Risk of Head and Neck Cancers from Gastroesophageal Reflux Disease: A Single Institution Study

Nicolas Jo, BS[1]; Janice Huang, MS[2]; Garrett Forman, BS[2]; Isildinha M Reis, PhD[2], Elizabeth Franzmann, MD[2]

[1]Florida International University Herbert Wertheim College of Medicine, [2]University of Miami Miller School of Medicine

Introduction

Gastroesophageal reflux disease (GERD), affects 20% of the US population and occurs when stomach contents reflux into the esophagus, causing a range of acute and chronic symptoms.[1] Barrett's esophagus, a well-understood complication of GERD, often plays a role as a precursor for esophageal adenocarcinoma through the metaplasia-dysplasia-carcinoma sequence[2]. The literature of Barrett's esophagus has shown effects and role of acid reflux in inflammation, oxidative stress, and other cellular changes in carcinogenesis of the esophagus.[3]

While adenocarcinoma progression is well-defined, associations with squamous cell carcinoma and cancers of other sites along the upper aero-digestive tract (UADT) such as in the pharynx, oropharynx, hypopharynx, nasopharyngeal, and larynx are less clear.[4] Previous reviews identified a potential positive association between GERD and laryngeal squamous cell carcinoma.[4] This study is aimed towards identifying the risk of developing various head and neck cancers from a diagnosis of GERD from a single center, patient-chart database.
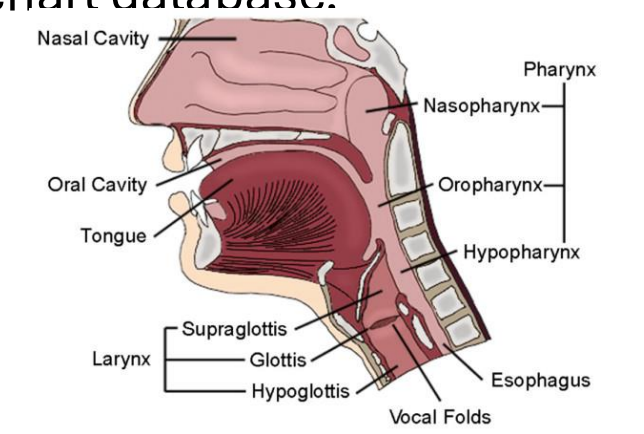
Figure 1. UADT Track[5]

Methods

We analyzed a dataset of patient visits at various University of Miami outpatient clinics between 2010 to 2024. Data points were defined as patient clinic visits and the information collected from these visits. Data from visits were collapsed together by participant ID, which was used to determine associations between a history of GERD and a diagnosis of head/neck cancers.

Preliminary data analysis has been performed using R and SPSS. Descriptive analysis included summary statistics for age, gender distribution, tobacco use, and cancer history in individuals with and without GERD. The exposure variable was GERD or GERD-like symptom diagnosis, and the outcome variable was head/neck cancers diagnosis according to patient charts during the study timeframe. Risk analysis was calculated to determine OR. Patients with head/neck cancers were compared to all patients who did not develop head/neck cancers. Logistic regression was used to estimate odds ratio (OR) of head/neck cancer diagnostic and multinomial logistic regression was used to estimate ORs for anatomical subsites comparing GERD and non-GERD groups.

