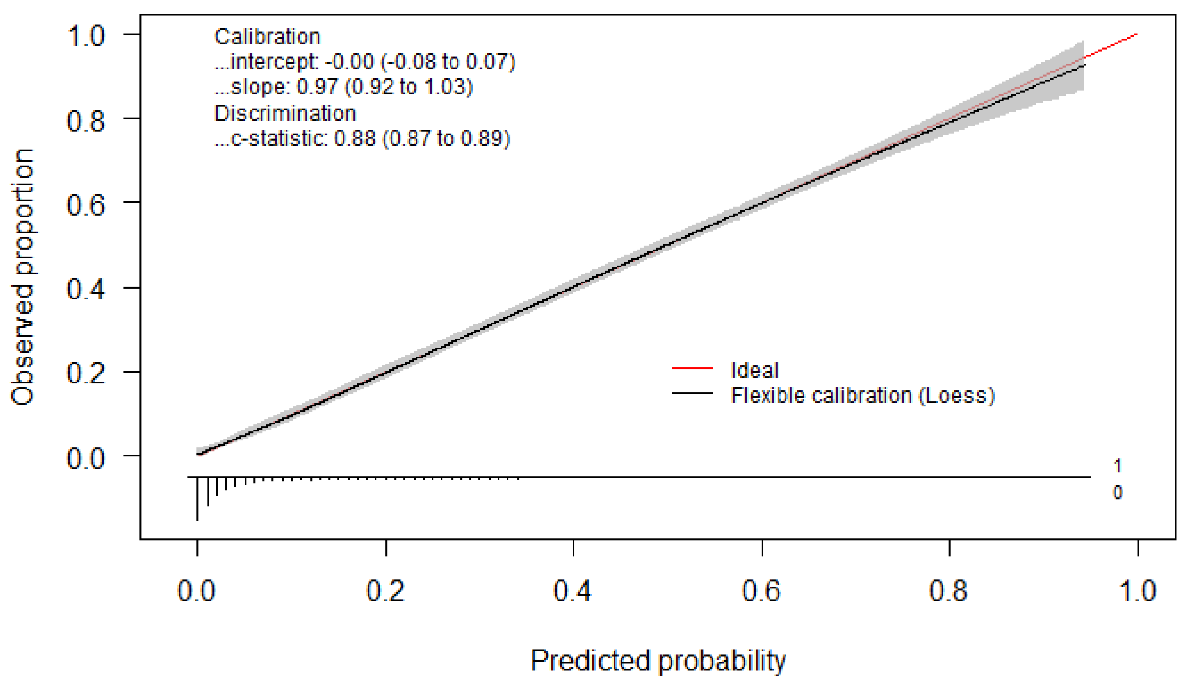
Female full model:



Male reduced model:

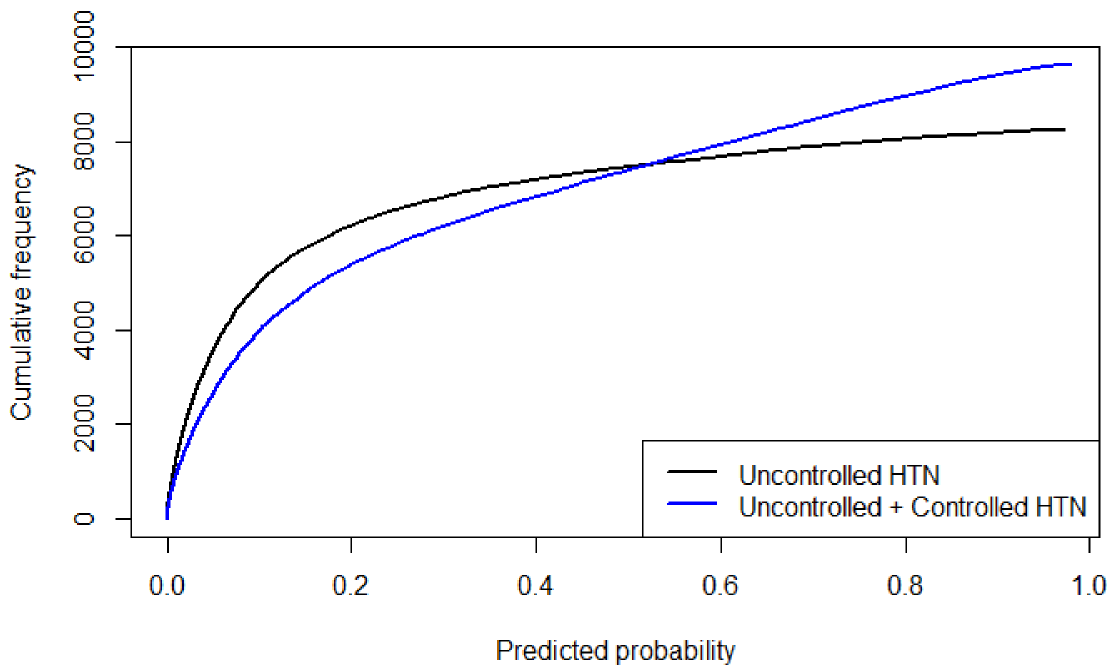


Female reduced model:

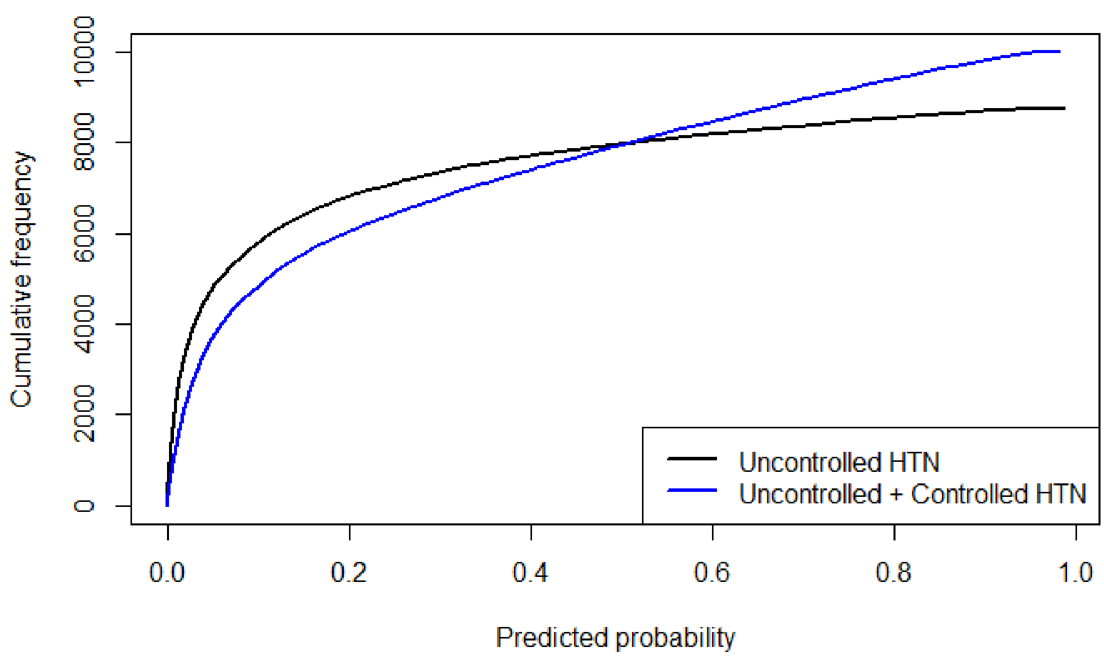


Cumulative predicted probability curves of models excluding respondents with controlled hypertension:

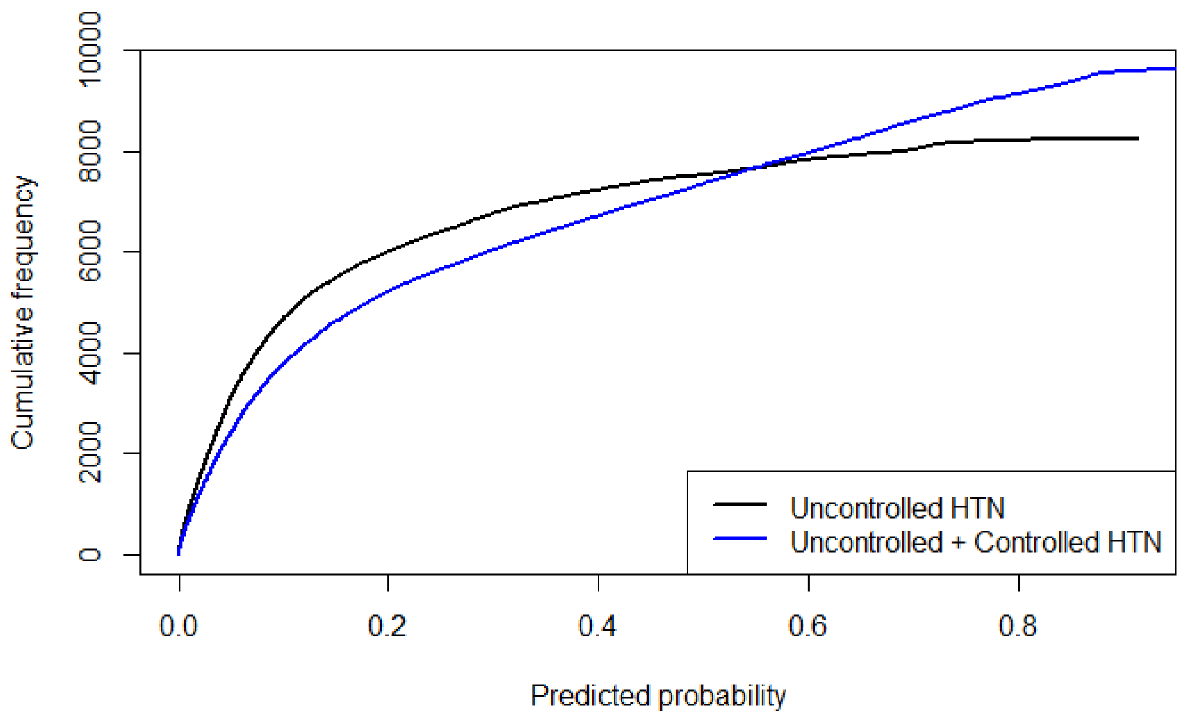
Male full model:



