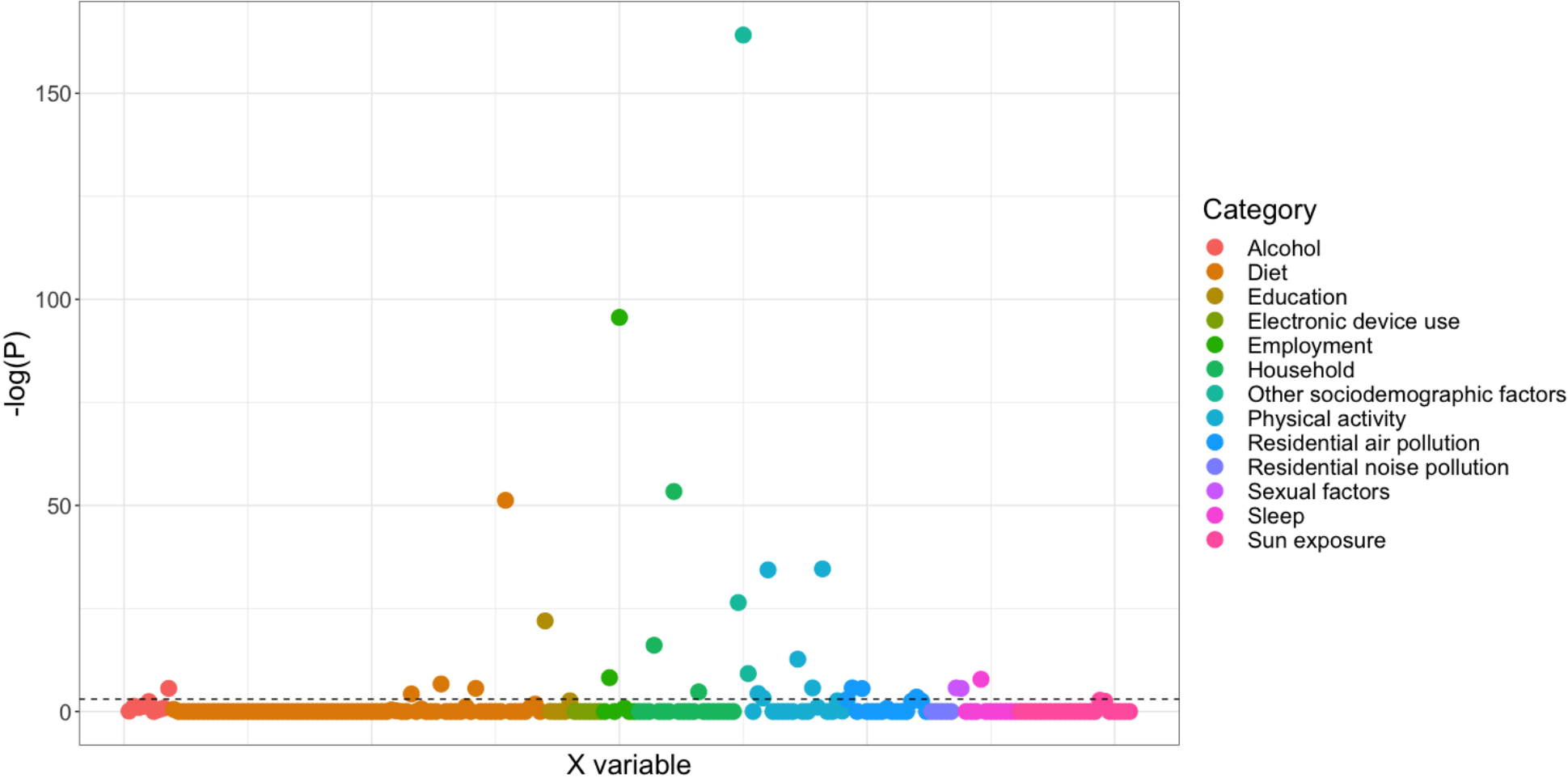
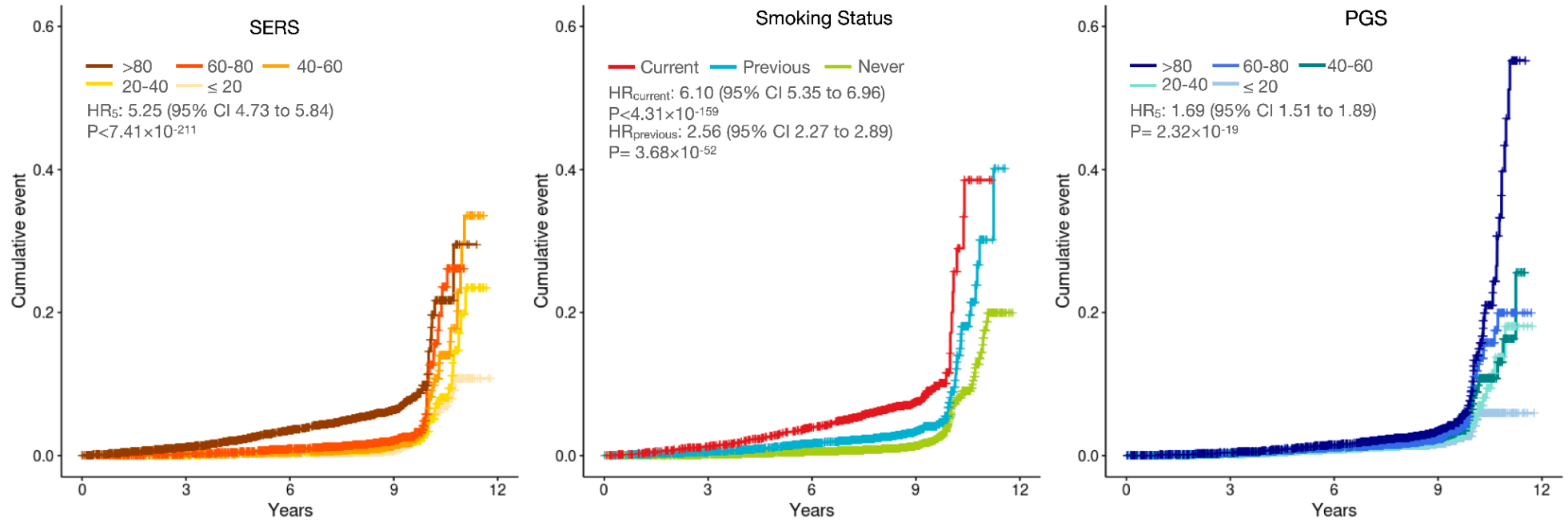


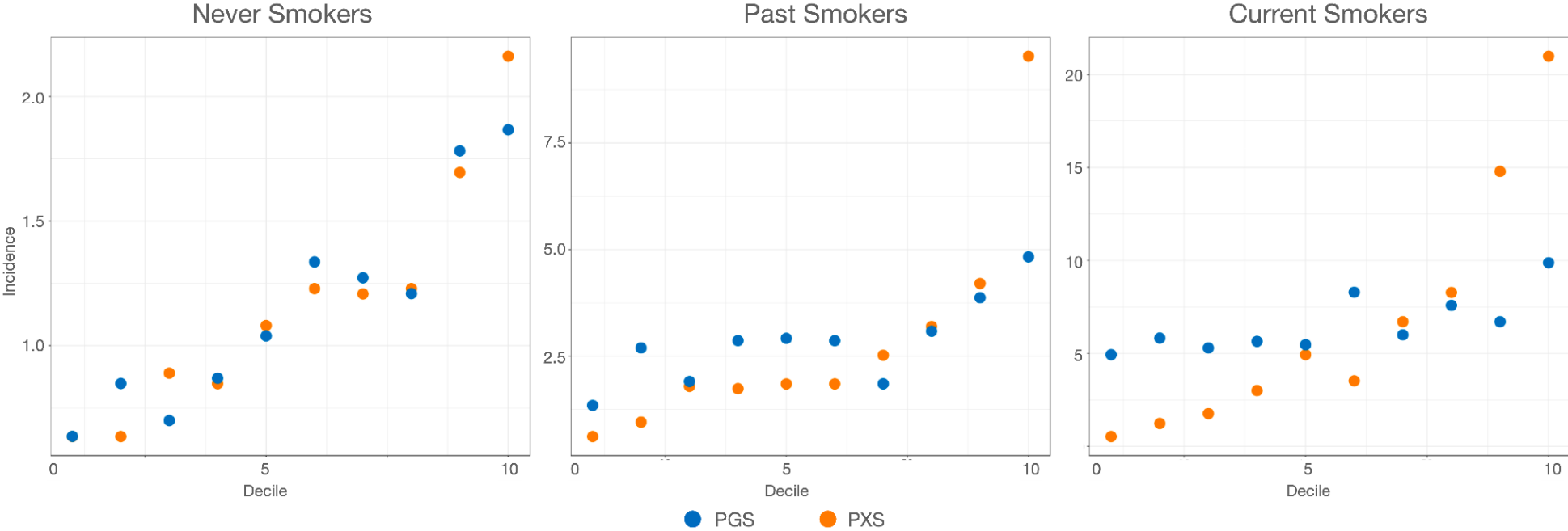
Supplementary Figure 1: Manhattan plot of XWAS results. The negative log of the FDR-adjusted P value is plotted for each factor. The horizontal line indicates where the P value=0.05 (FDR-adjusted and two-sided). The color