Results

289,597 unique patients from 581,416 patient visit data points were collected. Of these, 27,457 patients were included in the GERD group, and 289,597 patients were included in the non-GERD group. Data points included ICD-9 and ICD-10 codes of GERD or GERD-like symptoms, cancer diagnosis and type, diagnosis year, and reflux medication use.
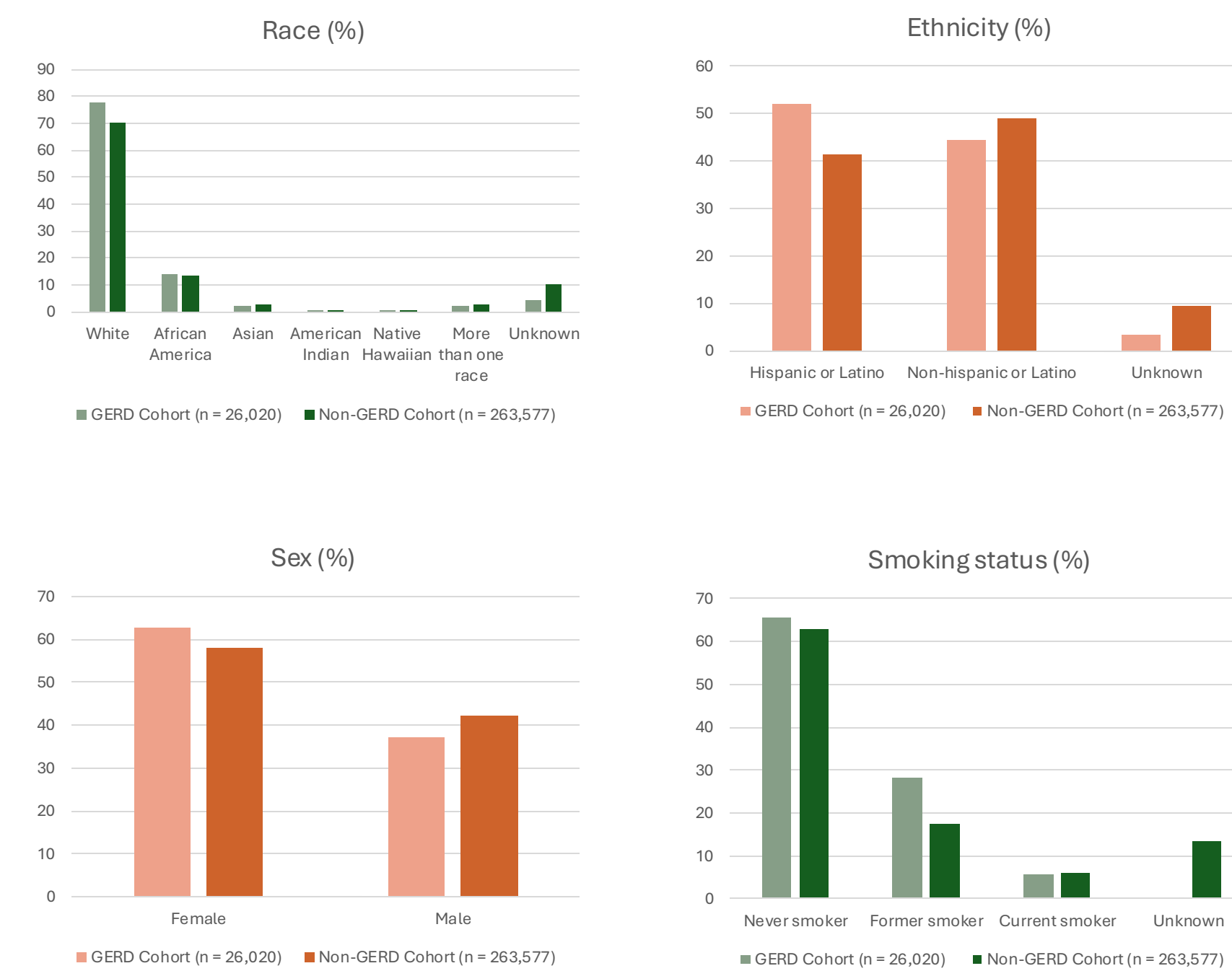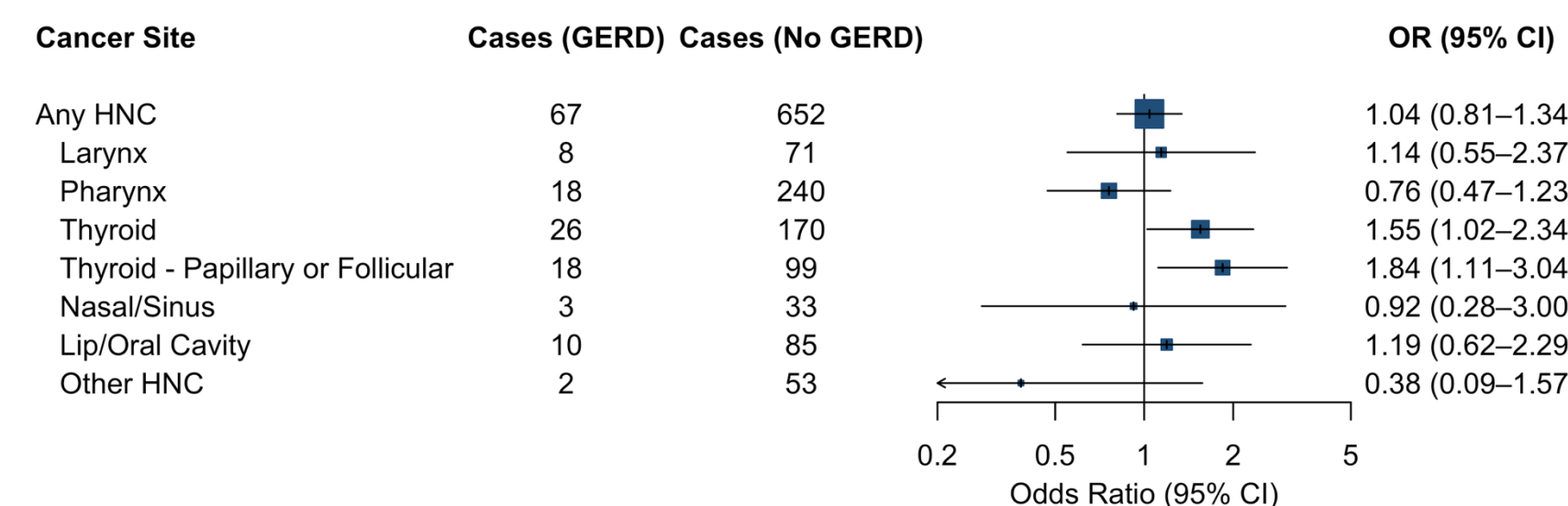
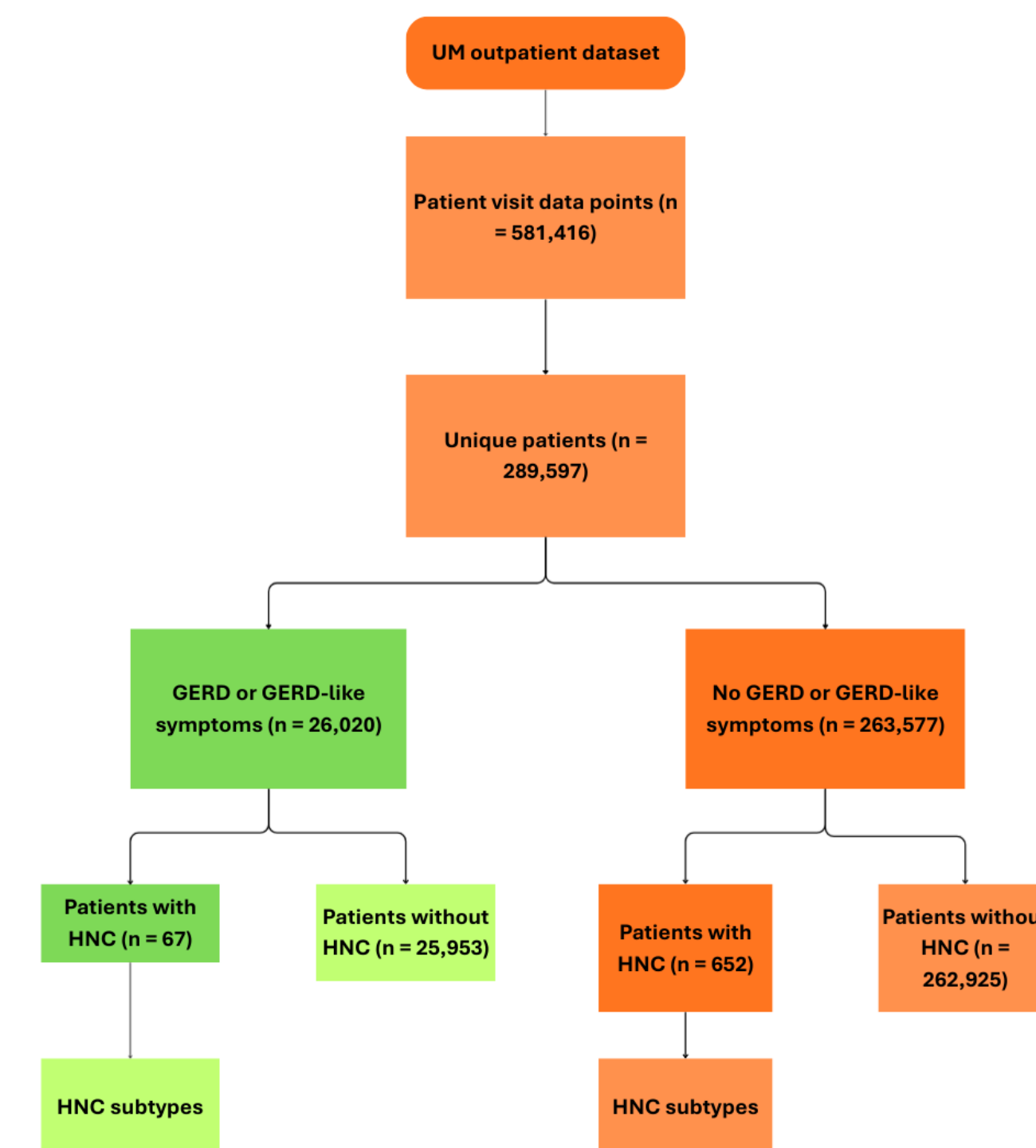**Figure 2. Demographics of study population**

