# Patients with Primary Immunodeficiencies Have Higher Rates of Head and Neck Cancer and Worse Outcomes

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## BACKGROUND

- Primary immunodeficiency disorders (PID) are associated with an increased risk of malignancy (skin and hematologic) potentially due to decreased surveillance of dysplastic cells and/or increased risk of persistent oncogenic infection[1,2]
- Immunocompromised patients are at an increased risk of head and neck cancer (HNC)[3,4]
- HNC incidence and outcomes in patients with PID has not been investigated

## OBJECTIVES

1) Determine the rate of HNC among patients with PID compared to the general US population
2) Determine the rate of mortality, lung metastases, failure to thrive and malnutrition in patients with HNC and PID, compared to those without PID
3) Determine the rate of post-operative infection and sepsis in patients with HNC and PID, compared to those without PID

## METHODS

*Data sources*
- TriNetX: global health research network of deidentified EMRs
- NCI SEER 22-registry database[5]

*Incidence Study*
- Created PID cohort using TriNetX and general population cohort using SEER database
- TriNetX Cohort
  - Patients with PID ≥1 year and no HIV history; 2017–2021
  - Determined annual incidence of oral cavity/pharyngeal & laryngeal cancers via TriNetX "Incidence & Prevalence" function
- SEER Cohort – general population
  - Pooled US HNC incidence from 2017–2021, calculated incidence rate per 100,000 by age using *SEER*Stat*
- Determined standardized incidence ratio (SIR) and 95% CI

*Overall Outcomes*
- PID cohort: Age ≥ 18, PID diagnosis preceding HNC
- No PID cohort: Age ≥ 18, HNC without PID
- Exclusion criterion: HIV infection
- Index event: HNC diagnosis
- Compared the following HNC outcomes by PID status: rate of mortality, lung metastasis, failure to thrive, malnutrition

*Post-Operative Outcomes*
- PID HNS Cohort: Age ≥ 18, PID preceding HNC + surgery
- No PID HNS Cohort: Age ≥ 18, HNC + surgery, no PID
- Exclusion criterion: HIV infection
- Index event: first head & neck surgery
- Compared the following by PID status: rate of infection, sepsis, skin/soft tissue infection

*Statistical Analysis for Outcomes Analysis*
- 1:1 propensity matching (age, sex, race, ethnicity, tobacco/alcohol use, AJCC stage)
- Advanced analytics for association[6]
- Statistical significance $p \leq 0.05$

## CONTACT

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## RESULTS

- **PID patients**: ↑ risk of oral/pharyngeal (4.9x) and laryngeal (4.4x) cancers, especially in younger cohorts
- After 1:1 propensity matching, cohorts of patients with HNC with and without PID each contained 7,057 patients
  - Average age 62.5, 65.2% male, ~75% white, 78.3% non-Hispanic, 13.5% alcohol users, and 10.2% tobacco users
- **HNC + PID**: ↑ mortality, recurrence, failure to thrive, malnutrition
- After 1:1 propensity matching, cohorts of patients with HNC and head and neck surgery with and without PID each contained 4,145 patients
  - Average age 62.4, ~66% male, ~75% white, ~77% non-Hispanic, 17.5% alcohol users, and 14.6% tobacco users
- **HNC surgery + PID**: ↑ post-op complications (e.g., infections)

## FIGURES & TABLES

**Table 1:** HNC incidence PID patients vs. general US population

| Cancer Subsite | Age Cohort | Population | No. observed cases | No. expected cases | US Incidence per 100,000 | SIR (95% CI) |
|---|---|---|---|---|---|---|
| Oral cavity and pharynx | 40-44 | 20,176 | 19 | 1.08 | 5.37 | 17.6 (10.5-26.3) |
| | 45-49 | 24,407 | 19.5 | 2.52 | 10.3 | 7.74 (4.69-11.6) |
| | 50-54 | 30,247 | 41.8 | 5.67 | 18.8 | 7.37 (5.30-9.77) |
| | 55-59 | 37,954 | 58.8 | 10.9 | 28.8 | 5.37 (4.09-6.83) |
| | 60-64 | 42,426 | 74 | 15.8 | 37.3 | 4.68 (3.67-5.80) |
| | 65-69 | 42,861 | 82.8 | 18.5 | 43.3 | 4.47 (3.56-5.48) |
| | 70-74 | 33,177 | 61.6 | 15.2 | 45.9 | 4.04 (3.10-5.12) |
| | 75-79 | 20,351 | 40.4 | 9.63 | 47.3 | 4.20 (3.00-5.59) |
| | 80-84 | 9,765 | 16 | 4.64 | 47.5 | 3.45 (1.97-5.35) |
| | Overall | | | | | **4.93 (4.43-5.37)** |
| Larynx | 55-59 | 38,857 | 18.3 | 2.57 | 6.62 | 7.12 (4.24-10.8) |
| | 60-64 | 42,651 | 18.6 | 4.15 | 9.73 | 4.48 (2.68-6.75) |
| | 65-69 | 42,983 | 19 | 4.92 | 11.5 | 3.86 (2.32-5.79) |
| | 70-74 | 32,930 | 14.8 | 4.14 | 12.6 | 3.58 (1.99-5.63) |
| | 75-79 | 22,362 | 12 | 2.83 | 12.7 | 4.24 (2.18-6.97) |
| | Overall | | | | | **4.44 (3.58-5.51)** |