represents the exposure category, and exposures are ordered alphabetically. Source data are provided as a Source Data file.



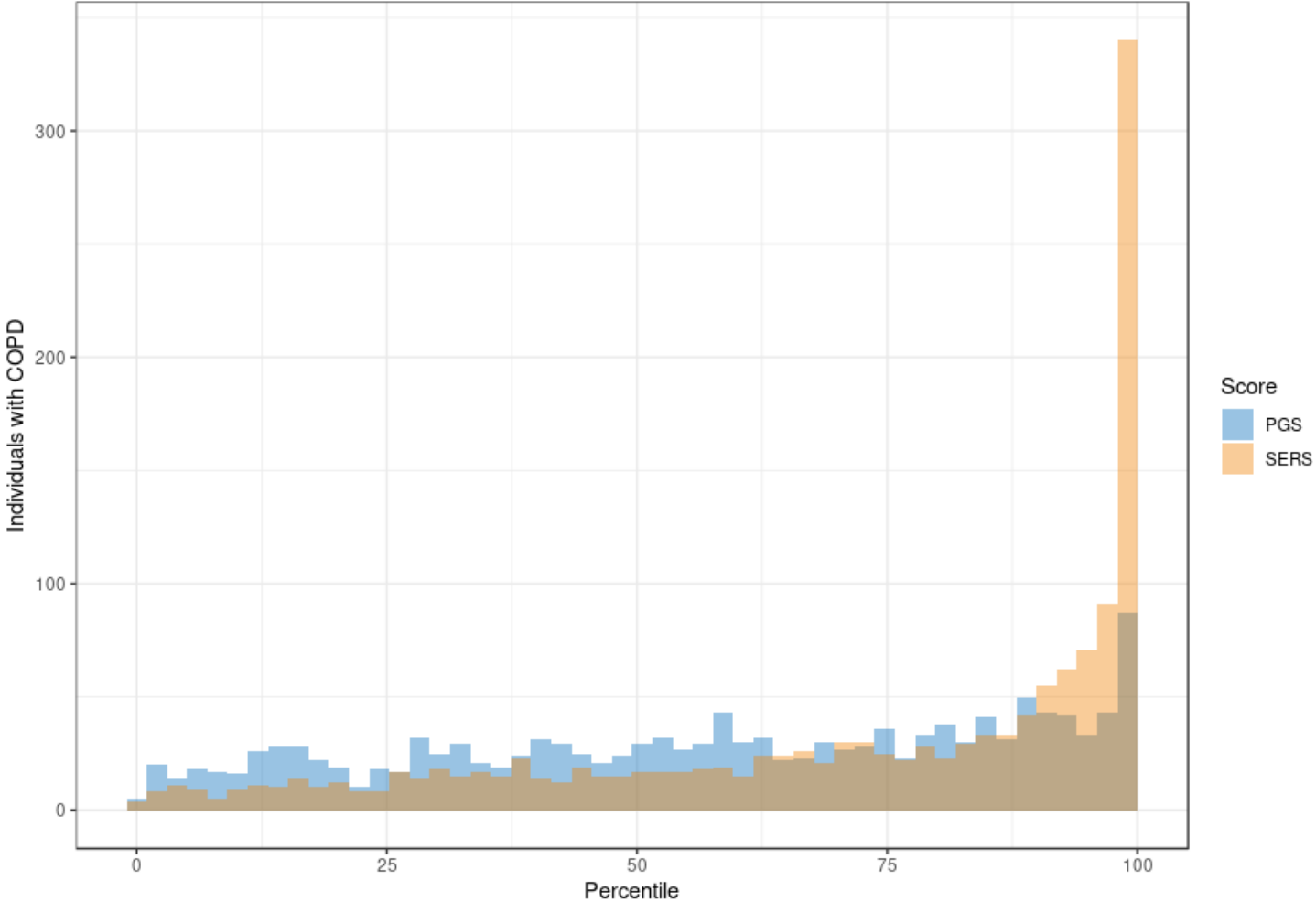
Supplementary Figure 2: Cumulative incidence plot stratified by SERS quintile, smoking status, and PGS quintile in the EUR evaluation set. Hazard ratios (HR) are reported in