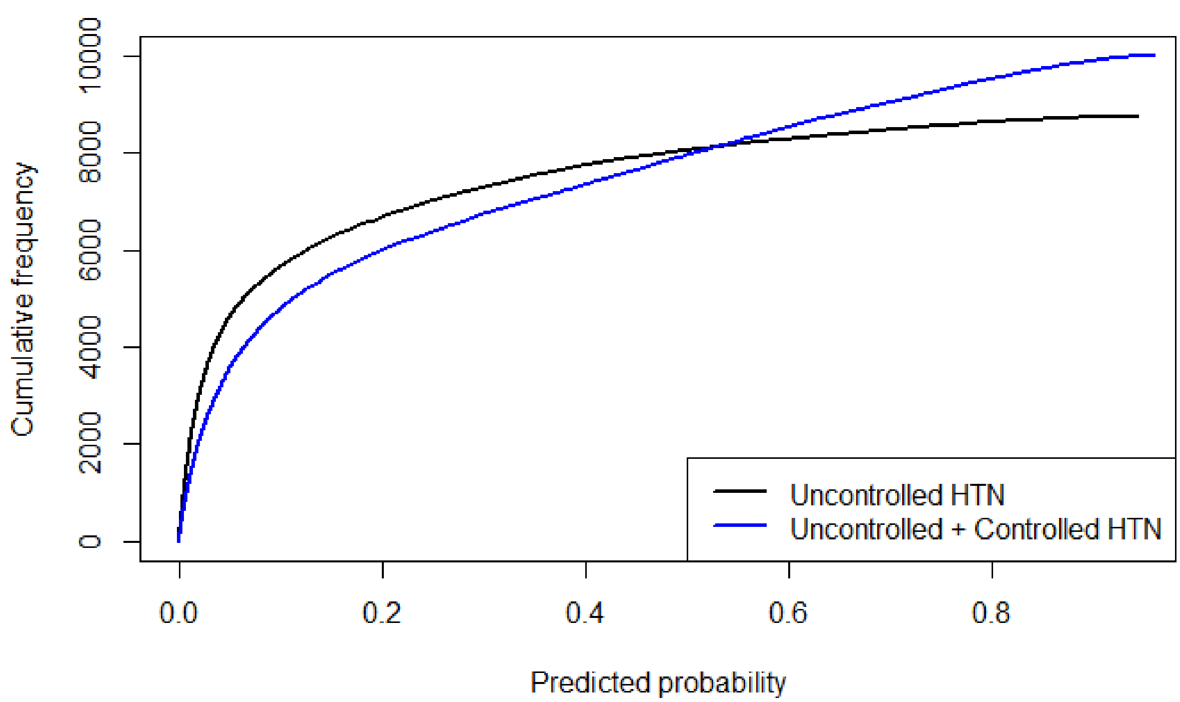
Female full model:



Male reduced model:



Female reduced model:



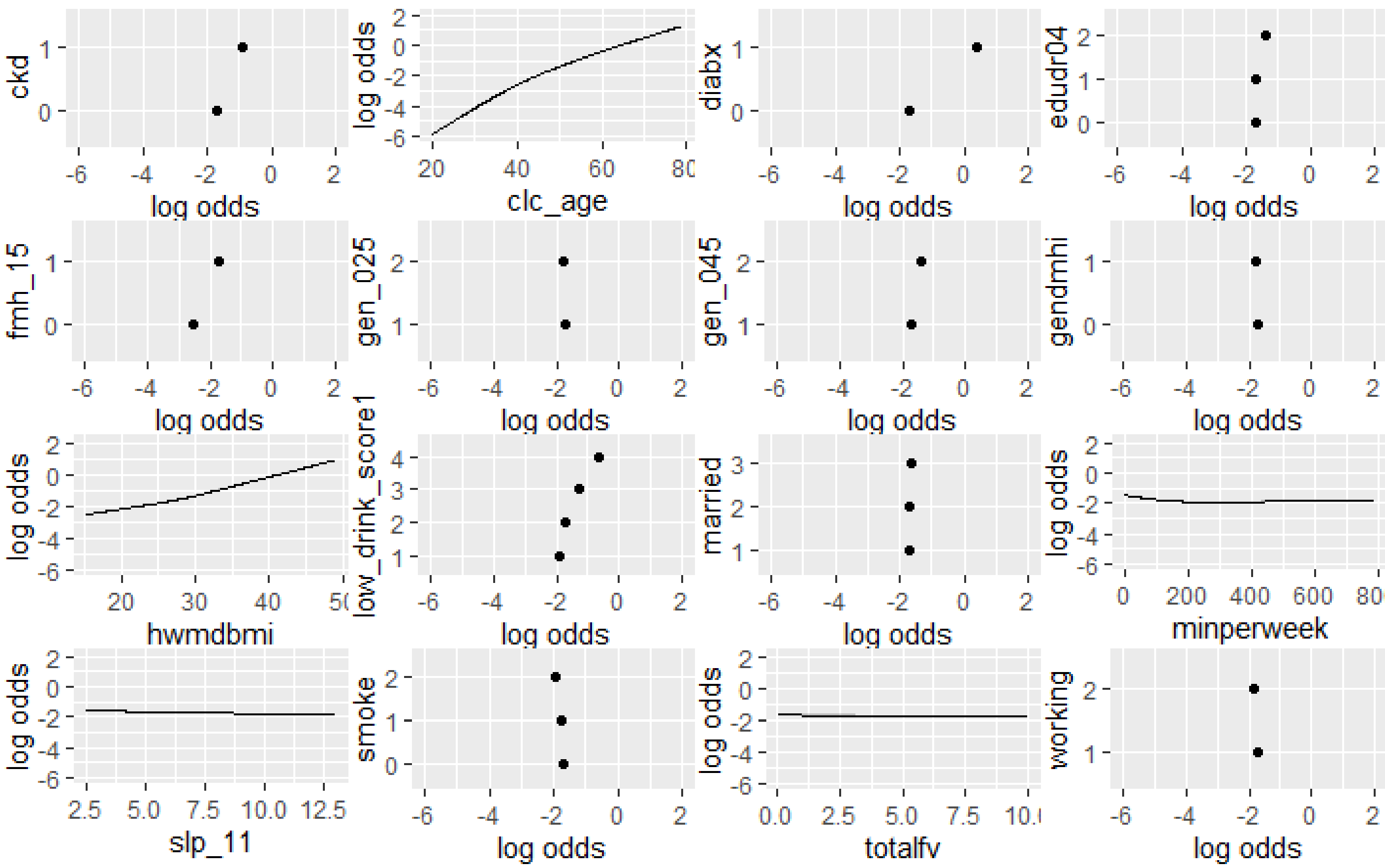
Appendix 10 – Partial effects plots

Legend

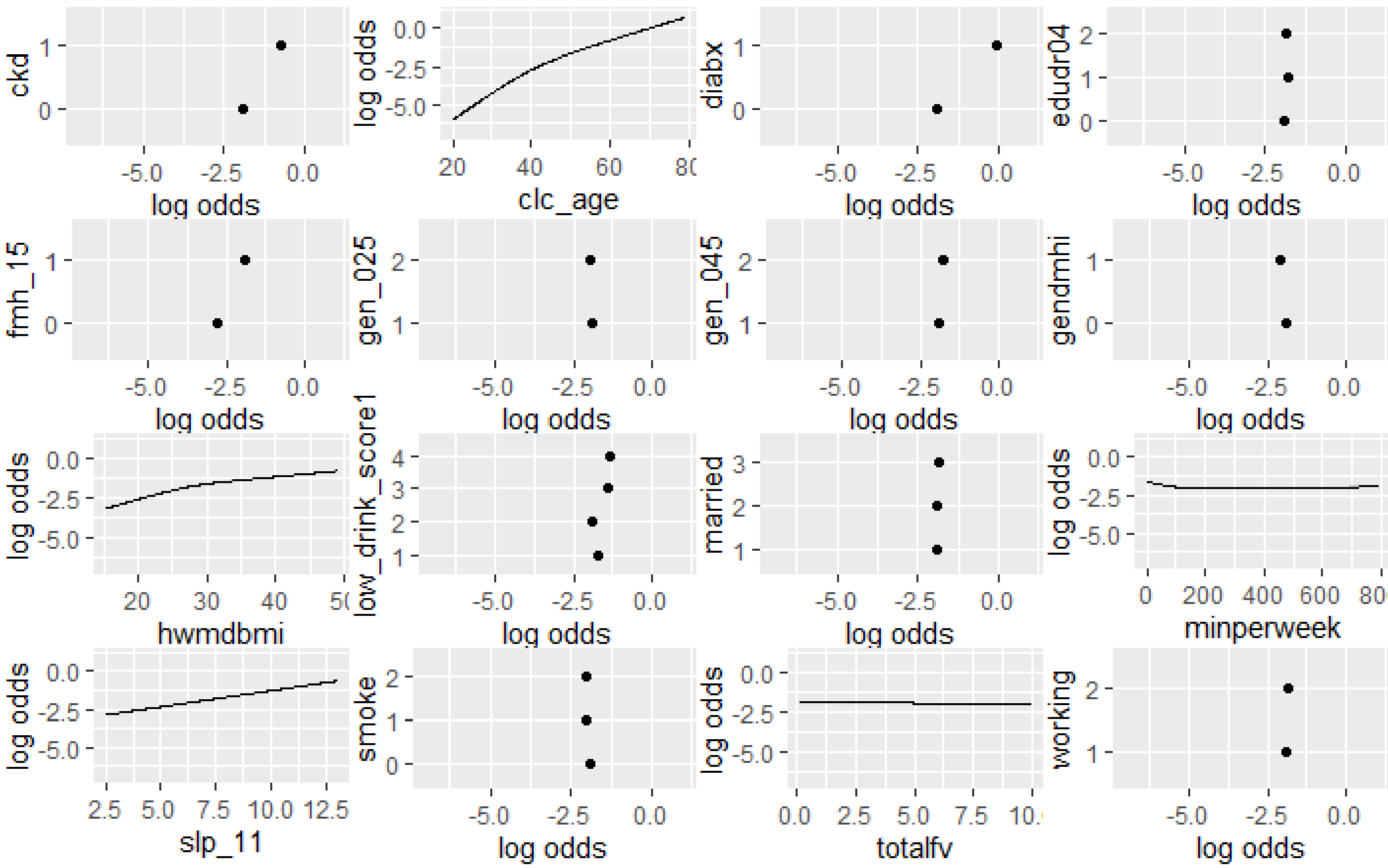
Variable Label (Variable on Plot)	Categories
Chronic kidney disease (ckd)	1 – Yes 0 – No[1]
Age (clc_age)	N/A
Diabetes (diabx)	1 – Yes 0 – No[1]
Highest education level (edudr04)	2 – Less than secondary school graduation 1 – Secondary school graduation 0 – Post-secondary school graduation[1]
Hypertension family history (fmh_15)	1 – Yes 0 – No[1]
Self-perceived stress (gen_025)	1 – Not at all to a bit 2 – Quite a bit or extremely
Sense of belonging (gen_045)	1 – Strong 2 – Weak
Self-rated mental health (gendmhi)	1 – Poor or fair 0 – Good, very good, or excellent [1]
Body mass index (hwmdbmi)	N/A
Alcohol consumption (low_drink_score1)	1 – Never drinker 2 – Former drinker 3 – Light drinker 4 – Moderate to heavy drinker
Marital status (married)	1 – Married or common-law 2 – Widowed, separated, or divorced 3 – Single and never married
Physical activity minutes (minperweek)	N/A
Smoking status (smoke)	2 – Current smoker 1 – Former smoker 0 – Never smoker[1]
Sleep duration (slp_11)	N/A
Daily fruit and vegetable consumption (totalfv)	N/A
Working status (working)	1 – Has a job 2 – Does not have a job

