**Polygenic risk score across distinct colorectal cancer screening outcomes: from premalignant polyps to colorectal cancer.**

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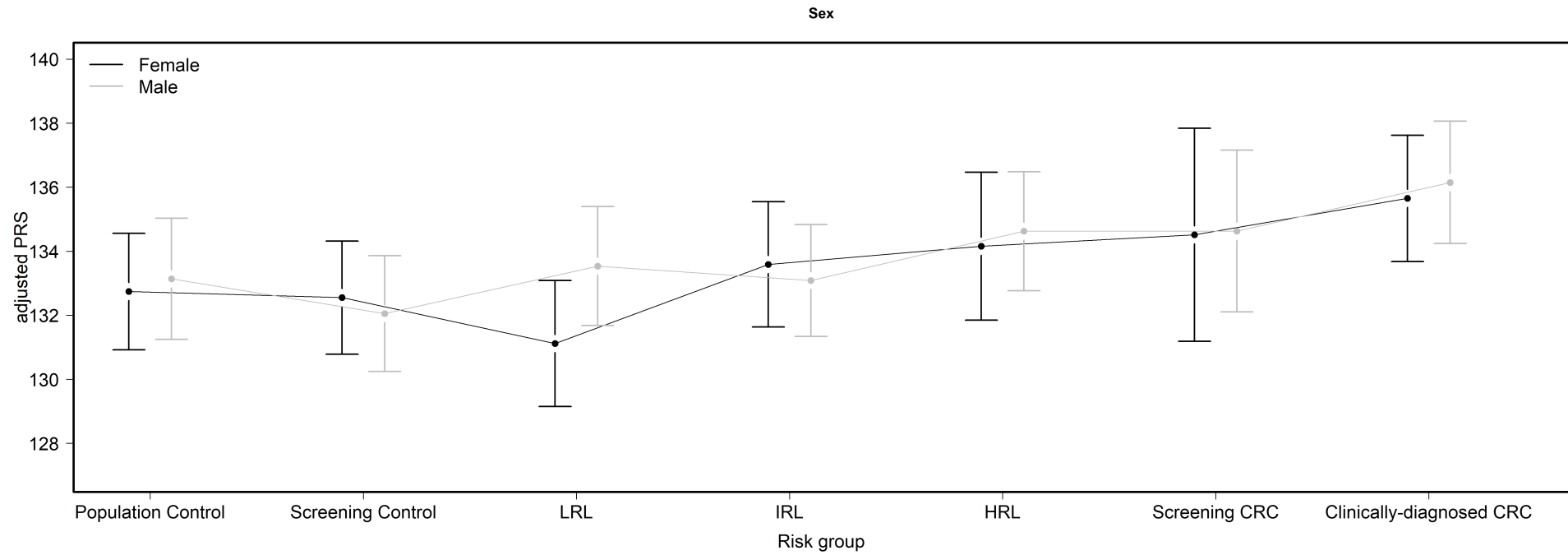
Supplementary Figure Captions

**Supplementary Figure 1** Ancestry PCA of HapMap and our samples
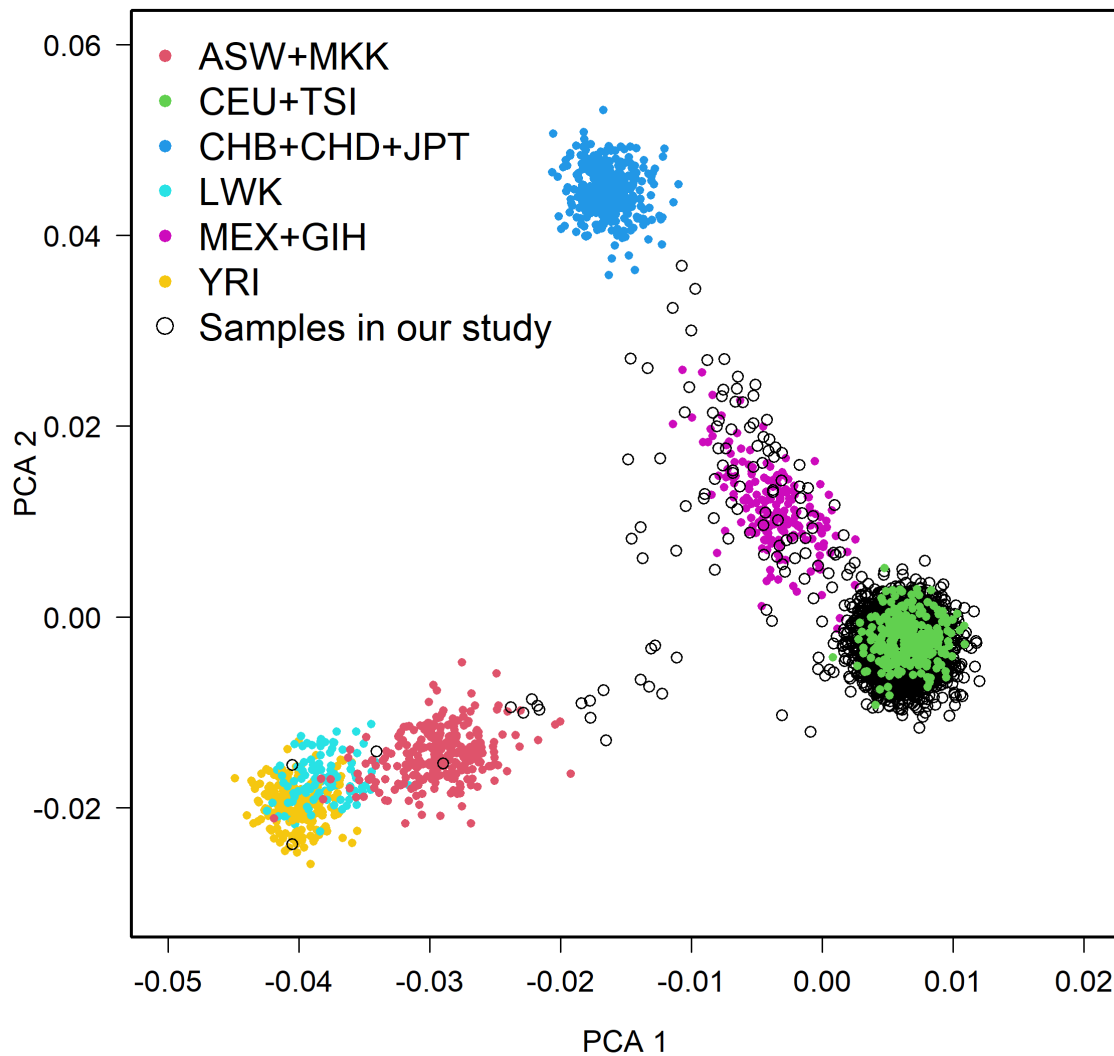
Supplementary Figure 1 legend: **ASW**: African ancestry in Southwest USA; **CEU**: Utah residents with Northern and Western European ancestry from the CEPH collection, **CHB**: Han Chinese in Beijing, China, **CHD:** Chinese in Metropolitan Denver, Colorado, **GIH:** Gujarati Indians in Houston, Texas, **JPT:** Japanese in Tokyo, Japan, **LWK:** Luhya in Webuye, Kenya, **MEX:** Mexican ancestry in Los Angeles, California, **MKK:** Maasai in Kinyawa, Kenya, **TSI:** Toscani in Italia and **YRI**: Yoruba in Ibadan, Nigeria.

Supplementary Figure 2 Distribution of the polygenic risk score according to the different 7 risk groups by sex.