comparison between the top quintile of PGS and SERS compared to the remaining population, and between current and previous smokers compared to never smokers. All displayed p-values are two-sided without adjustment for multiple comparisons.



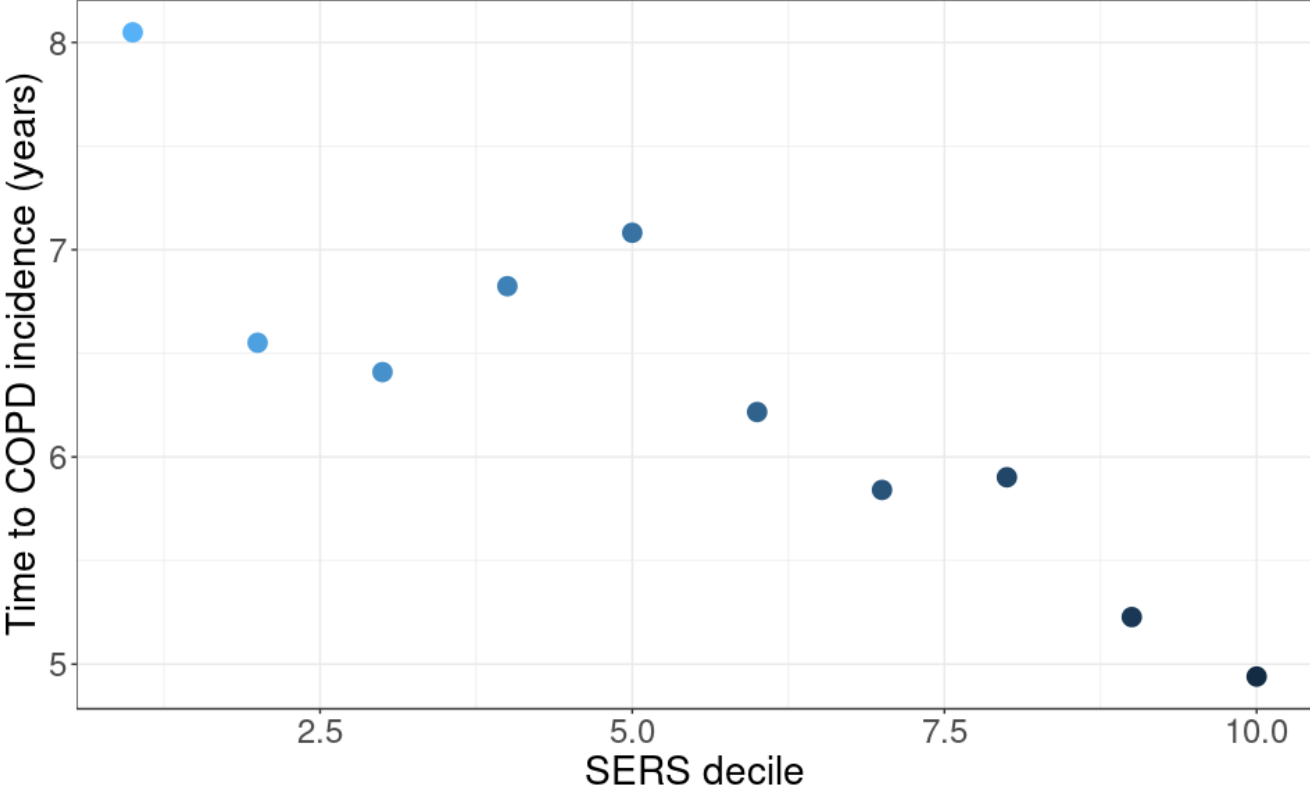
Supplementary Figure 3: Stratification of COPD incidence