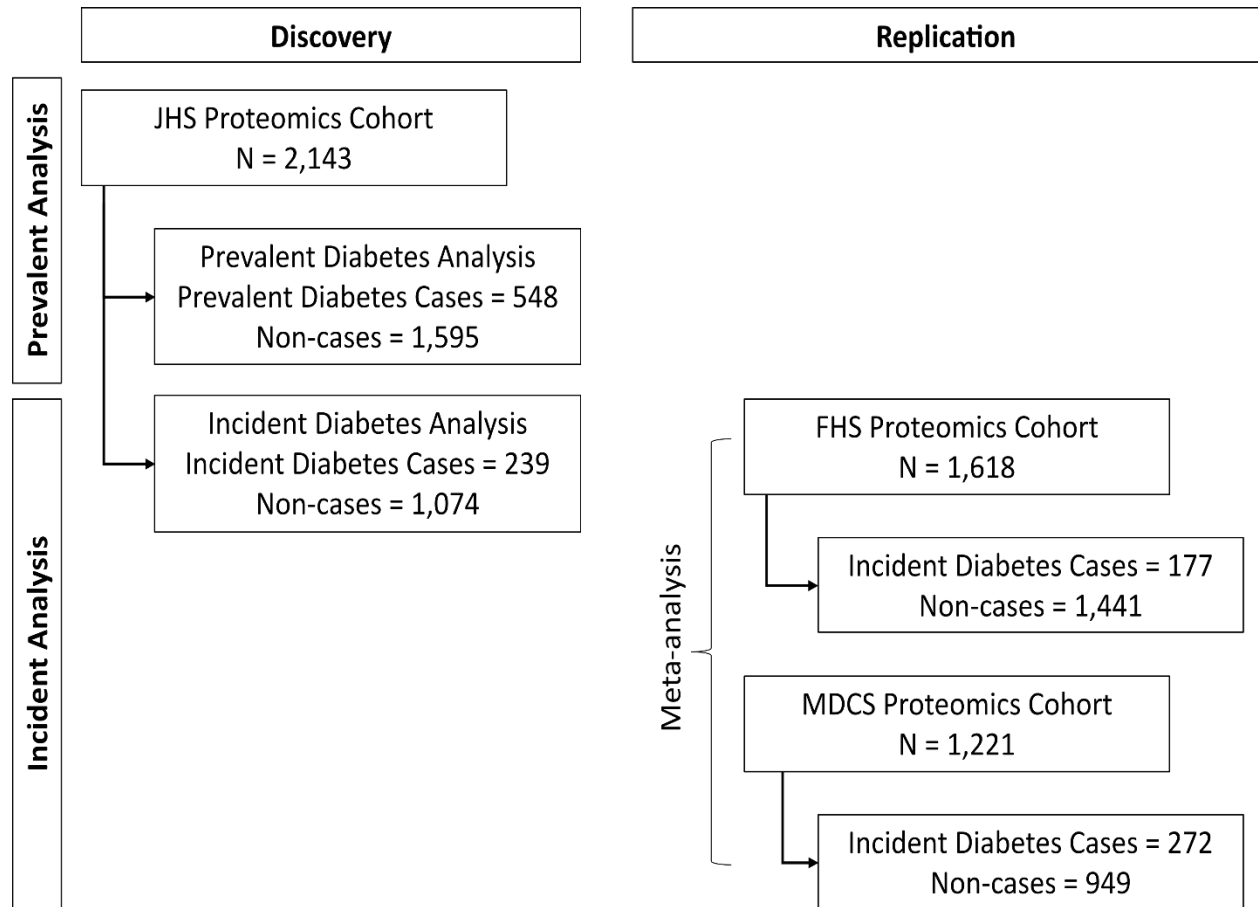


Supplemental Materials

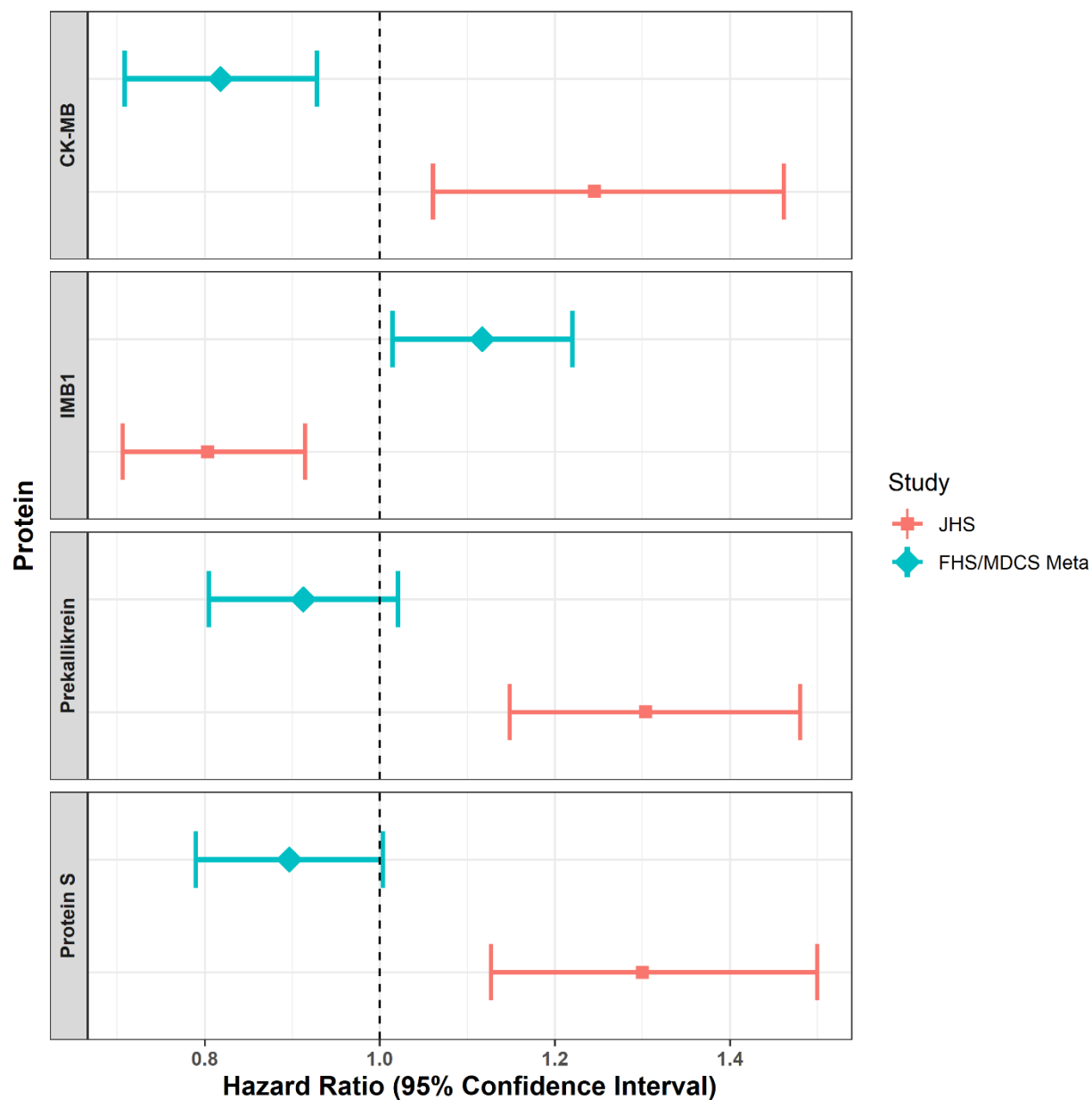
For quality control, each proteomic plate contained 3 pooled plasma samples derived from the JHS cohort, 5 calibrator controls created from external pooled plasma samples of healthy human donors, and 3 buffer samples without proteins. These were used to monitor the success of the different steps of the method and used to normalize and standardize the protein relative concentrations to correct for systemic variability caused by technical reasons. The calibrator controls were used for intraplate median signal normalization to control for variability within a plate due to sample protein concentration variability. This could be caused by pipetting variation, reagent concentration differences, and/or differences in the timing of assays in the method. Inter-plate variability was controlled for using the measurement of each protein in the JHS cohort derived pooled plasma samples measured across all plates.

