**Case-Only Analysis**

Among 707 cancer cases, early-onset (<50) patients were more likely to have higher PHQ-9 scores compared to late-onset cases. Depression was associated with increased odds of early-onset cancer (OR = 1.47, 95% CI: 1.11–1.93, AUC = 0.73). CRP showed no significant association (OR = 1.03, 95% CI: 0.69–1.55).

**Age-Stratified Models**

* ≥50 years (n = 3,188): Depression was not significantly associated with cancer (OR = 1.05, 95% CI: 0.96–1.15). CRP was inversely associated (OR = 0.74, 95% CI: 0.65–0.84), with modest model performance (AUC = 0.59).
* <50 years: Continuous models yielded less consistent results; depression effects attenuated, and CRP associations weakened.

**Sensitivity Analysis (<50 Excluding hsCRP >10 mg/L)**

After removing participants with very high CRP values, the results for CRP remained stable, indicating that the associations were not driven solely by acute inflammatory outliers.

**Younger Cutoff Analyses**

When focusing on progressively younger patients:

* <45 years (n ≈ 1,498): PHQ-9 was null (OR = 1.00), and CRP trended inversely (OR = 0.71, 95% CI: 0.49–1.03, AUC = 0.65).
* <40 years (n ≈ 1,160): Depression trended below 1 (OR = 0.90, 95% CI: 0.56–1.45), while CRP was significantly below 1 (OR = 0.61, 95% CI: 0.41–0.90, AUC = 0.75).

These findings do not support the hypothesis that stress and inflammation play a stronger role in the youngest cancer patients. Instead, CRP showed inverse associations in very early-onset cases.

**Stratified Analyses**

In subgroup analyses among <50 participants, PHQ-9 and CRP associations varied modestly by sex and race/ethnicity. However, wide confidence intervals and reduced sample sizes limited interpretability. No single demographic group showed consistently more potent effects.

**Propensity Score Weighting (Robustness Check for <50)**

To account for confounding by sex, race, education, smoking, and income, propensity score weighting was applied:

* **High CRP (>3 mg/L):** Weighted OR = 0.81 (95% CI: 0.59–1.12); unweighted OR = 0.83 (95% CI: 0.49–1.38). Both estimates were below 1 and not significant, suggesting no robust association between CRP and cancer in younger adults.
* **High Stress (PHQ-9 ≥10):** Weighted OR = 0.63 (95% CI: 0.43–0.91); unweighted OR = 1.09 (95% CI: 0.54–2.20). After adjusting for confounders, high stress was significantly associated with lower odds of cancer, reversing the direction observed in the unadjusted models.

This indicates that **apparent stress–cancer links in < confounding factors may explain 50 adults**, and once balanced, high stress is not a risk factor and may even show an inverse association.