across never smokers (N=47,190), previous smokers (N=17,835), and current smokers (N=5,675) in the EUR evaluation set . The polygenic (blue) and polyexposure (orange) risk scores were binned into 10 deciles for individuals in each smoking status group. The incidence of COPD for each decile is plotted on the y-axis. Source data are provided as a Source Data file.



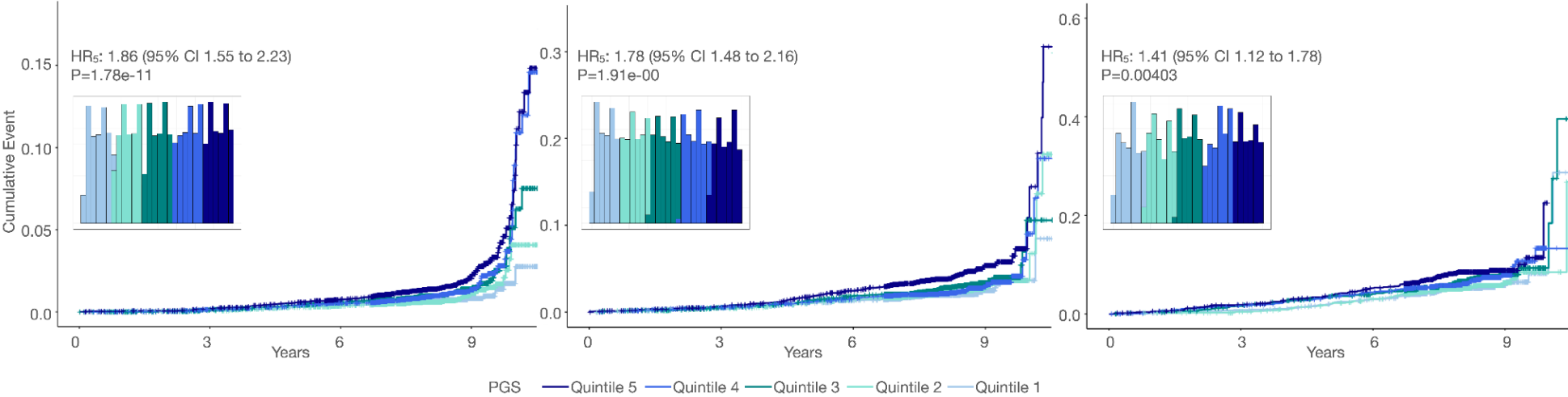
Supplementary Figure 4: Distribution of risk scores in EUR individuals with COPD (N=1425). All EUR evaluation set individuals were binned into 100 percentiles based on their SERS or PGS. The distribution of the percentile for individuals who were later diagnosed with COPD is shown.



