



Impact of Psychiatric Comorbidities on Outcomes in Young Adults with Head and Neck Squamous Cell Carcinoma

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Introduction / Background

Head and neck squamous cell carcinoma (HNSCC) is the 7th most common cancer worldwide; tobacco, alcohol, and HPV are the principal risk factors, and incidence is rising in young adults (ages 18–45), especially oropharynx and oral cavity cancers.^{1,2} HNSCC treatment (surgery, radiation, chemotherapy, immunotherapy) affects speech, swallowing, and appearance, compounding psychosocial burden.¹ Head and neck cancer survivors carry a higher burden of anxiety and depression than many other cancer types, higher rates of smoking/heavy drinking (24.6% vs 18.0%) and a greater mental health burden (18.6% vs 13.0%), and the strongest cross-cancer link to substance use disorder (SUD).^{3,4,10} Depression in cancer is associated with treatment non-adherence and higher mortality, mediated by inflammation, immune suppression, and HPA-axis dysregulation.⁵ Anxiety and depression diagnoses have risen sharply post-COVID, particularly in adults aged 18–29,⁷ and young adults with cancer face disproportionate financial and psychological burden.⁶ Pre-existing mental health disorders are linked to increased cancer mortality and perioperative opioid use,^{8,9} while treatment of anxiety/depression is associated with reduced mortality in HNC survivors.¹¹ The independent effects of SUD, anxiety, and depression on outcomes in young adults with HNSCC remain poorly defined.

Objective / Purpose

To evaluate the association between pre-existing SUD, anxiety, and depression and post-diagnosis outcomes—mortality, healthcare utilization, and pain burden—in young adults (18–45) with HNSCC at 1-, 2-, and 5-year intervals.

Methods

- Design: Retrospective, propensity score–matched cohort study
- Data source: TriNetX Research Network — 116 healthcare organizations, ~57.2 million patients (predominantly U.S.). Data pulled June 29, 2026. IRB-exempt (de-identified data).
- Population: Patients aged 18–45 diagnosed with HNSCC 2016–2026 (ICD-10-CM).
- Exposure cohorts (each vs. controls with no SUD/anxiety/depression): SUD (F10–F19)
- Anxiety (F40–F41)
- Depression (F32–F33)
- Matching: 1:1 nearest-neighbor greedy caliper on demographics (age, sex, race, ethnicity), comorbidities (circulatory disease, diabetes, BMI, COPD, hypertension), and tumor site; SMD <0.1 = optimal balance.
- Matched cohort sizes (per group): SUD n=1,562; Anxiety n=1,568; Depression n=492.
- Outcomes at 1, 2, 5 yr: Primary — all-cause mortality. Secondary — ED visits, opioid analgesic use, cancer-related pain, chronic pain, outpatient visits (patients with the outcome before the interval excluded to assess incidence).
- Analysis: Risk ratios (RR) with 95% CI; significance p<0.05. Suicide attempt/ideation could not be analyzed (insufficient sample size).

Results

- All three comorbidities were independently associated with increased mortality across every time point. SUD showed the broadest range of adverse outcomes; anxiety and depression carried the highest mortality risk ratios.

Mortality — Risk Ratio (95% CI)

Cohort	1 year	2 years	5 years
SUD	1.59 (1.22–2.06)	1.64 (1.31–2.05)	1.49 (1.22–1.83)
Anxiety	2.40 (1.80–3.21)	2.21 (1.73–2.82)	2.07 (1.65–2.59)
Depression	2.75 (1.57–4.81)	1.87 (1.22–2.86)	1.85 (1.25–2.76)

All p<0.01.

Secondary outcomes at 5 years — Risk Ratio (95% CI)