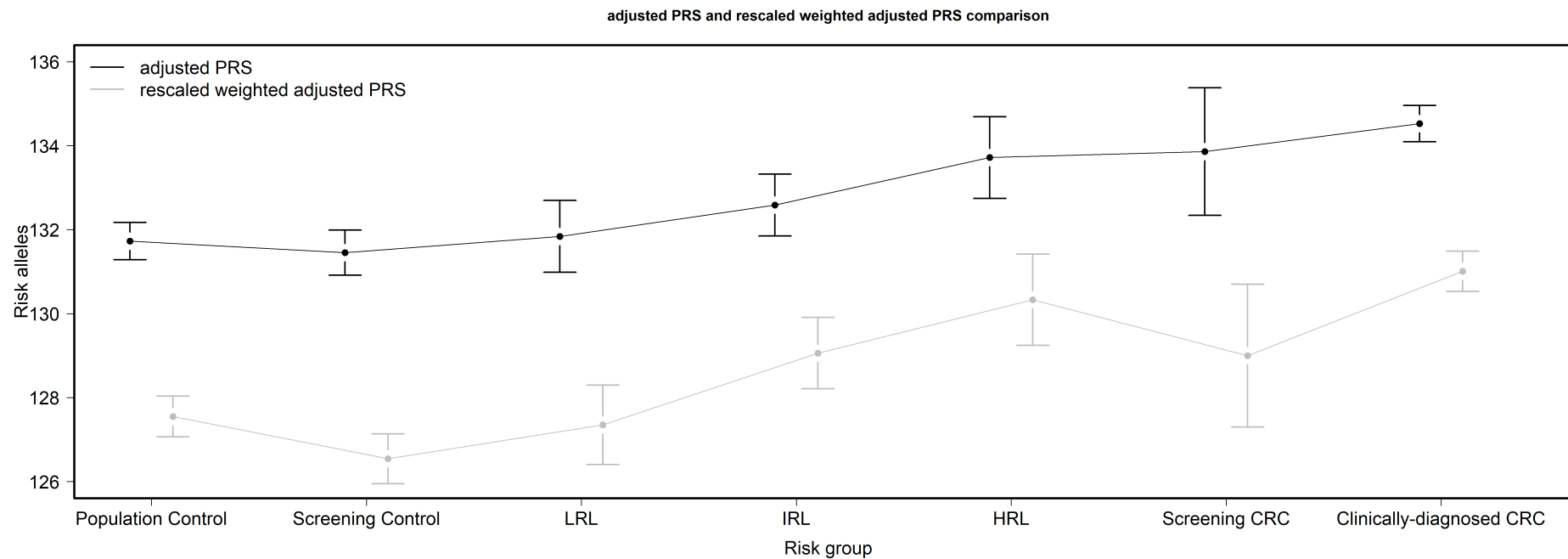

Supplementary Figure 2 legend: Data are represented as the mean and 95% CI for each group.

Supplementary Figure 3 Distribution of the polygenic risk score according