Figure 3. Flow chart of data stratification

Cancer Site	Cases (GERD)	Cases (No GERD)	OR (95% CI)
Any HNC	67	652	1.04 (0.81–1.34)
Larynx	8	71	1.14 (0.55–2.37)
Pharynx	18	240	0.76 (0.47–1.23)
Thyroid	26	170	1.55 (1.02–2.34)
Thyroid - Papillary or Follicular	18	99	1.84 (1.11–3.04)
Nasal/Sinus	3	33	0.92 (0.28–3.00)
Lip/Oral Cavity	10	85	1.19 (0.62–2.29)
Other HNC	2	53	0.38 (0.09–1.57)

Figure 4. OR of Head/Neck Cancers

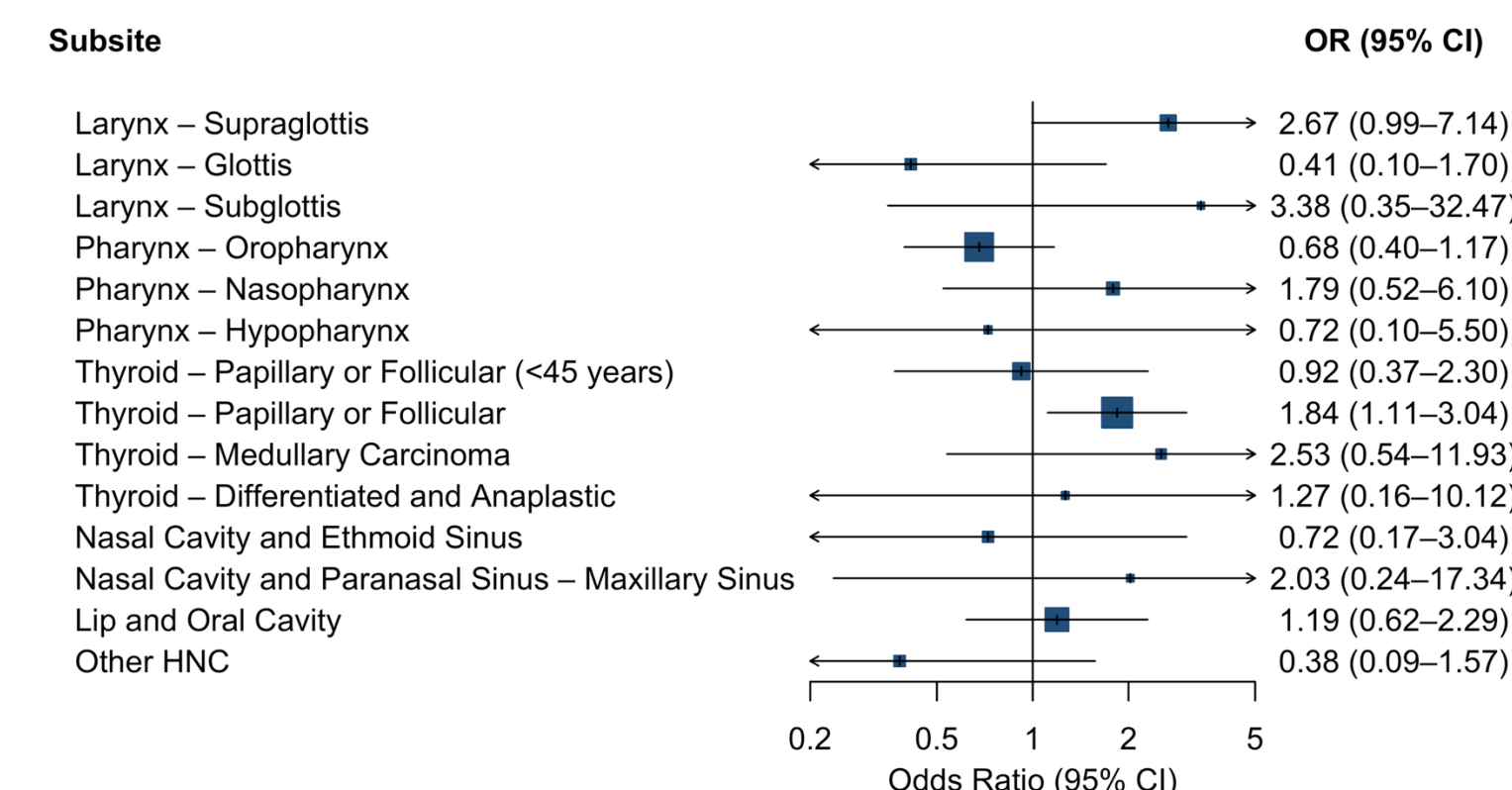| Subsite	OR (95% CI)
Larynx – Supraglottis	2.67 (0.99–7.14)
Larynx – Glottis	0.41 (0.10–1.70)
Larynx – Subglottis	3.38 (0.35–32.47)
Pharynx – Oropharynx	0.68 (0.40–1.17)
Pharynx – Nasopharynx	1.79 (0.52–6.10)
Pharynx – Hypopharynx	0.72 (0.10–5.50)
Thyroid – Papillary or Follicular (<45 years)	0.92 (0.37–2.30)
Thyroid – Papillary or Follicular	1.84 (1.11–3.04)
Thyroid – Medullary Carcinoma	2.53 (0.54–11.93)
Thyroid – Differentiated and Anaplastic	1.27 (0.16–10.12)
Nasal Cavity and Ethmoid Sinus	0.72 (0.17–3.04)
Nasal Cavity and Paranasal Sinus – Maxillary Sinus	2.03 (0.24–17.34)
Lip and Oral Cavity	1.19 (0.62–2.29)
Other HNC	0.38 (0.09–1.57)