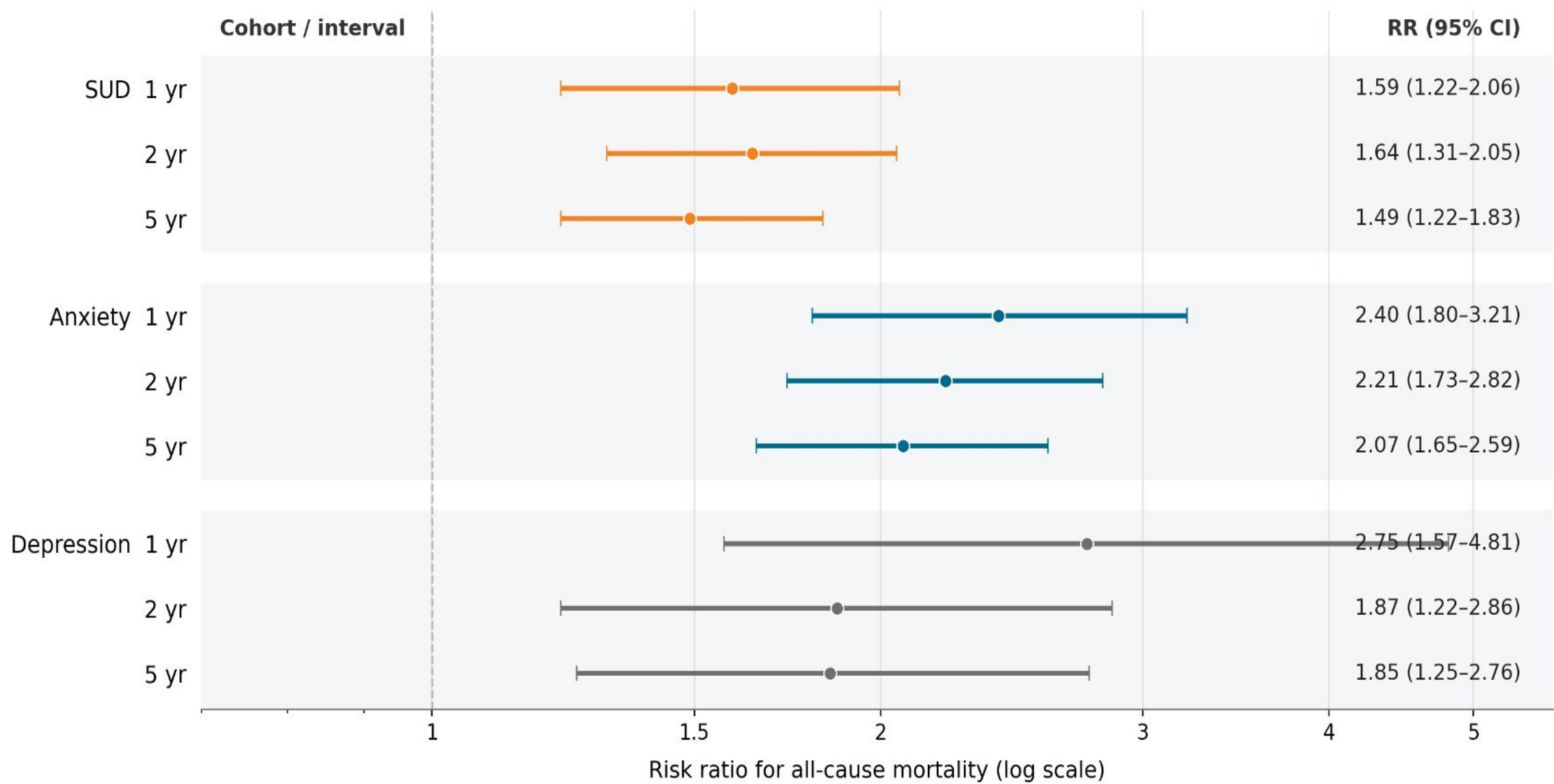
Outcome	SUD	Anxiety	Depression
ED visits	1.60 (1.42–1.80)	1.38 (1.22–1.56)	1.29 (1.05–1.60)
Opioid analgesics	1.29 (1.15–1.44)	NS	NS
Cancer-related pain	2.19 (1.76–2.71)	2.16 (1.70–2.75)	1.67 (1.08–2.58)
Chronic pain	1.98 (1.45–2.72)	2.44 (1.74–3.42)	NS
Outpatient visits	1.39 (1.17–1.65)	1.34 (1.10–1.63)	NS

NS = not statistically significant. SUD elevated for all outcomes at all intervals. Anxiety: opioid use NS at all intervals; outpatient visits significant at 2 and 5 yr only. Depression: ED visits significant at 2 and 5 yr only; opioid use, chronic pain, and outpatient visits NS at all intervals.

Results

Mortality risk ratios by comorbidity and follow-up interval

Points show RR and bars show 95% CI versus matched controls; dashed line marks RR = 1. All p < 0.01.



Conclusion

- Pre-existing SUD, anxiety, and depression are each independently associated with increased mortality, healthcare utilization, and pain burden in young adults with HNSCC.
- Anxiety and depression demonstrated the highest mortality risk ratios; SUD was uniquely associated with increased opioid analgesic use and the broadest range of adverse outcomes.
- Findings support routine screening for SUD, anxiety, and depression at HNSCC diagnosis in young adults, with tailored, integrated behavioral health, addiction medicine, pain management, and supportive oncology care; treatment of anxiety/depression has been linked to reduced mortality in HNC survivors.¹¹
- Prospective studies are needed to determine whether early identification and intervention improve survival and utilization.

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