[1] Reference category in model, hence 0 coding

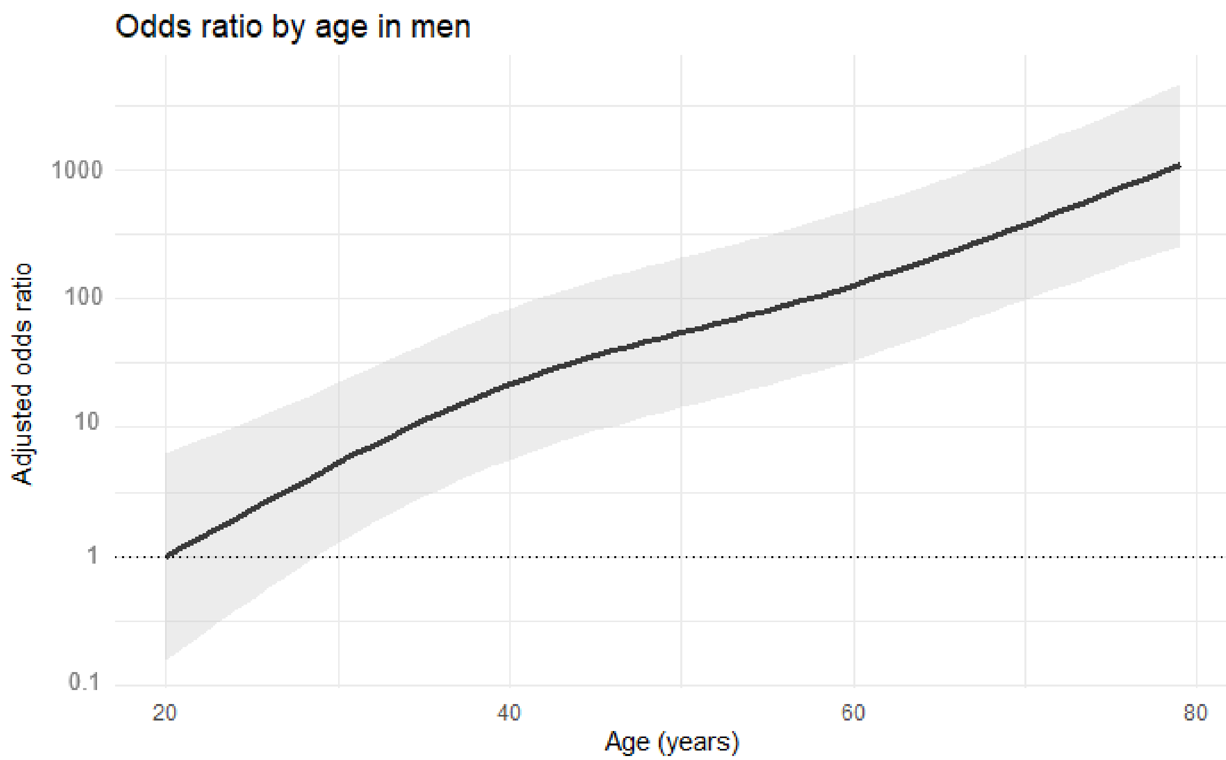
Male partial effects plots:

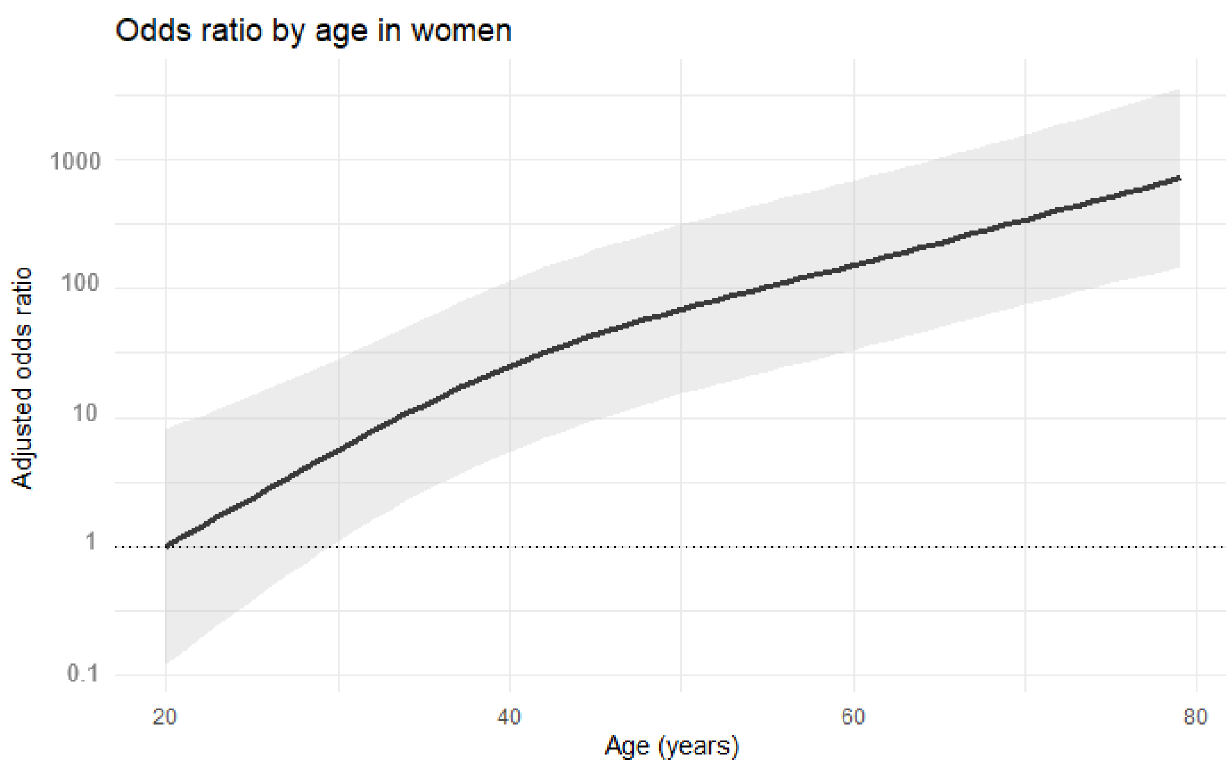


Female partial effects plots:

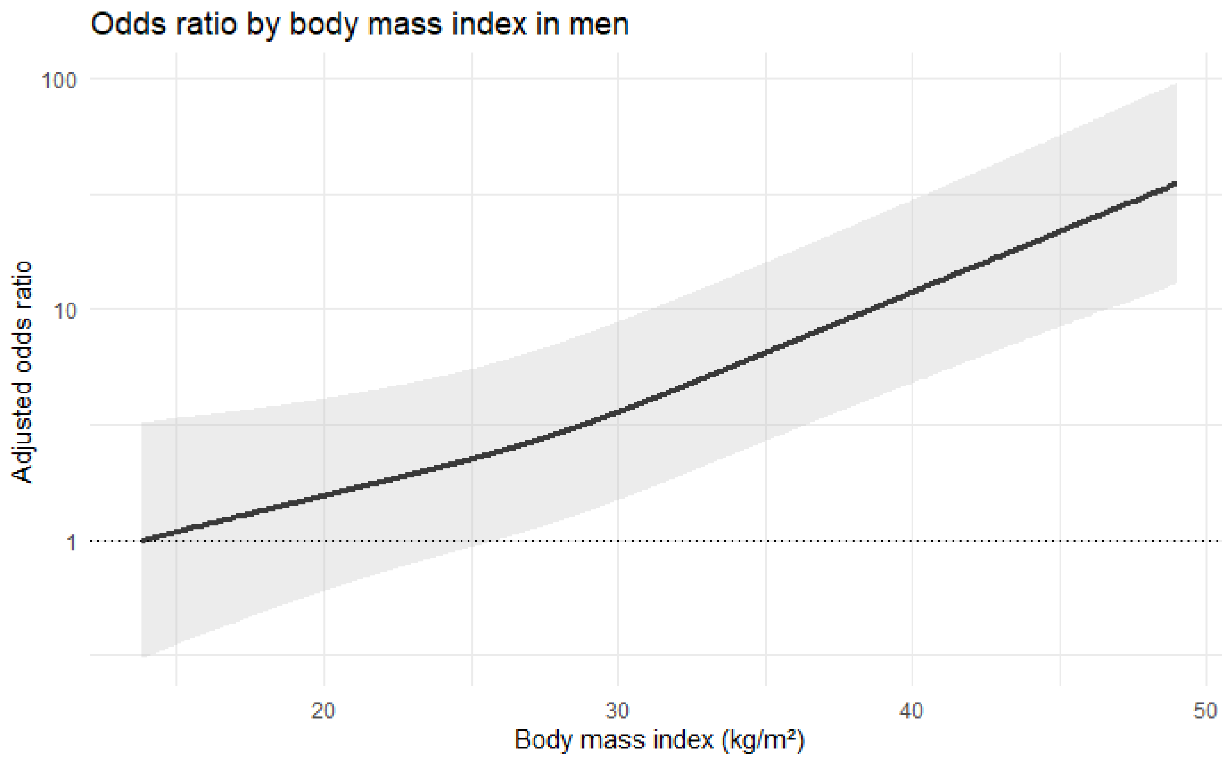


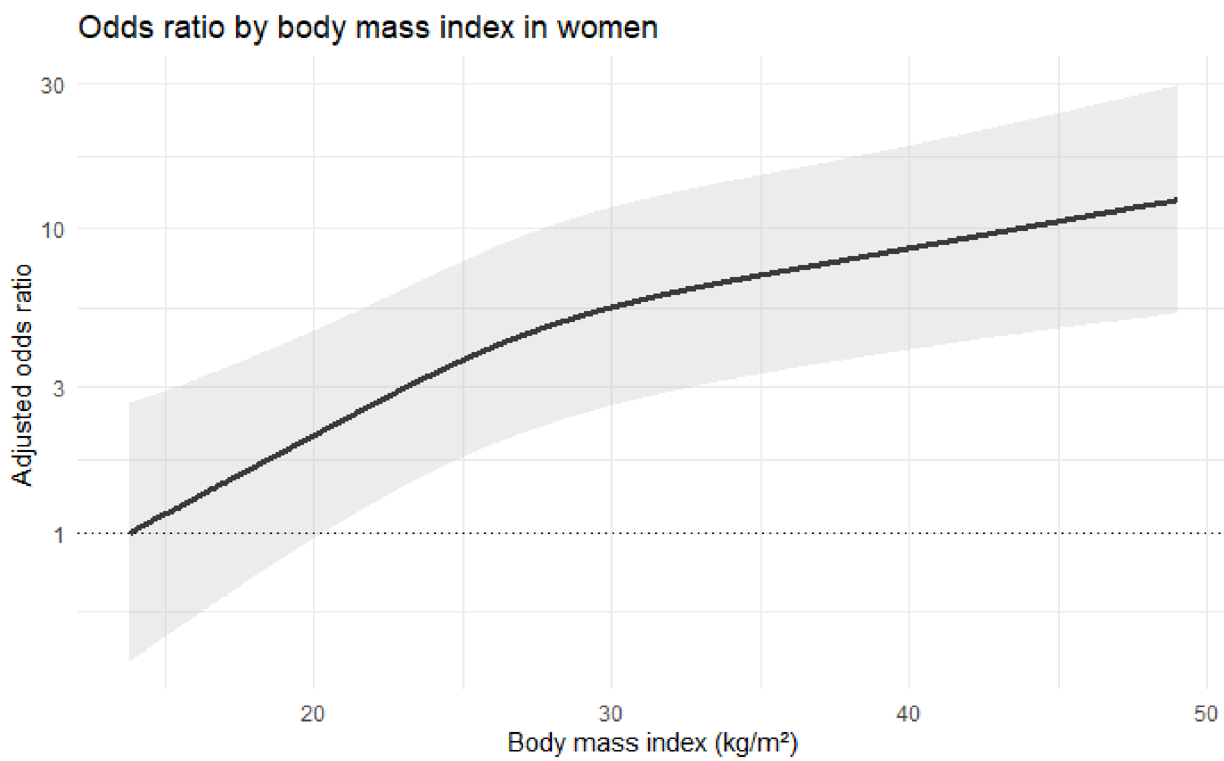
Appendix 11 – Model-adjusted odds ratio plots