Figure 5. OR of Head/Neck Cancer by subsite

Discussion

Preliminary logistic regression demonstrated an overall head/neck cancer OR of 1.042 (95% CI = 0.81, 1.34). Multinomial logistic regression by head/neck cancer subsite demonstrates a notable increase in risk for supraglottic and subglottic cancers, but this association is not significant and lacks power (OR = 2.667, 95% CI = 0.995 – 7.141; OR = 3.378, 95% CI = 0.351 – 32.467). There is a suggestion of association with papillary and follicular thyroid cancer, but the sample size is too small to conclude this (OR = 1.842, 95% CI = 1.115 – 3.044, n = 26). Previous studies have demonstrated adjusted hazard ratio of 1.91 between GERD and thyroid cancers[6], but this association was statistically insignificant after controlling for surveillance bias and further study is required to determine the significance of the finding in this study.

Further analysis is planned with multivariate regression as well as matching cases to controls to account for smoking, gender, age, and other covariates that may also influence risk. These factors can contribute to the complexity of these associations, such as in smoking, as a known risk factor for GERD[7] as well as various head/neck cancers.[8] Smoking status could function as a potential confounder or even as a mediator between GERD and head/neck cancers. Other potential relationships between these factors requires further analysis. Overall, current analysis suggests no significant associations between GERD and head/neck cancer

References

[1] Antunes C, Aleem A, Curtis SA. Gastroesophageal Reflux Disease(Archived) [Updated 2023 Jul 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441938/

[2] Richter JE, Rubenstein JH. Presentation and epidemiology of gastroesophageal reflux disease. Gastroenterology. 2018;154(2):267-276. doi:10.1053/j.gastro.2017.07.045

[3] O'Riordan JM, Abdel-latif MM, Ravi N, et al. Proinflammatory cytokine and nuclear factor kappa-B expression along the inflammation-metaplasia-dysplasia-adenocarcinoma sequence in the esophagus. The American Journal of Gastroenterology. 2005;100(6):1257-1264. doi:10.1111/j.1572-0241.2005.41338.x

[4] Eells AC, Mackintosh C, Marks L, Marino MJ. Gastroesophageal reflux disease and head and neck cancers: A systematic review and meta-analysis. American Journal of Otolaryngology. 2020;41(6):102653. doi:10.1016/j.amjoto.2020.102653

[5] Liebertz DJ, Lechner MG, Masood R, et al. Establishment and characterization of a novel head and neck squamous cell carcinoma cell line USC-HN1. Head & Neck Oncology. 2010;2(1). doi:10.1186/1758-3284-2-5

[6] Tran CL, Han M, Kim B, Park EY, Kim YI, Oh J. Gastroesophageal reflux disease and risk of cancer: Findings from the Korean National Health Screening Cohort. Cancer Medicine. 2023;12(18):19163-19173. doi:10.1002/cam4.6500

[7] Maret-Ouda J, Markar SR, Lagergren J. Gastroesophageal reflux disease. JAMA. 2020;324(24):2536. doi:10.1001/jama.2020.21360

[8] Lander DP, Kallogjeri D, Piccirillo JF. Smoking, drinking, and dietary risk factors for head and neck cancer in prostate, Lung, colorectal, and ovarian cancer screening trial participants. JAMA Otolaryngology–Head & Neck Surgery. 2024;150(3):249. doi:10.1001/jamaoto.2023.4551

Acknowledgements