Supplemental Figure 1. Diagram of cohorts included in the analyses.



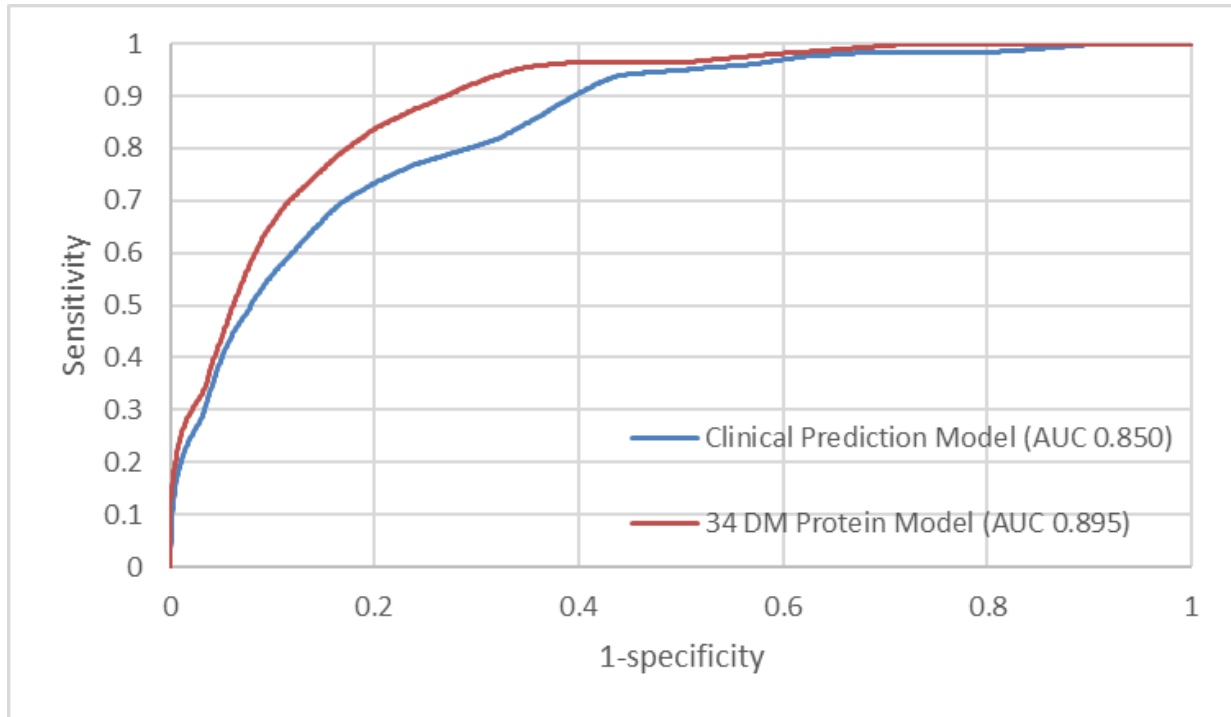
Of note, 282 individuals that had proteomics profiling that did not have prevalent diabetes were also excluded from the incident diabetes analysis due to missing data. JHS: Jackson Heart Study. FHS: Framingham Heart Study. MDCS: Malmö Diet and Cancer Study.

Supplemental Figure 2. Proteins with differences in incident T2D associations when comparing the JHS and the FHS/MDCS metanalysis.