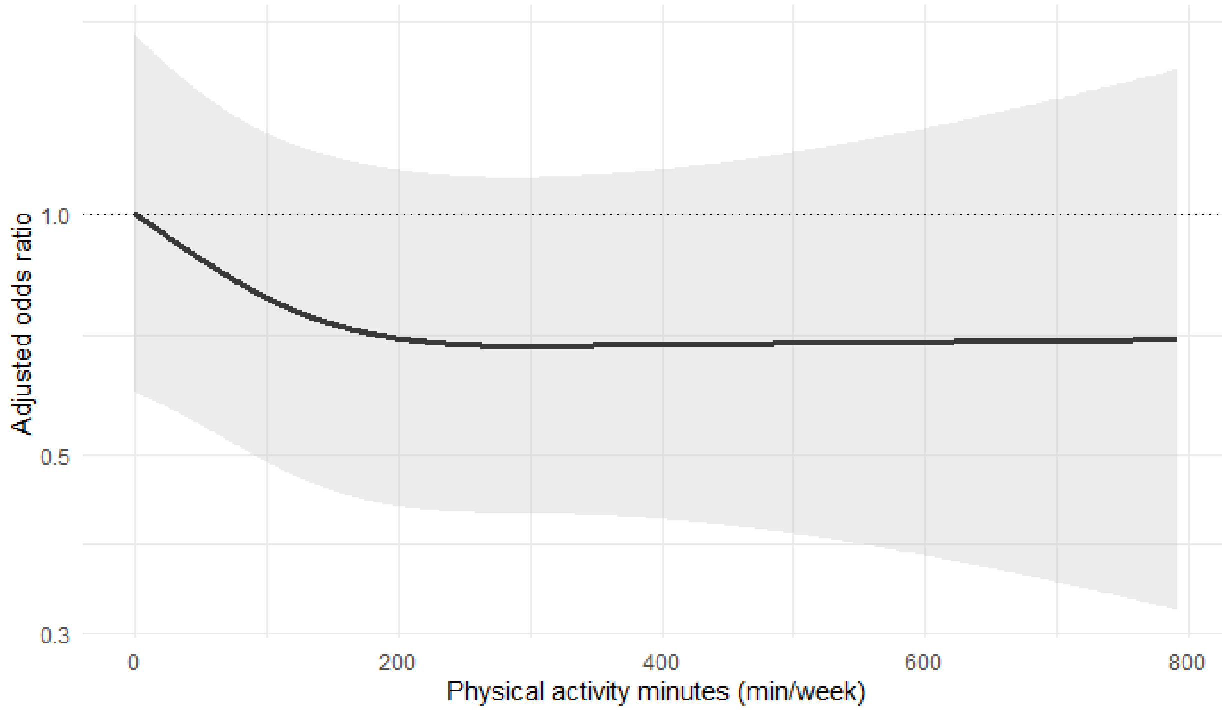
Reference: Age = 20 years



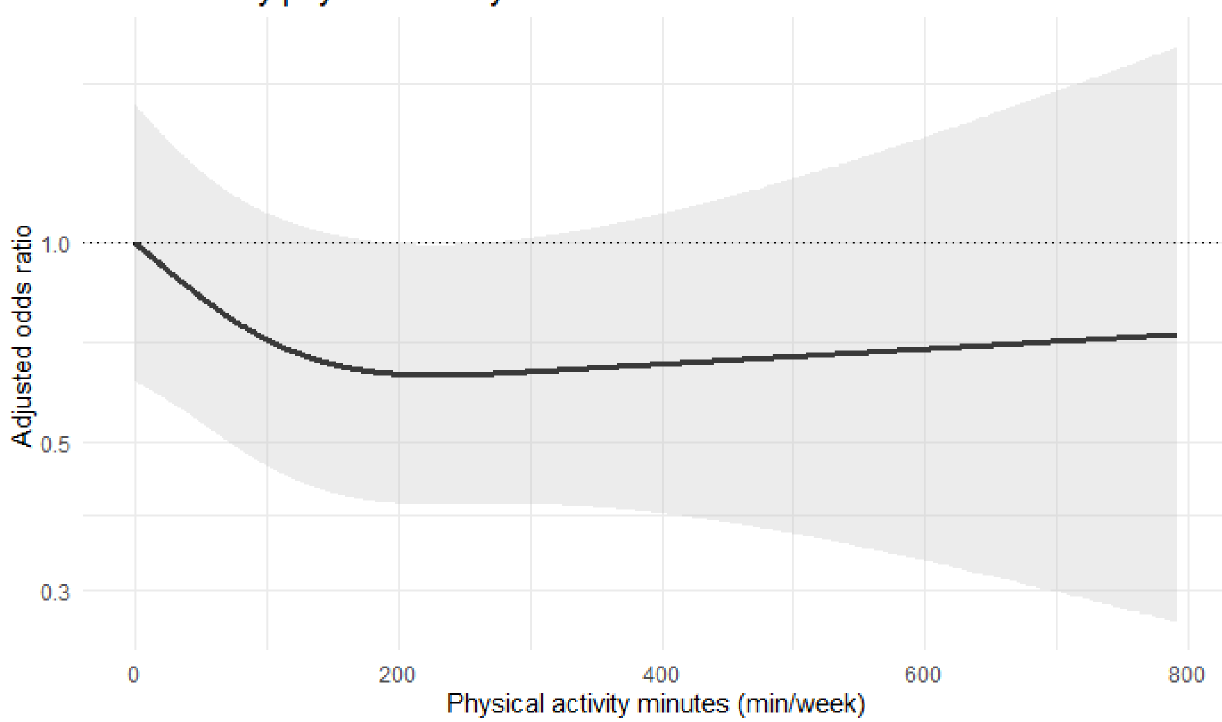


Reference: Body mass index = 13.83 kg/m^2 in men 14.90 kg/m^2 in women

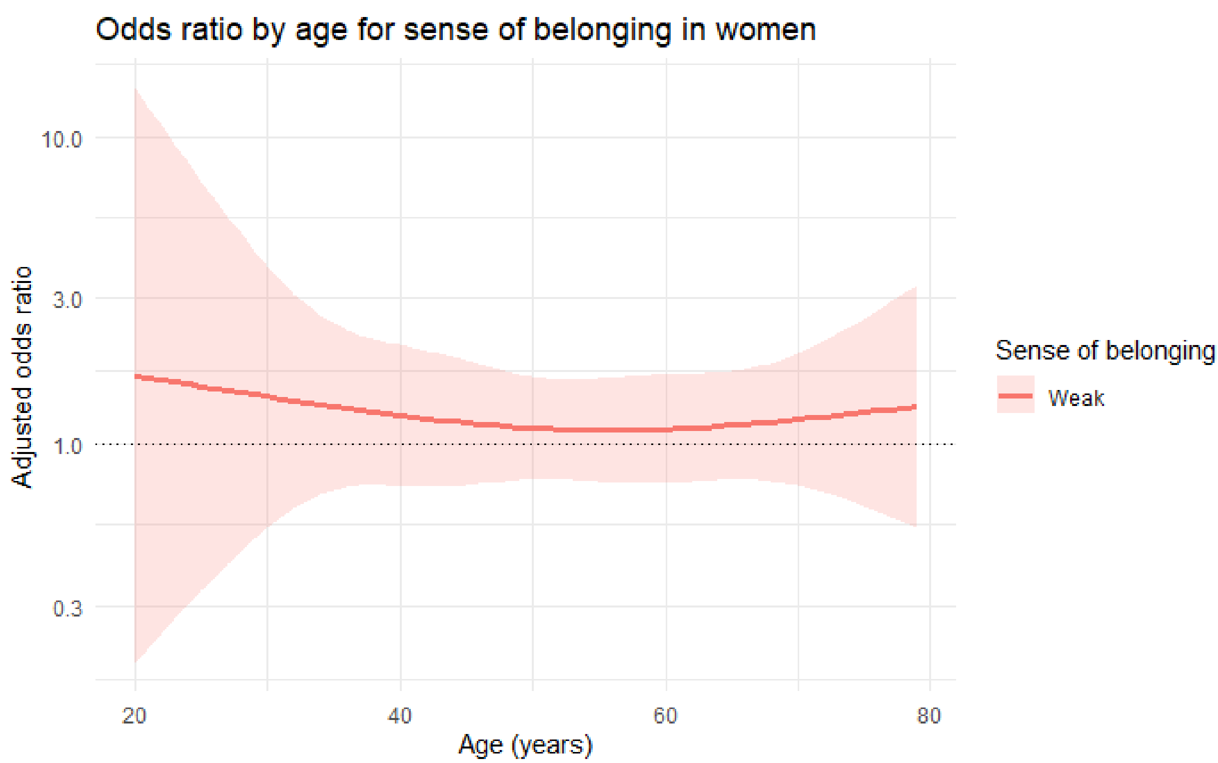
Odds ratio by physical activity minutes in men



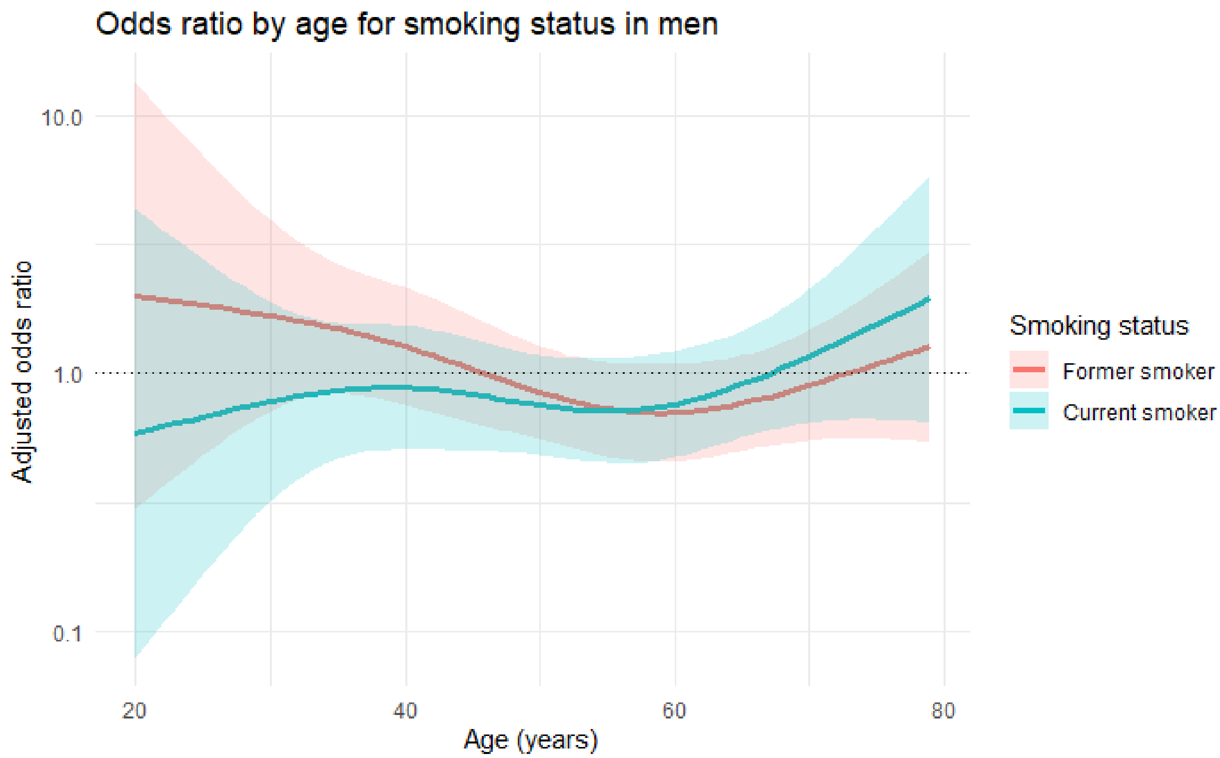
Odds ratio by physical activity minutes in women

