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Abstract

Introduction
Dental restorations represent chronic oral exposures to various materials, yet their oncologic safety profile remains incompletely characterized. With billions of fillings placed annually, understanding associations with oral cavity cancer, salivary gland tumors, and precancerous lesions is essential for patient counseling and materials selection.

Methods
Retrospective cohort analysis using TriNetX US Collaborative evaluated whether dental restorations modified incident oral cavity cancer, salivary gland cancer, and oral leukoplakia risk. Patients receiving fillings (direct: amalgam/resin; indirect: crowns/inlays) before 2021 with ≥5-year follow-up were compared to controls receiving other dental care without restorations. Cohorts were propensity score-matched 1:1 for demographics, BMI, HbA1c, tobacco/alcohol/cannabis use, socioeconomic factors, comorbidities, and dental caries burden. Analyses stratified by age and restoration type.

Results
Dental fillings were associated with significantly increased oral leukoplakia (HR 1.50 [95% CI 1.12–2.00], p=0.006) and salivary gland cancer (1.93 [1.02–3.67], p=0.04) among 97,342 matched pairs. Direct restoration was associated with increased oral cavity cancer (1.48 [1.02–2.15], p=0.037) and leukoplakia (1.46 [1.09–1.96], p=0.010). Material-specific analysis showed elevated leukoplakia with resin composites (1.70 [1.23–2.34], p=0.001) and amalgam (1.62 [0.96–2.73], p=0.070). Indirect restorations showed the most pronounced leukoplakia elevation (2.21 [1.18–4.12], p=0.011) in 16,747 pairs. Age-stratified analysis revealed younger patients (18–60) had particularly elevated leukoplakia risk (1.79 [1.11–2.90], p=0.015), while patients aged 60+ showed no significant associations.

Conclusion
Dental restorations demonstrate material-specific and age-dependent associations with oral cavity malignancies and precancerous lesions. Consistent leukoplakia elevation and significantly increased salivary gland cancer risk warrant enhanced surveillance and investigation into carcinogenic mechanisms of chronic dental material exposure.

Table 1 Baseline Characteristics of Matched Dental Filling and Control Cohorts Following 1:1 Propensity Score Matching			
Characteristic	Dental Filling (n=97,884)	Control (n=97,884)	Std. Diff
Demographics			
Age at index, mean ± SD (y)	35.4 ± 21.6	35.4 ± 21.6	0.002
Female sex	53,583 (54.7%)	53,596 (54.8%)	<0.001
Male sex	44,301 (45.3%)	44,288 (45.2%)	<0.001
White	54,424 (55.6%)	53,977 (55.1%)	0.010
Black or African American	25,342 (25.9%)	25,779 (26.3%)	0.010
Hispanic or Latino	9,352 (9.6%)	9,177 (9.4%)	0.010
Asian	4,335 (4.4%)	4,360 (4.5%)	0.001
Laboratory Values			
Body mass index, mean ± SD	28.5 ± 7.8	28.2 ± 8.1	0.040
Hemoglobin A1c, mean ± SD (%)	6.22 ± 1.55	6.21 ± 1.71	0.005
Comorbid Conditions			
Essential hypertension	14,237 (14.5%)	14,335 (14.6%)	0.003
Hyperlipidemia	13,348 (13.6%)	13,119 (13.4%)	0.007
Overweight / obesity	10,963 (11.2%)	10,172 (10.4%)	0.030
Dental caries	10,773 (11.0%)	10,750 (11.0%)	0.001
GERD	9,861 (10.1%)	10,844 (11.1%)	0.030
Diabetes mellitus	6,348 (6.5%)	6,224 (6.4%)	0.005
Nicotine dependence	6,658 (6.8%)	6,897 (7.0%)	0.010
Personal history of cancer	2,576 (2.6%)	2,403 (2.5%)	0.010
Ischemic heart disease	2,627 (2.7%)	3,386 (3.5%)	0.050
Alcohol-related disorders	2,482 (2.5%)	2,577 (2.6%)	0.010
Family history of malignancy	2,477 (2.5%)	2,497 (2.6%)	0.001
Chronic kidney disease	1,819 (1.9%)	2,416 (2.5%)	0.040
Heart failure	1,337 (1.4%)	1,919 (2.0%)	0.050
Cannabis-related disorders	942 (1.0%)	938 (1.0%)	<0.001
Bariatric surgery history	400 (0.4%)	485 (0.5%)	0.010
Crohn disease	310 (0.3%)	518 (0.5%)	0.030
Social and Exposure History			
Occupational exposure (Z57)	137 (0.14%)	64 (0.07%)	0.020
Genetic susceptibility to cancer (Z15.0)	45 (0.05%)	81 (0.08%)	0.010