to the different 7 risk groups by age
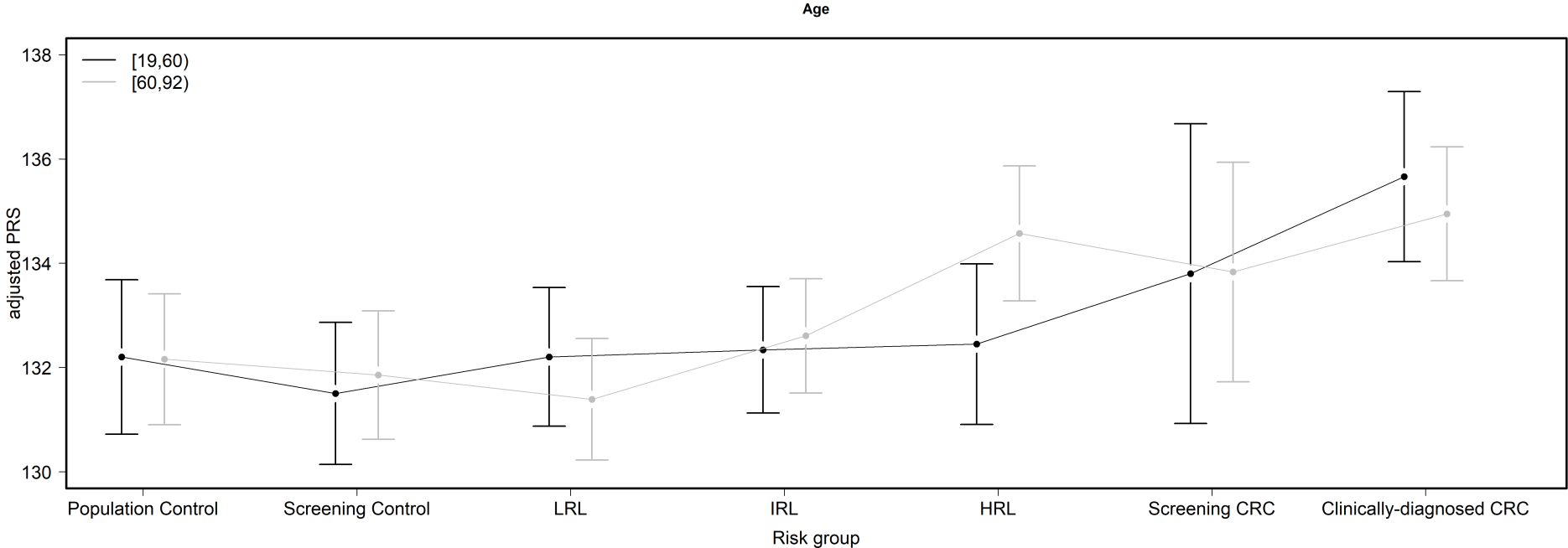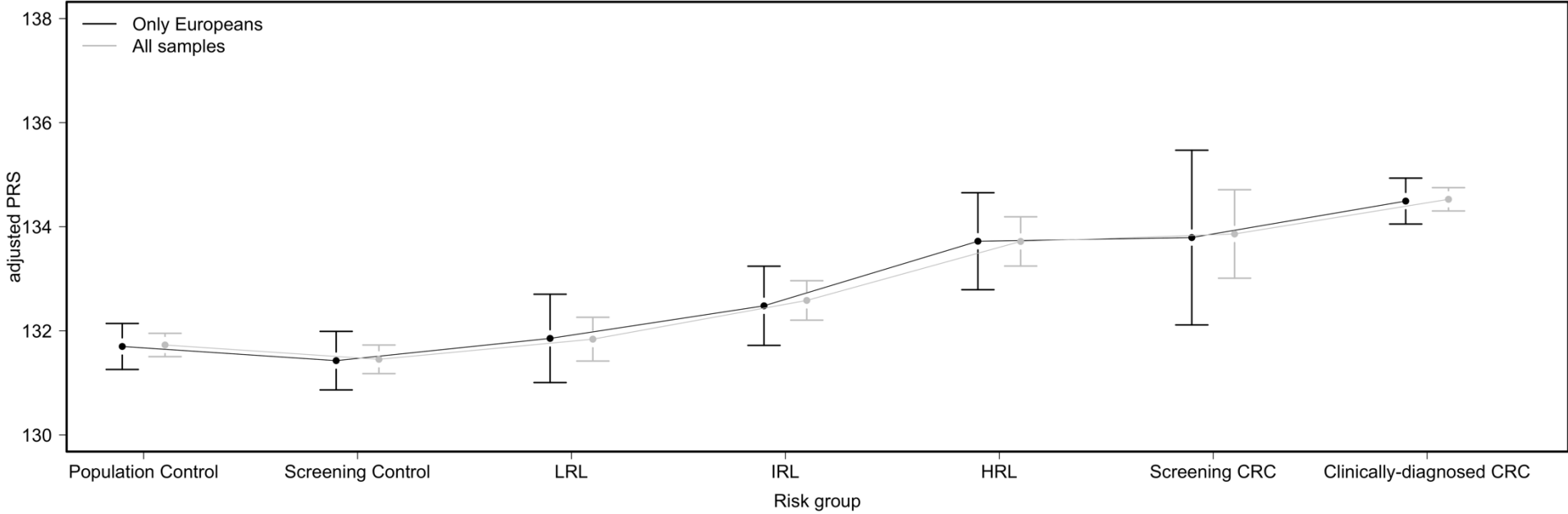

Supplementary Figure 3 legend: Data are represented as the mean and 95% CI for each group.

