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Supplementary information

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# Integrative proteomic analyses across common cardiac diseases yield mechanistic insights and enhanced prediction

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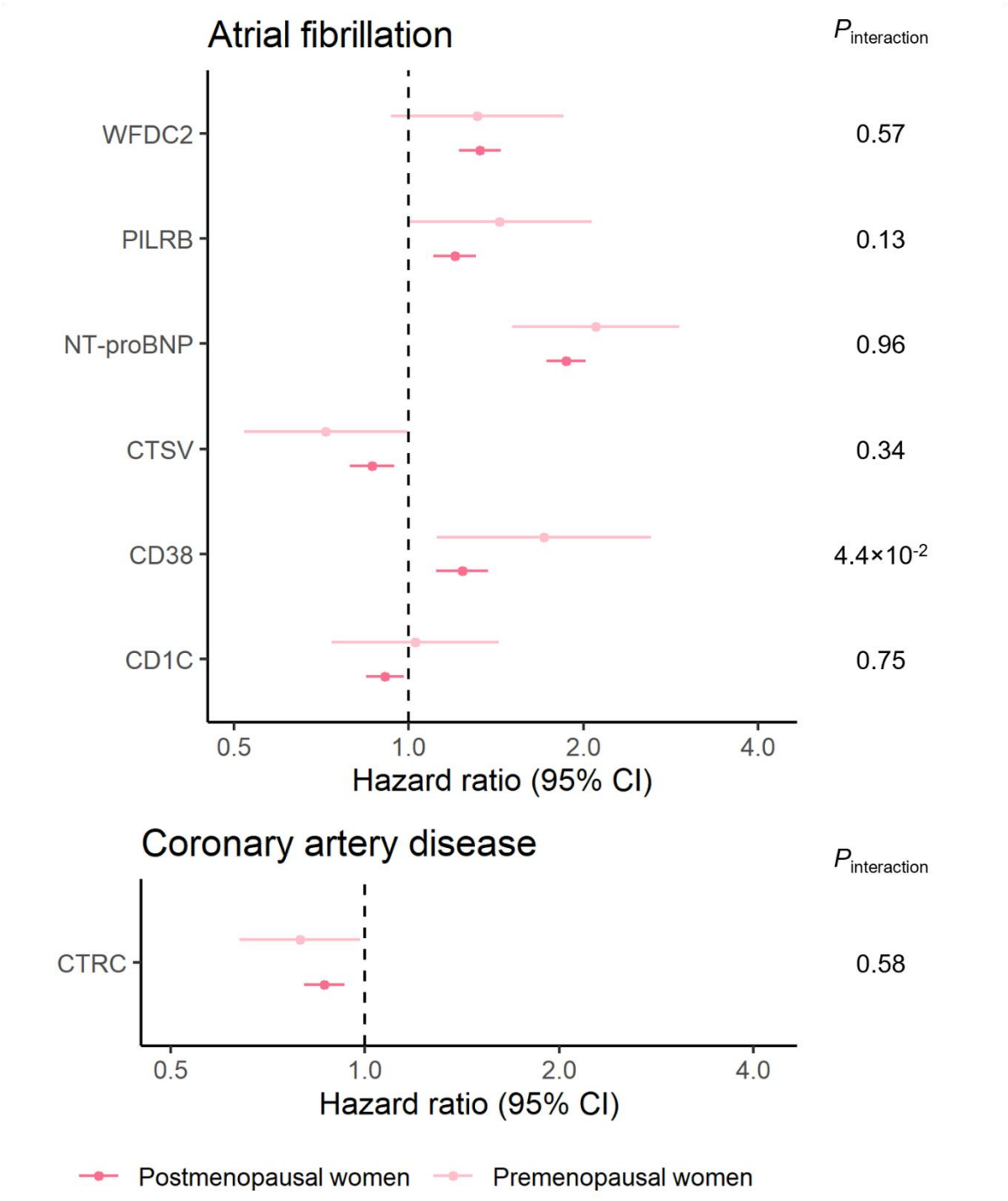
**SUPPLEMENTARY FIGURES**