Table 2 Oral Cavity Cancer and Oral Leukoplakia by Restoration Type			
Restoration Type	Pairs	Oral Cavity Cancer HR (95% CI)	Oral Leukoplakia HR (95% CI)
All fillings	97,342	1.30 (0.93–1.82) p=0.12	1.50 (1.12–2.00) p=0.006
Direct (all)	88,889	1.48 (1.02–2.15) p=0.037	1.46 (1.09–1.96) p=0.010
Resin composite	81,113	0.99 (0.69–1.42) p=0.956	1.70 (1.23–2.34) p=0.001
Amalgam	25,663	0.94 (0.52–1.69) p=0.832	1.62 (0.96–2.73) p=0.070
Indirect (crowns, inlays)	16,747	1.11 (0.57–2.16) p=0.754	2.21 (1.18–4.12) p=0.011

Matched pairs shown for the largest analysis in each stratum; denominators vary slightly by outcome after exclusion of prevalent cases. Red = p<0.05 (log-rank). Salivary gland cancer (all fillings: HR 1.93, 1.02–3.67, p=0.04) had too few events for material-specific estimates.

Methods

- Retrospective 1:1 propensity-matched cohort study using the TriNetX US Collaborative Network. Patients who received a dental filling before 2021 (direct: amalgam or resin composite; indirect: crowns or inlays) with ≥5 years of follow-up were compared with patients receiving other dental care without restorations.
- Matched on age, sex, race/ethnicity, BMI, HbA1c, tobacco, alcohol and cannabis use, socioeconomic factors, comorbidities, and dental caries burden (all SMDs <0.1). Cox proportional hazards models; analyses stratified by restoration type, material, and age (18–60 vs 60+).