Supplementary Figure 4 Distribution of the adjusted polygenic risk score and the weighted polygenic risk score according to the different 7 risk groups.

adjusted PRS and rescaled weighted adjusted PRS comparison

Supplementary Figure 4 legend: Data are represented as the mean and 95% CI for each risk group. To plot the weighted polygenic risk score in polygenic risk score scale, the weighted polygenic risk needed to be divided by the sum of the reported weights and multiplied by the total number of SNPs.

Supplementary Figure 5 Distribution of the adjusted polygenic risk score and distribution of the polygenic risk score excluding non-European samples according to the different 7 risk groups.


Supplementary Figure 5 legend: Data are represented as the mean and 95% CI for each group.

Supplementary Figure 6 Analysis of the weighted adjusted polygenic risk score (A) Distribution in cases and controls. (B) Receiver Operating Characteristic curve based on 133 SNPs used to measure the area under the curve in cases compared to controls. (C) Positive and negative predicted values for the number of CRC risk alleles weighted by fecal immunochemical test (positive weight = 0.06 and negative weight = 0.94).
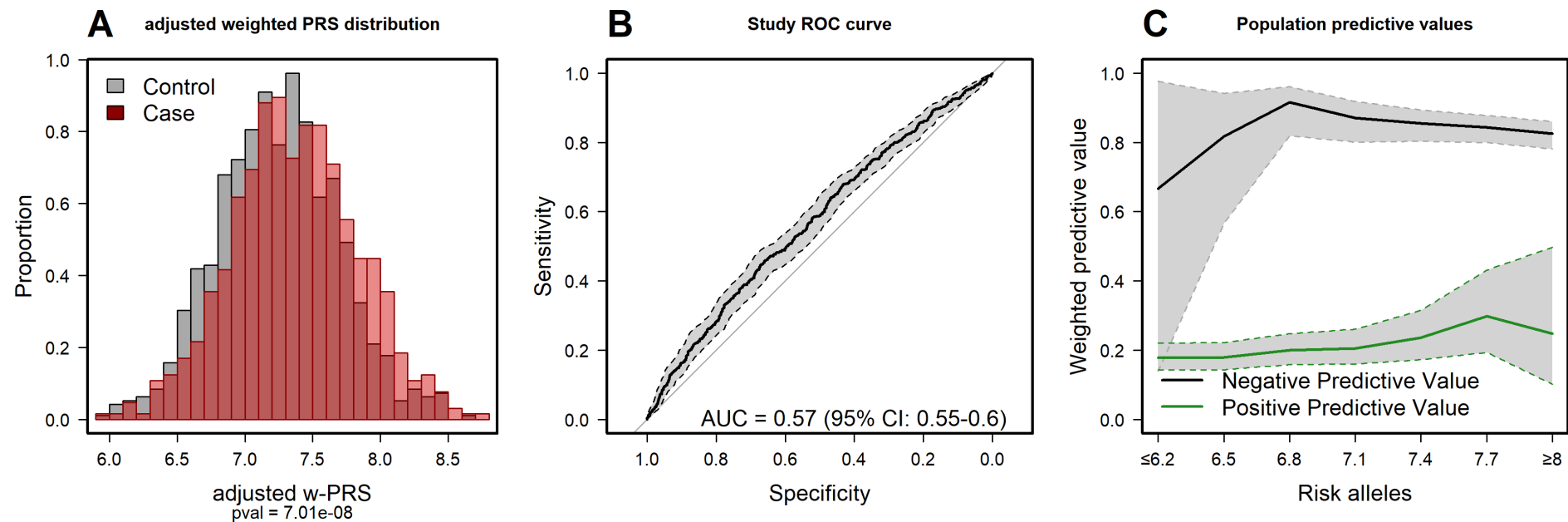
Supplementary Figure 7 Analysis of high-risk lesions and CRC cases (A) Distribution of the adjusted polygenic risk score in cases (high-risk lesions and CRC cases) and controls (low-risk lesions, intermediate-risk lesions, and controls). (B) Receiver Operating Characteristic curve based on 133 SNPs used to measure the area under the curve in cases compared to controls. (C) Positive and negative predicted values for the number of CRC risk alleles weighted by fecal immunochemical test (positive weight = 0.06 and negative weight = 0.94).