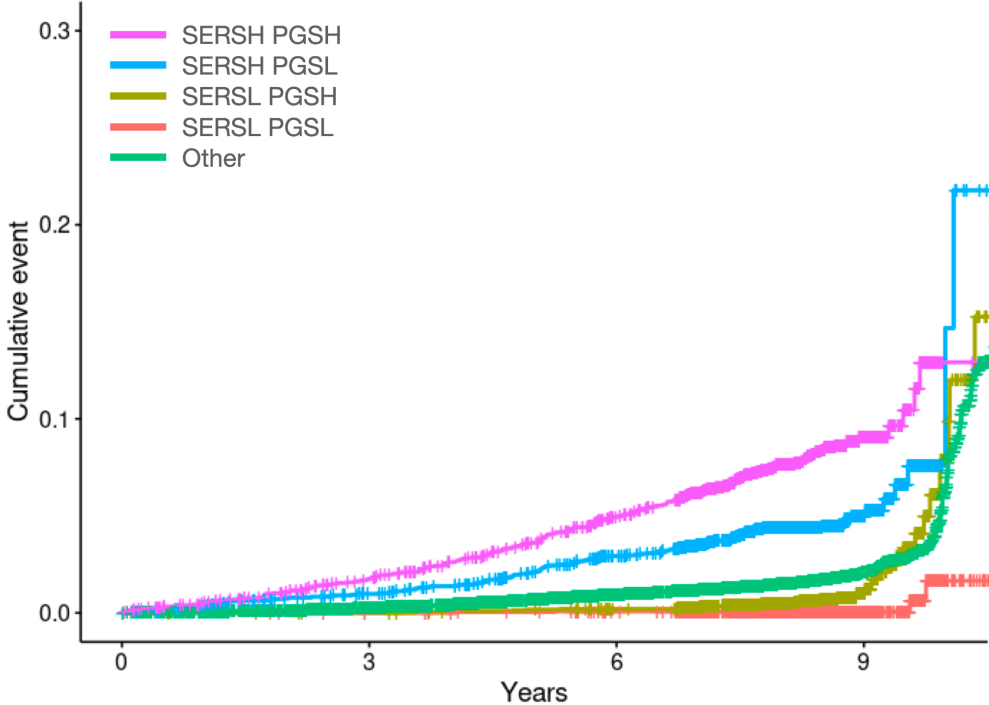
Supplementary Figure 5: Average time to event for individuals who are later diagnosed with COPD for each SERS decile. Source data are provided as a Source Data file.



Supplementary Figure 6: Cumulative incidence plots for never smokers (left), previous smokers (middle), and current smokers (right) stratified by PGS (blue shades) quintiles. The distribution of PGS for each smoking status is shown in each panel. All displayed p-values are two-sided without adjustment for multiple comparisons. 22



Supplementary Figure 7: Cumulative event plot stratified by different combinations of PXS and PGS in the EUR evaluation set. High- and low-risk scores are defined as being in the top and bottom quintiles, respectively. PXSH PGSH: high PXS and high PGS. PXSH PGSL: high PXS and low PGS. PXSL PGSH: low PXS and high PGS. PXSL PGSL: low PXS and low PGS.



Supplementary Figure 8: Venn diagram of individuals with incident COPD who have the highest (top quintile) and lowest (bottom quintile) risk scores in EUR evaluation set. SERSH: highest socioeconomic and economic risk score, SERSL: lowest socioeconomic and economic risk score, PGSH: highest polygenic risk score, PGS�: lowest polygenic risk score.