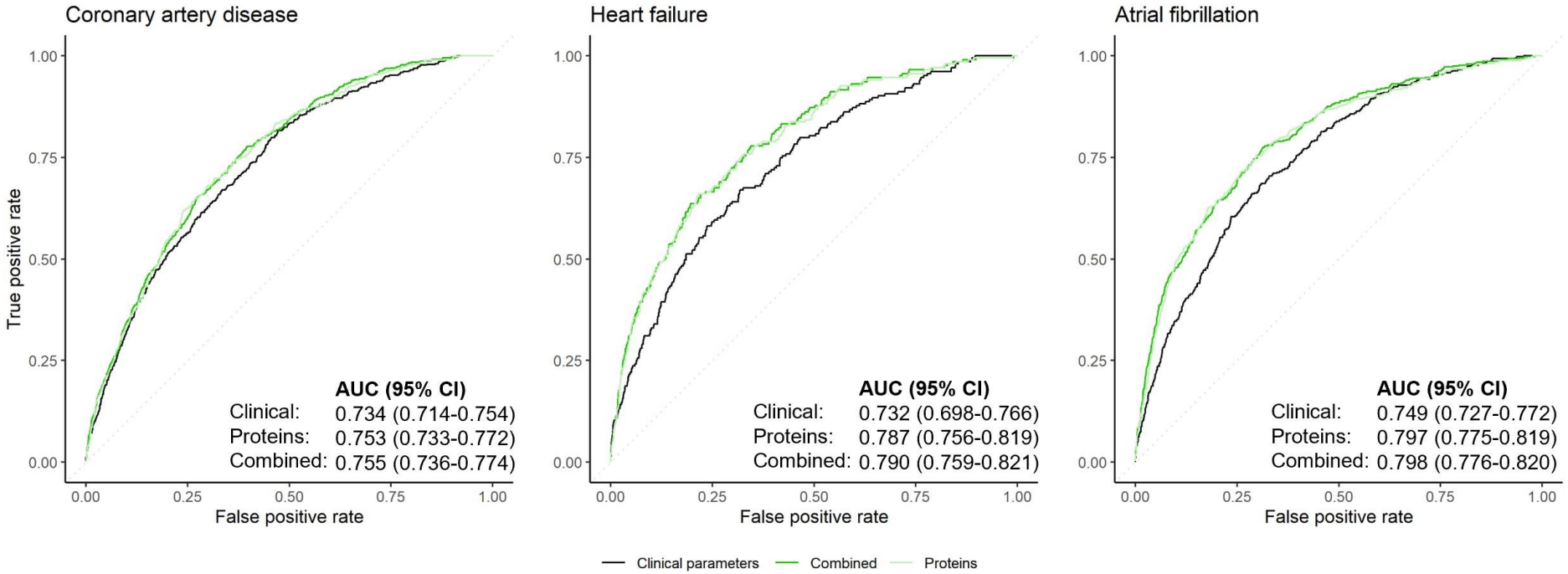
**Supplementary Fig. 1. Associations of proteins with sex-differential effects on cardiac disease risk in premenopausal vs. postmenopausal women.**




Forest plots depict protein-disease associations with "sex-differential effects" in premenopausal (*n*=5,838) and postmenopausal women (*n*=15,026) from the UKB-PPP. Menopause status was ascertained at baseline by self-report and unknown for 3,837 women. All associations are indicate using hazard ratios with corresponding 95% confidence intervals (CIs) for the indicated protein (per standard deviation) on the indicated outcome in

premenopausal and postmenopausal separately. $P_{interaction}$ indicates the two-sided *P*-value for the interaction term between “sex” and the indicated protein on the corresponding outcome. *P*-values were not adjusted for multiple comparisons. All associations were tested using multivariable-adjusted Cox proportional hazards models (see *Methods*).

**Supplementary Fig. 2. Risk prediction of incident coronary artery disease, heart failure, and atrial fibrillation in the UKB-PPP by risk scores based on clinical risk factors and/or circulating proteins that were also measured in the WHI-LLS.**




The receiver-operating characteristics curves depict the accuracy of the clinical, proteomic, and combined risk scores in predicting coronary artery disease, heart failure, and atrial fibrillation in the UKB-PPP testing set (*n*=8,863). Areas under the curve (AUCs) and corresponding 95% confidence intervals (95% CIs) quantify the performance of each model. Models with multiple candidate features were constructed using logistic least absolute shrinkage and selection operator (LASSO) models; the combined models included all clinical predictors (see *Methods*) as well as the circulating proteins that were also measured in the WHI-LLS as potential covariates in the final model. Participants were followed for a median (interquartile range) follow-up of 11.1 (10.4-11.8) years.