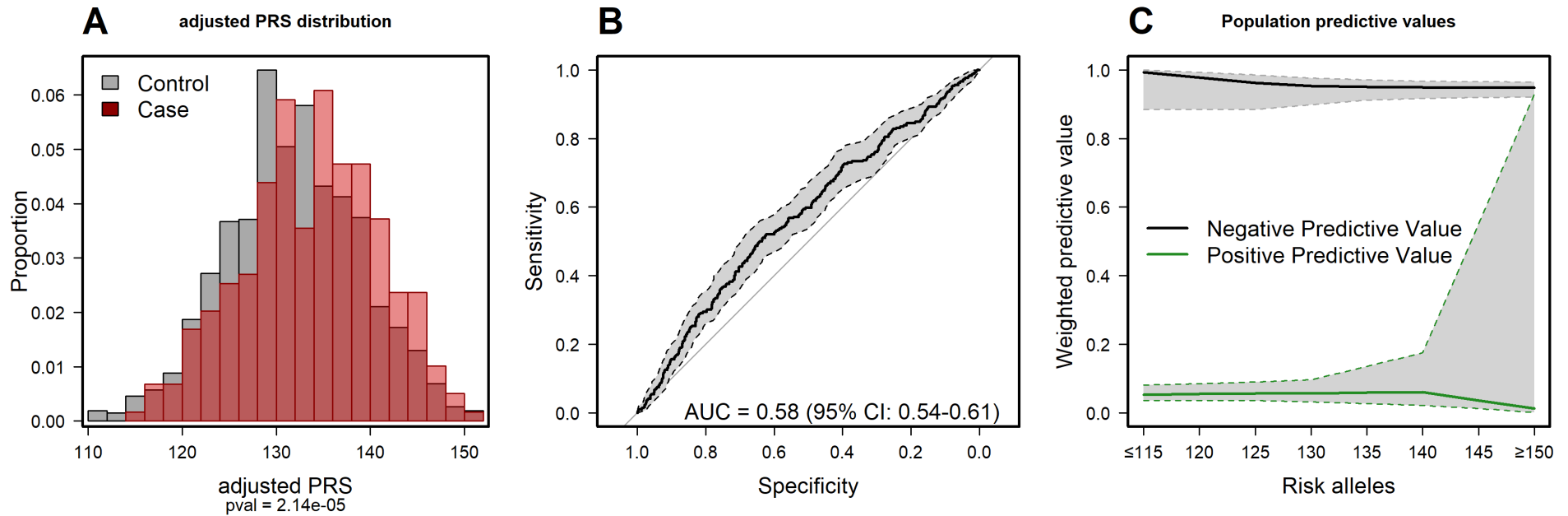
Supplementary Figure 8 Risk of premalignant polyps and colorectal cancer risk among screening population according to the adjusted polygenic risk score.