Figure 1

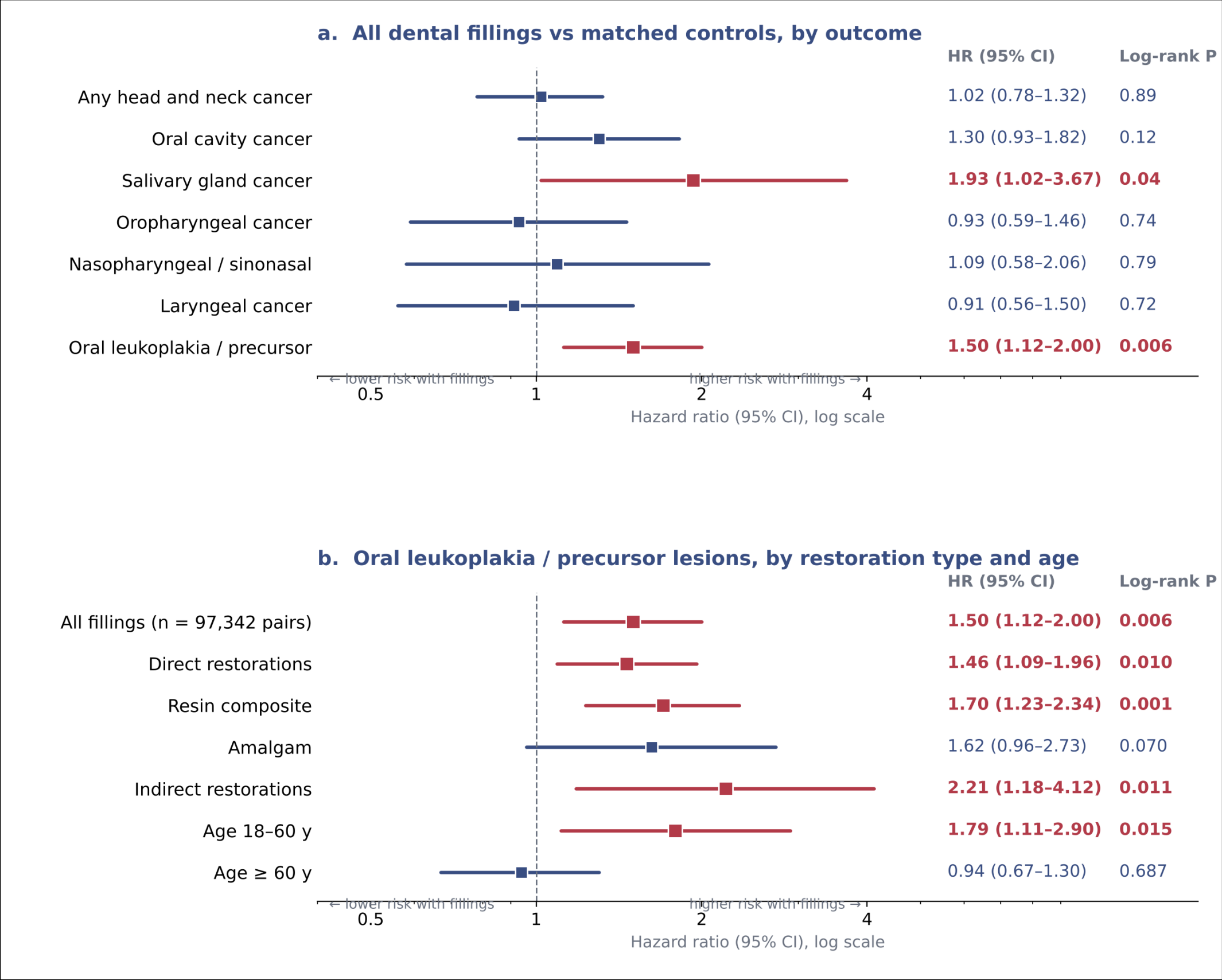


Fig 1. Dental Fillings and Incident Head and Neck Malignancy and Precursor Lesions. Forest plots of hazard ratios (95% CI) from 1:1 propensity-matched Cox models. (a) All fillings vs matched controls, by head and neck cancer subtype and oral leukoplakia. (b) Oral leukoplakia by restoration type, material, and age stratum. Red = statistically significant (p<0.05). Hypopharyngeal cancer omitted (too few events).

Results

- Among 97,342 propensity-matched pairs, dental fillings were associated with a higher incidence of oral leukoplakia and precursor lesions (HR 1.50, 95% CI 1.12–2.00, p=0.006) and salivary gland cancer (HR 1.93, 1.02–3.67, p=0.04). Any head and neck cancer overall was not increased (HR 1.02, 0.78–1.32) (Figure 1).
- Direct restorations were associated with increased oral cavity cancer (HR 1.48, 1.02–2.15, p=0.037) and leukoplakia (HR 1.46, 1.09–1.96, p=0.010). Resin composite carried a significant leukoplakia signal (HR 1.70, p=0.001); amalgam trended in the same direction (HR 1.62, p=0.070). Indirect restorations showed the largest leukoplakia elevation (HR 2.21, 1.18–4.12, p=0.011) (Table 2).

Subgroup Analyses

- Leukoplakia risk was elevated in patients aged 18–60 (HR 1.79, 1.11–2.90, p=0.015) but not in patients aged 60+ (HR 0.94, 0.67–1.30)
- No malignancies or precursor lesions were observed in the pediatric subgroup
- Oropharyngeal, nasopharyngeal/sinonasal, and laryngeal cancers were not associated with fillings in any stratum
- Oral cavity cancer was significantly increased only for direct restorations as a group; material-specific estimates (resin, amalgam) were null
- Salivary gland cancer was elevated for all fillings combined; material-specific analyses had too few events
- Indirect restorations showed the strongest leukoplakia association despite the smallest cohort (16,747 pairs)

Discussion/Conclusion

- Dental restorations were associated with higher rates of oral leukoplakia and salivary gland cancer, and direct restorations with higher rates of oral cavity cancer, compared with matched patients receiving dental care without restorations.
- The leukoplakia signal was consistent across direct, resin, amalgam, and indirect restorations, with the largest estimate for indirect restorations. A material-independent signal points toward shared mechanisms such as chronic mucosal irritation, lichenoid contact reactions, or persistent low-grade release of resin monomers and metal ions.
- Associations were concentrated in patients aged 18 to 60 and absent in patients 60 and older, where competing risk factors and higher baseline incidence may dilute any restoration-specific effect.
- Absolute risks remain low (incident leukoplakia 0.12% vs 0.08%). These findings do not argue against restorative care; they support routine mucosal examination adjacent to restorations and further study of the carcinogenic potential of long-term dental material exposure.
- Limitations include reliance on billing codes for exposures and outcomes, residual confounding by oral hygiene and HPV status, and the inability to characterize restoration size, location, or duration.

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