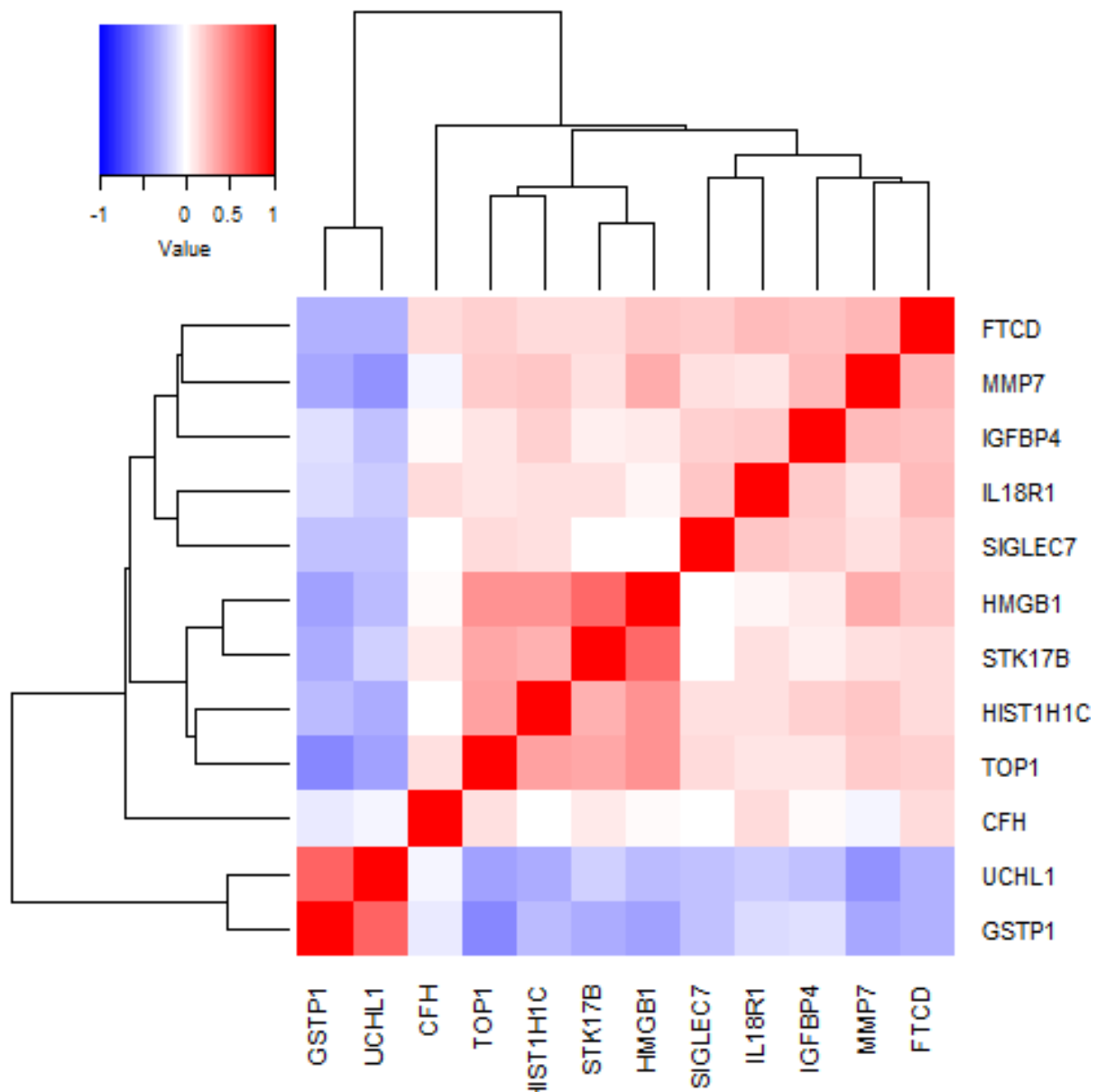
Hazard ratio for incident T2D for every 1 SD increase in standardized and transformed circulating aptamer level. The distribution of the standardized differences between beta effects using Cox proportional hazards models were different with a $p < 0.05$ for the proteins listed.

Supplemental Figure 3. Receiver operating characteristic curve (ROC) for the 34-protein incident diabetes prediction model compared to clinical factors alone in FHS



Clinical risk factors included in the clinical prediction model are age, gender, BMI, systolic blood pressure, HDL cholesterol, triglycerides, FPG, and family history of diabetes and were used in both models. The 34 DM protein model includes both the clinical risk factors detailed above, and the 34 proteins selected using elastic net regression from the 111 proteins associated with incident diabetes in JHS model 2 listed in **Table S15**.

Supplemental Figure 3. Heatmap of the 12 proteins associated with incident diabetes in JHS Model 2 that replicated in FHS/MDCS.



Spearman's rho value of the relative concentration of the 12 proteins are represented by the colors in the heatmap. Dark blue corresponding to values closer to -1 and dark red corresponds to values closer to 1.