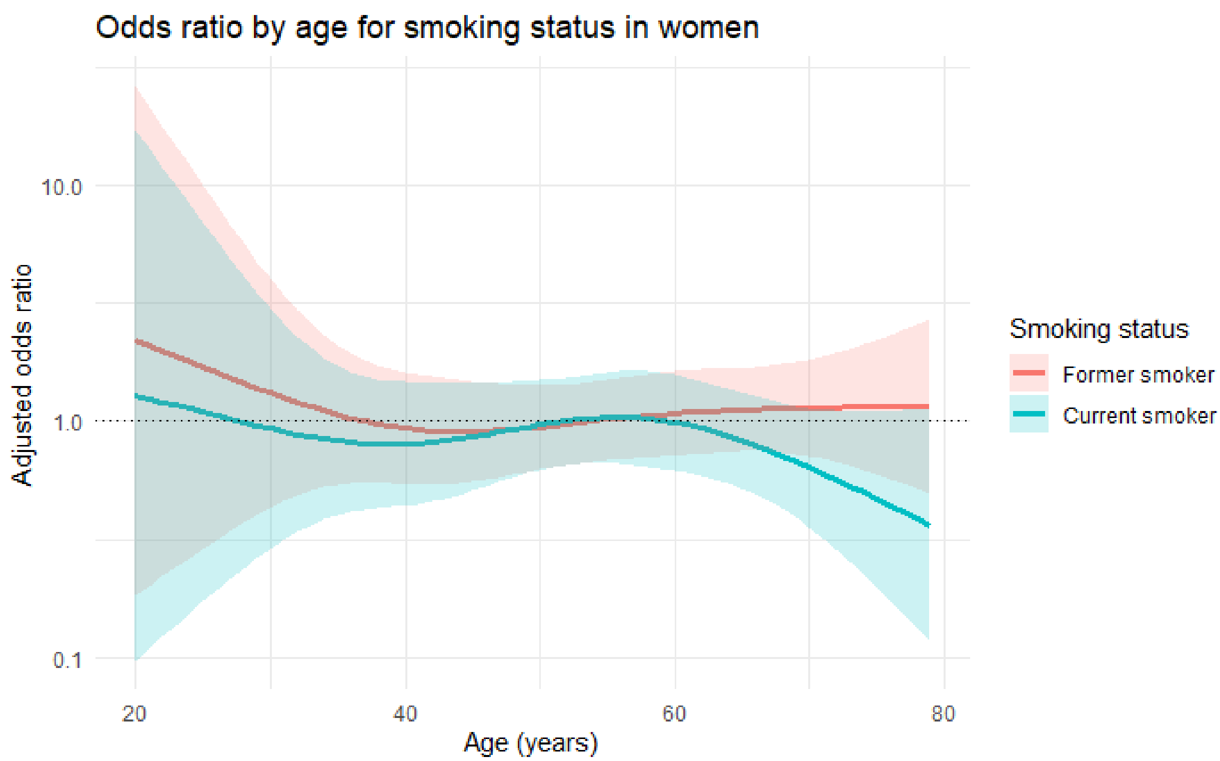


Reference = 0 min/week

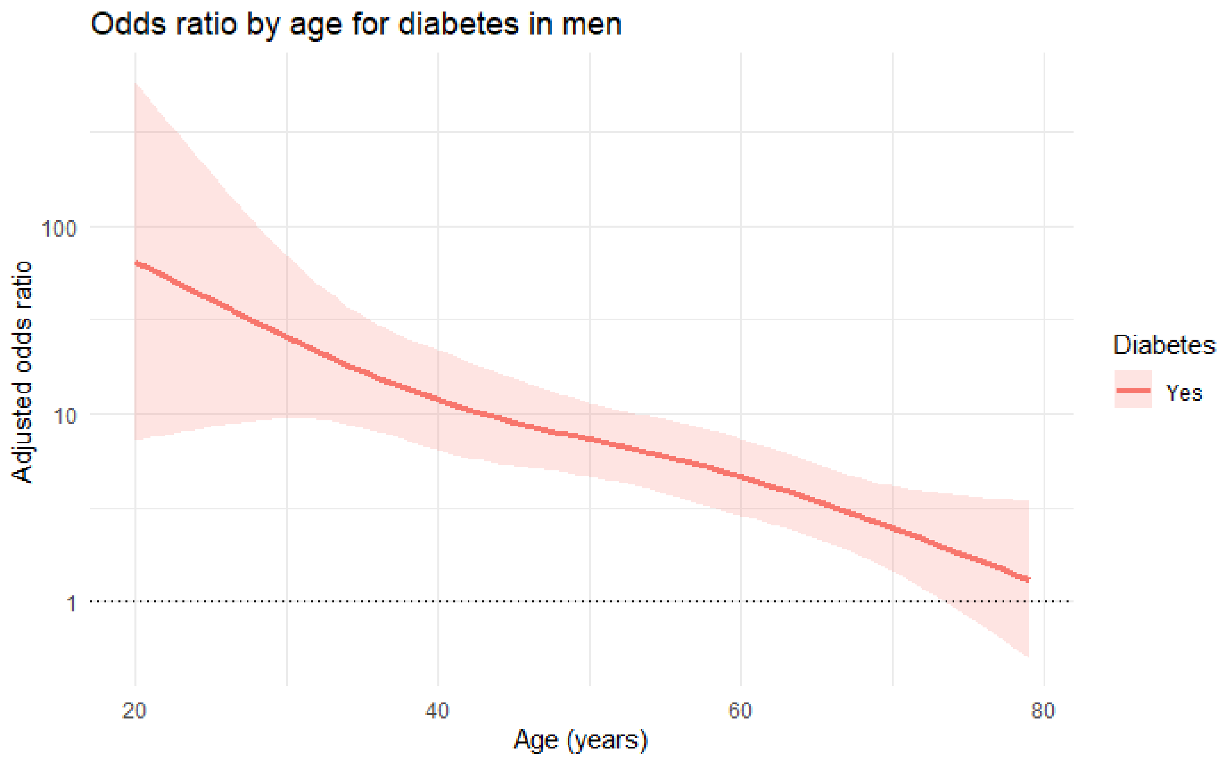


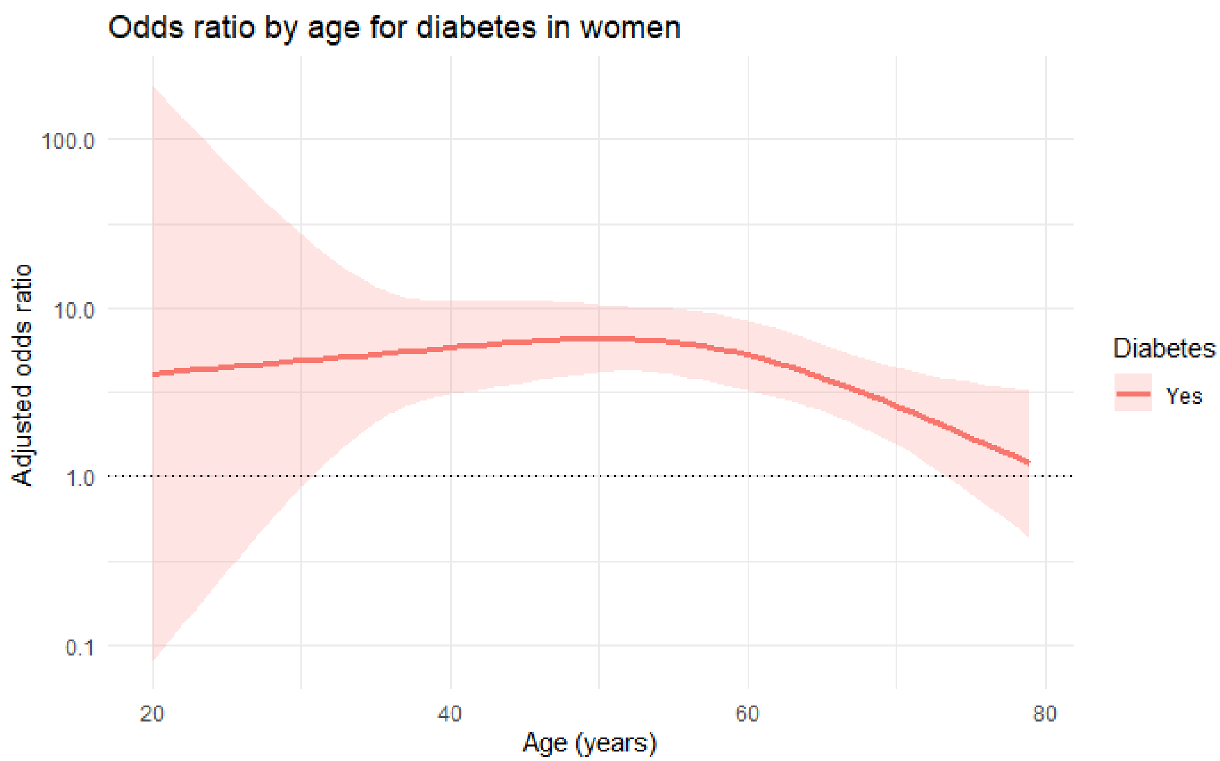
Reference = Strong sense of belonging



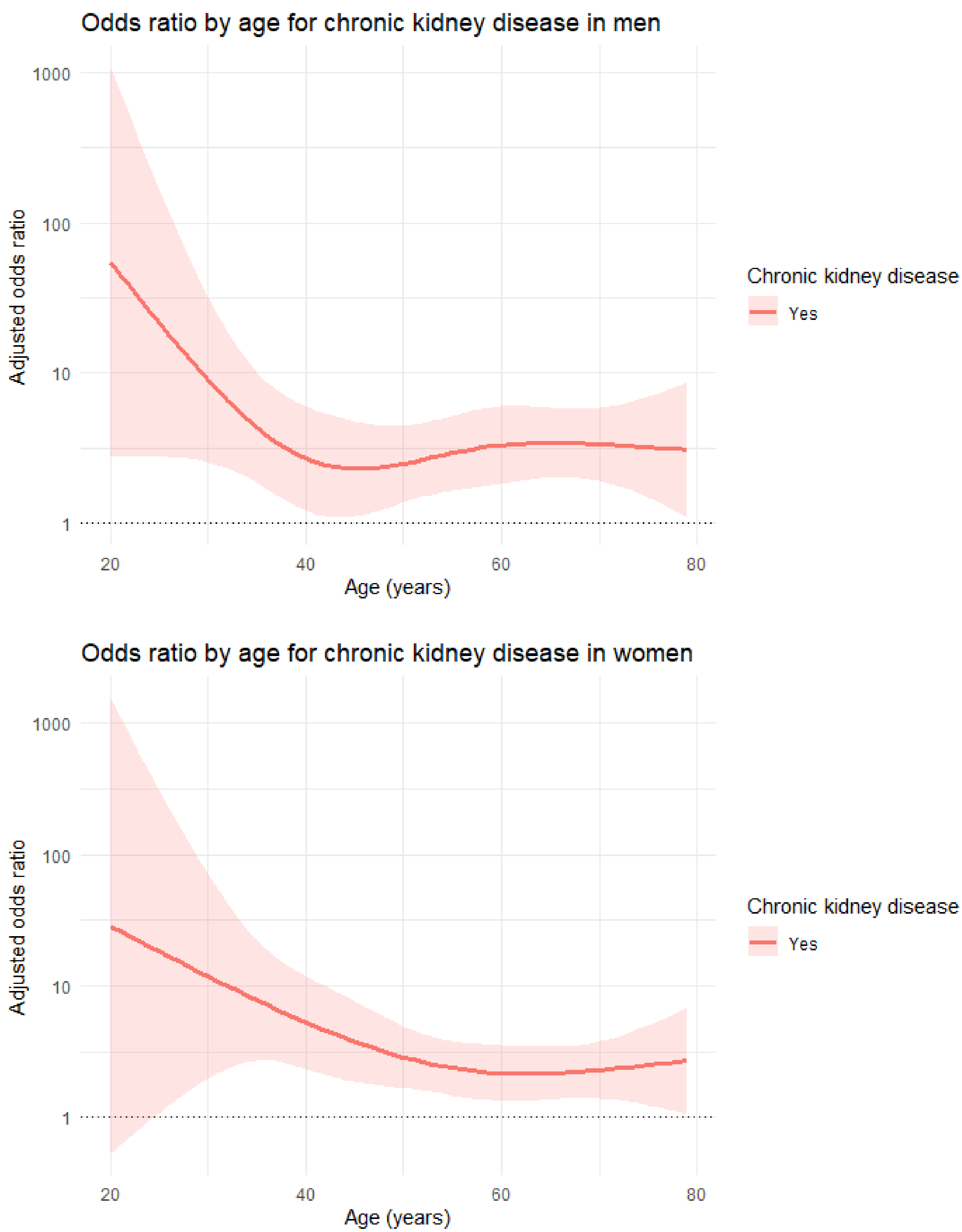


Reference = Never smoker

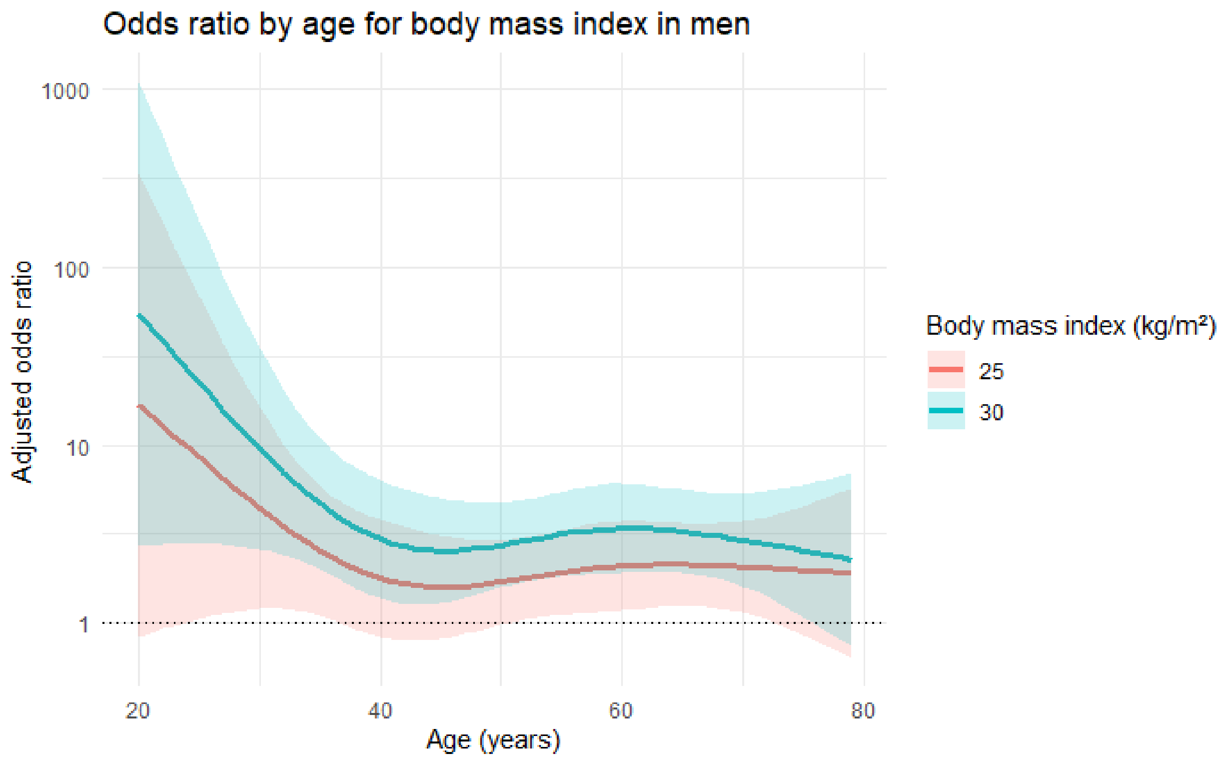


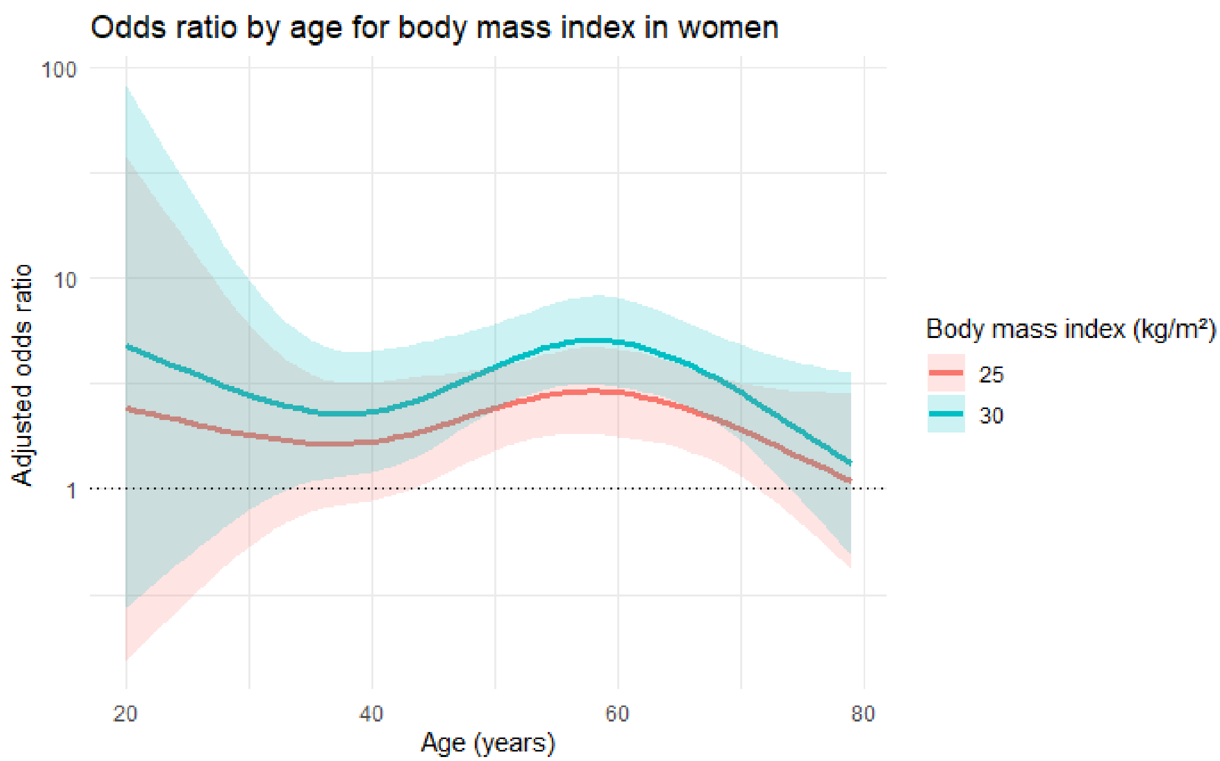