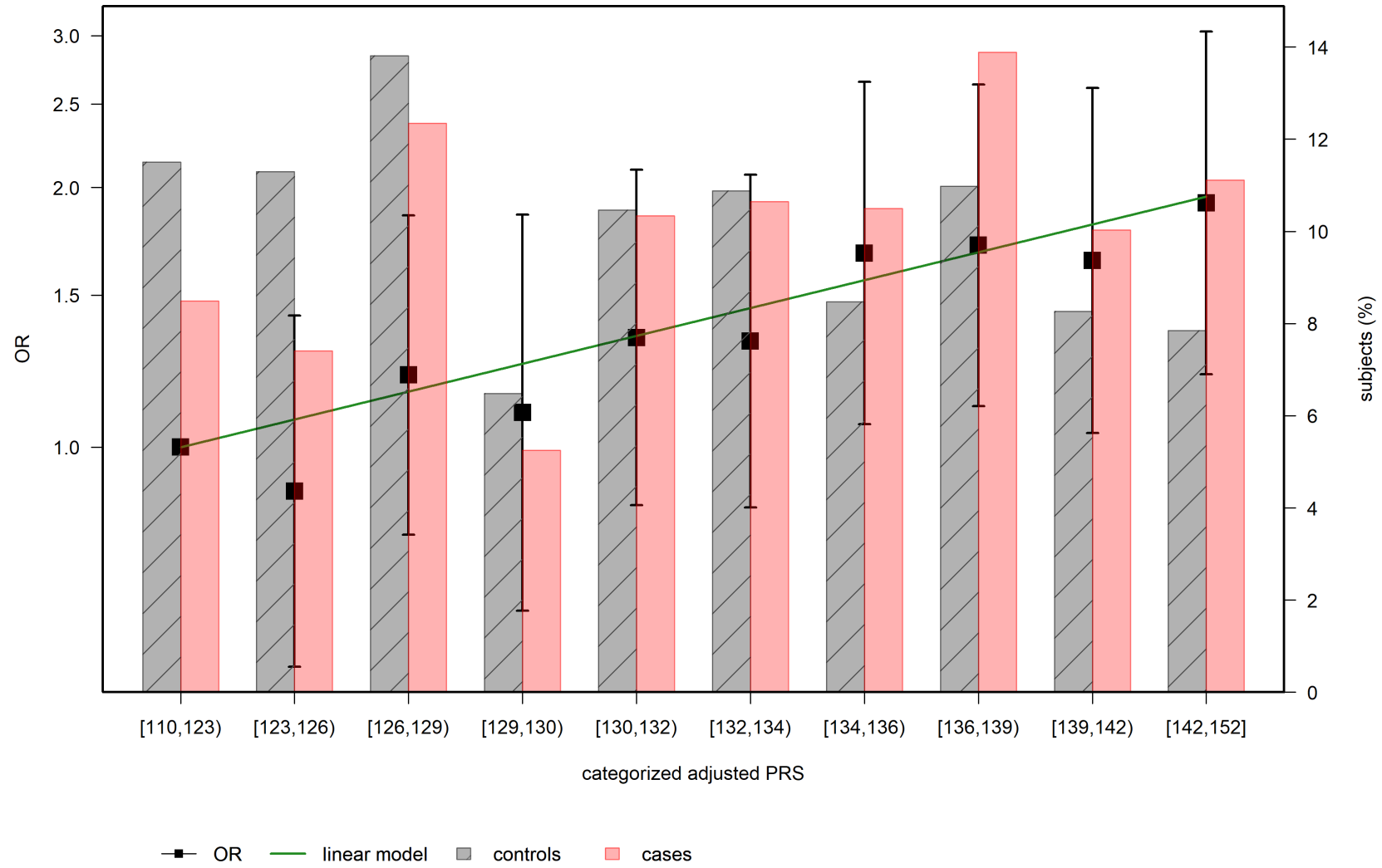
Supplementary Figure 9 (A) Distribution of the adjusted polygenic risk score among women in cases and controls. (B) Receiver Operating Characteristic curve for based on 133 SNPs used to measure the area under the curve in female cases compared to female controls. (C) Positive and negative predicted values for the number of CRC risk alleles in women weighted by fecal immunochemical test (positive weight = 0.06 and negative weight = 0.94). (D) Distribution of the polygenic risk score among men in cases and controls. (E) Receiver Operating Characteristic curve based on 133 SNPs used to measure the area under the curve in male cases compared to male controls (F) Positive and negative predicted values for the number of CRC risk alleles in men weighted by fecal immunochemical test (positive weight = 0.06 and negative weight = 0.94).