**Figure 2:** Post-operative outcomes of HNC in patients with vs. without PID

Odds ratio (95% CI) of sepsis, post-operative infections, and skin or soft tissue infections in the 30 days following initial head and neck surgery in HNC patients with vs. without PID

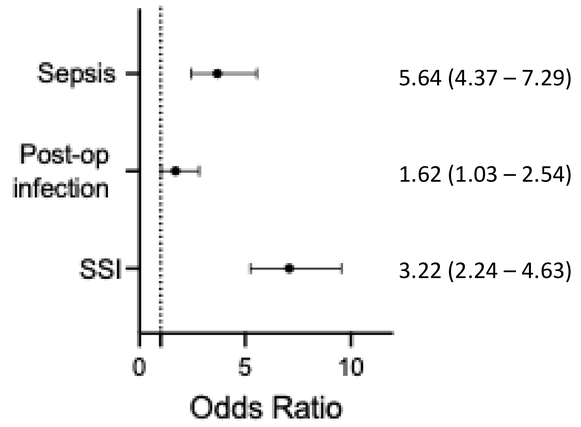
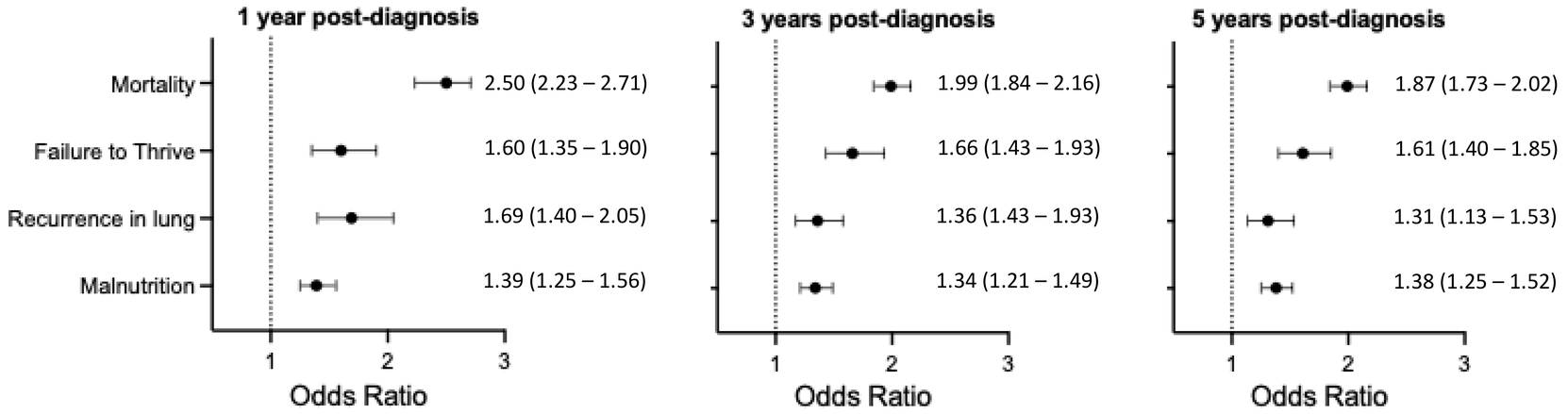



**Figure 1:** Overall HNC outcomes in patients with or without PID

Odds ratio (95% CI) of mortality, failure to thrive, recurrence in lung, and malnutrition in HNC patients with PID compared to patients without PID at 1-year, 3-years, and 5-years post-HNC diagnosis




## DISCUSSION & CONCLUSIONS

**Findings**
- PID patients: ↑ HNC risk, especially at younger ages
- PID + HNC: worse outcomes, ↑ mortality, recurrence, malnutrition, failure to thrive
- PID + HNC surgery: ↑ post-op risks, infection, sepsis

**Potential Mechanisms/Areas of Future Research**
- Impaired immunosurveillance of dysplastic cells
- ↑ rate of HPV infection & decreased clearance

**Implications for Patient Care**
- Consider increased HNC screening in patients with PID
- More aggressive treatment strategies may be warranted
- Explore the role of immunotherapy in this population

**Limitations**
- Unable to distinguish HPV+ vs. HPV- HNC in TriNetX/SEER
- TriNetX: limited data on rare outcomes to protect patient privacy, unable to assess HNC rates by PID subtype

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