Reference = No

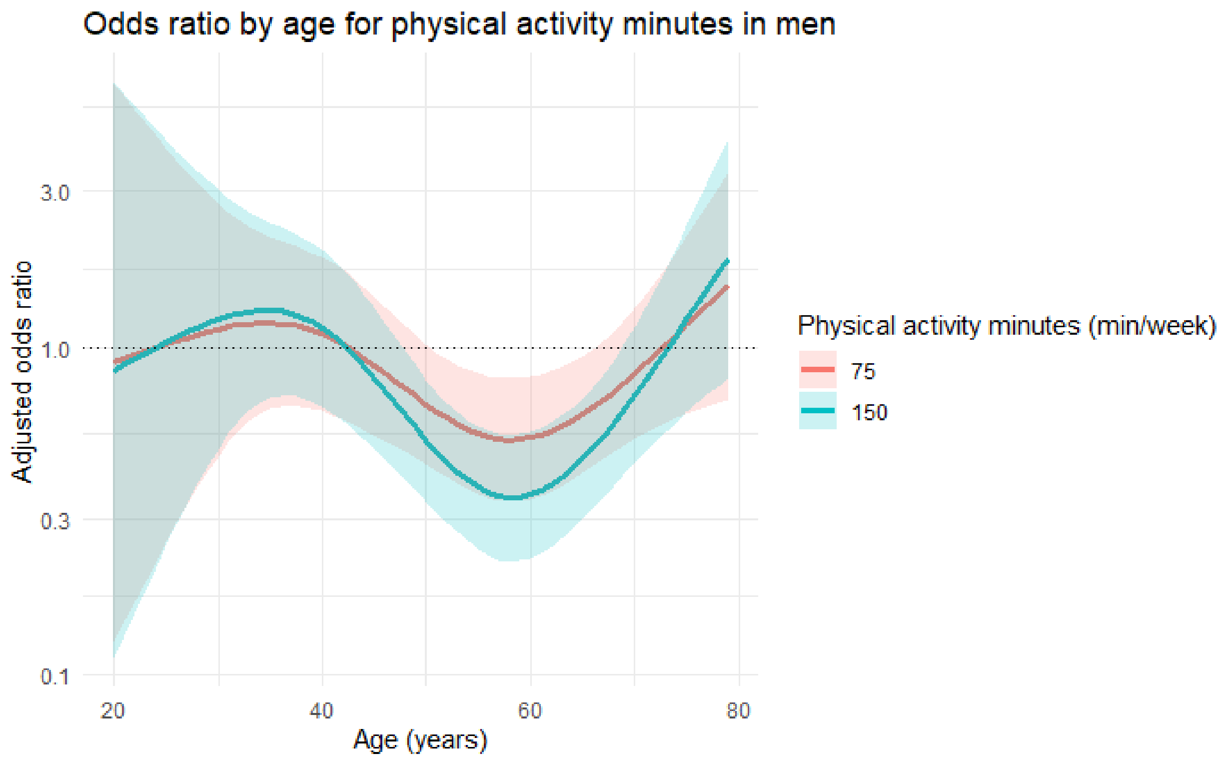


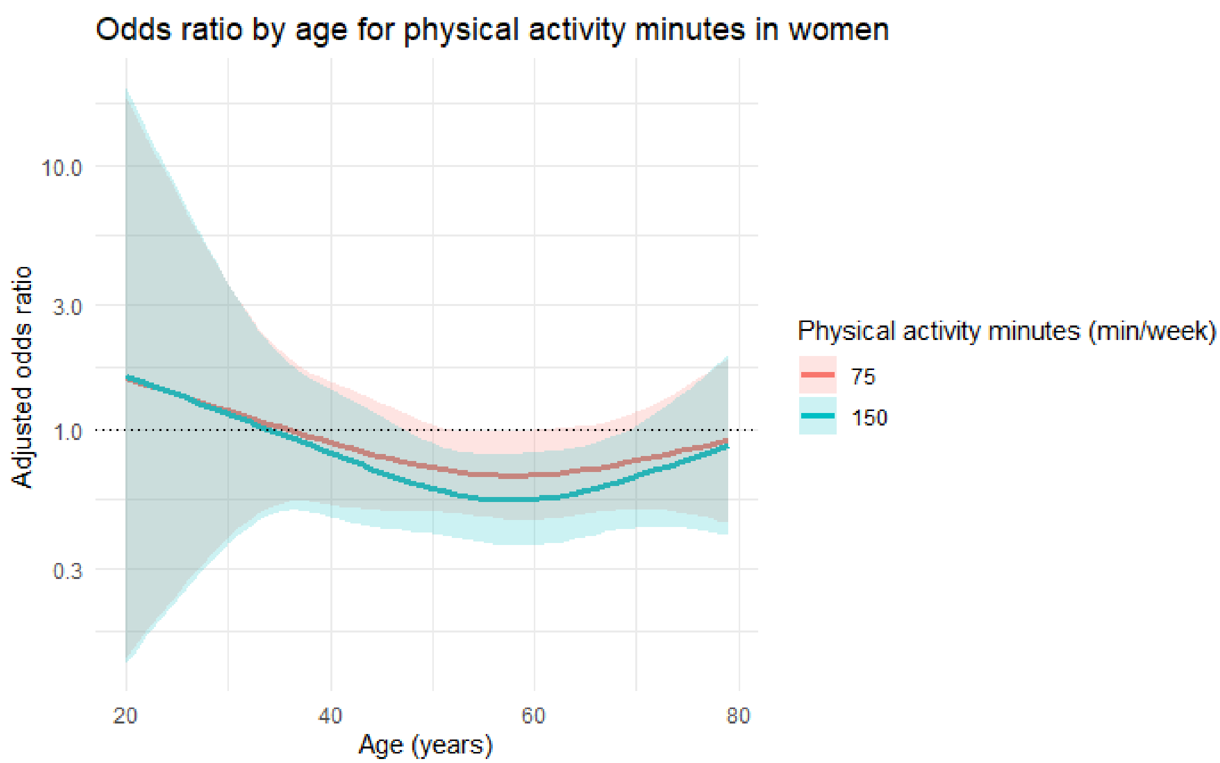
Reference = No



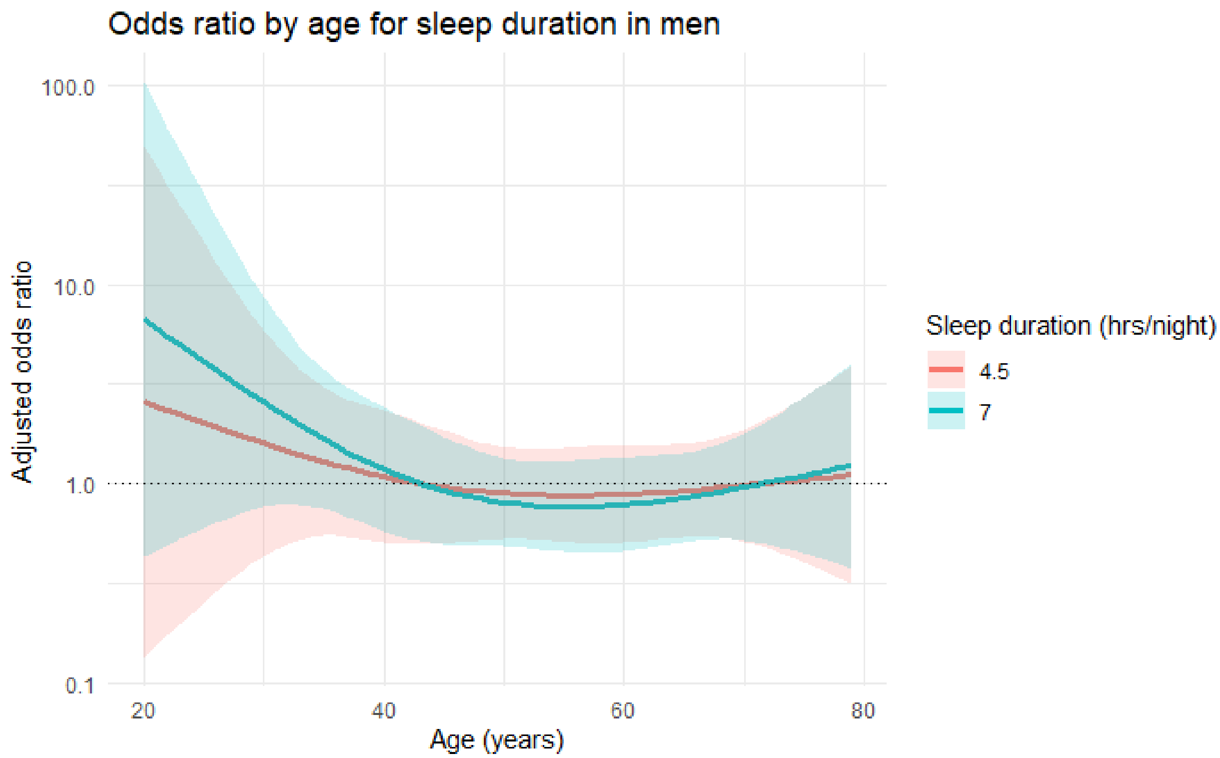


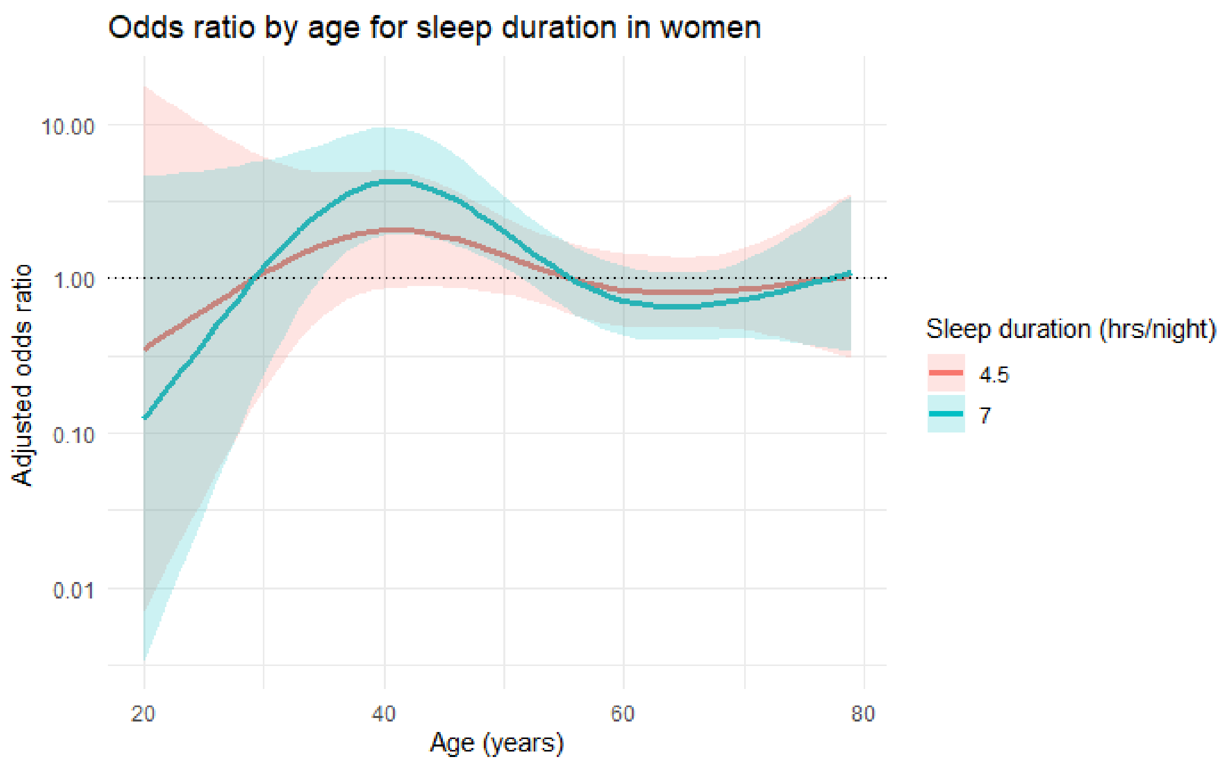
Reference = 18.5 kg/m^2





Reference = 0 min/week





Reference = 2 hrs/night

Appendix 12 – Mean age and body mass index within selected risk factors

	Mean age (years)	**Mean body mass index (kg/m^2)**
Psychological measures		
Self-rated mental health		
– Poor or fair	47.1	-
– Good, very good, or excellent	48.8	-
Self-perceived stress		
– Not at all to a bit	49.8	-
– Quite a bit or extremely	44.8	-
Health behaviours		
Smoking status		
– Current smoker	-	27.2
– Former smoker	-	28.5
– Never smoker	-	27.3