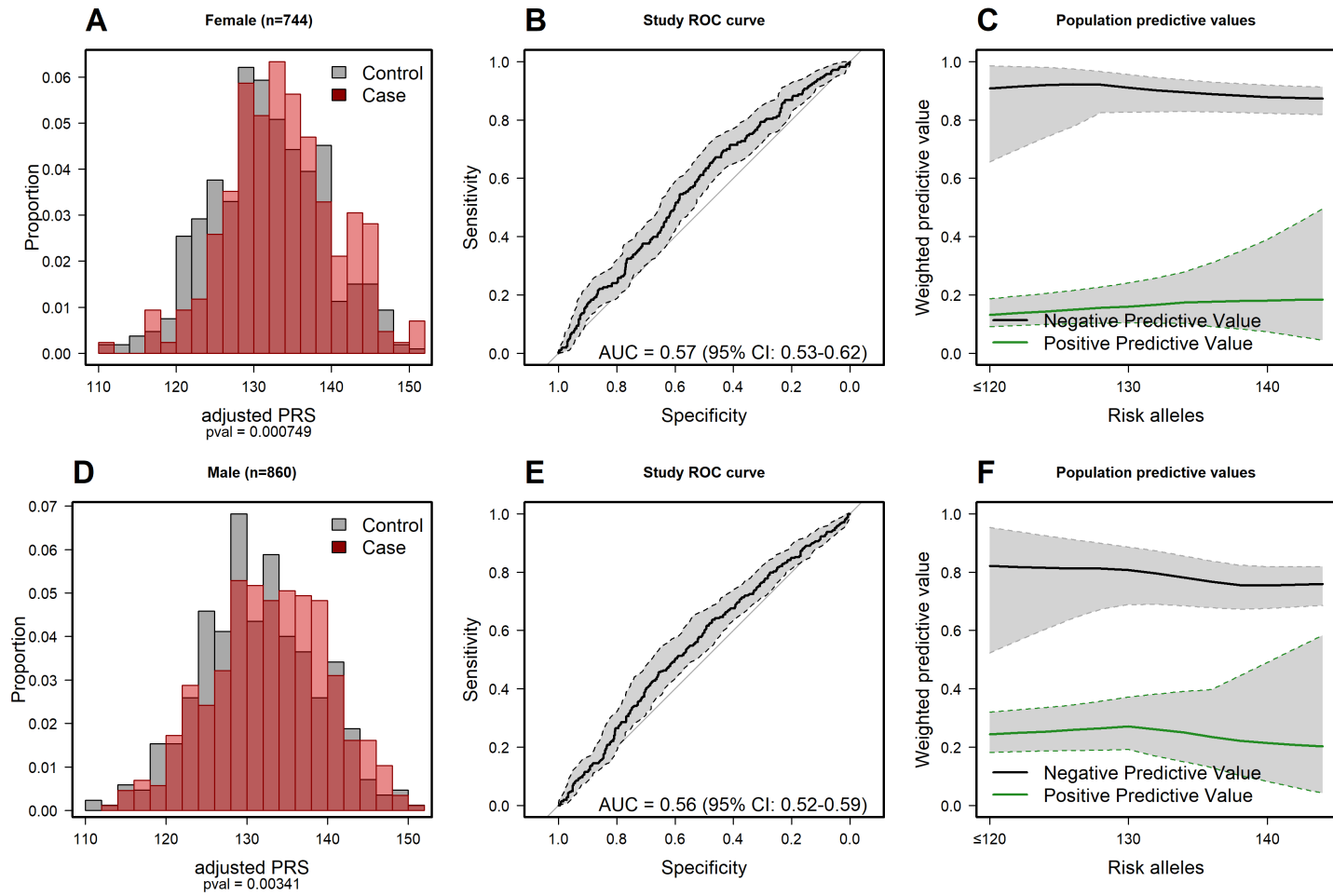
Supplementary Figure 10 (A) Distribution of the adjusted polygenic risk score among <60 years in cases and controls. (C) Receiver Operating Characteristic curve for based on 133 SNPs used to measure the area under the curve in <60 years cases compared to <60 years controls. (C) Positive and negative predicted values for the number of CRC risk alleles in <60y weighted by fecal immunochemical test (positive weight = 0.06 and negative weight = 0.94). (D) Distribution of the polygenic risk score among ≥60 years in cases and controls. (E) Receiver Operating Characteristic curve based on 133 SNPs used to measure the area under the curve in ≥60 years cases compared to ≥60 years controls (F) Positive and negative predicted values for the number of CRC risk alleles in ≥60y weighted by fecal immunochemical test (positive weight = 0.06 and negative weight = 0.94).