Evolving disparities in the epidemiology of oral cavity and oropharyngeal cancers

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Introduction

- Recent years have seen increasing recognition that HPV is a causative agent for some specific cancers within the head and neck cancer group (HNC).
- Incidence rates of HPVa HNCs are increasing while non-HPVa rates have declined.
- The scope of oral HPV infection is becoming better understood (e.g. 6.9% of those aged 14-69 have an oral HPV infection, with 1.0% having an infection with oncogenic variant HPV type 16).

Introduction - II

- Over the last 35 years, rates of oropharyngeal cancers have significantly declined for black men but increased for white men, resulting in significantly higher rates among white men.
- Between 1983 and 2002 HNC incidence rates were higher and increased more sharply among men than women.
- Patients with oral cavity cancer in rural settings had worse outcomes compared to patients residing in urban areas.
- There lacks an extensive evaluation of the effect of rurality on incidence of oropharyngeal and oral cavity cancers.

Introduction - III

- The lifetime risk of HPV for those with at least one opposite-sex partner is 84.6% for females and 91.3% for males.
- HPV is an etiological agent for the oropharynx (OPHY; present in 40%-90% of cancers). HPV type 16 is associated with ~90% of oropharyngeal squamous cell carcinomas
- Incidence rates for HPVa HNCs are increasing, while rates of tobacco-related HNCs are decreasing, resulting in a dramatic shift in the ratio of HPVa/non-HPVa cancers (e.g., 0.72 to 3.81 in Colorado from 1980-2004).
- Much of the increase in HPVa cancers is especially prominent among those of younger age and white race.

Introduction - IV

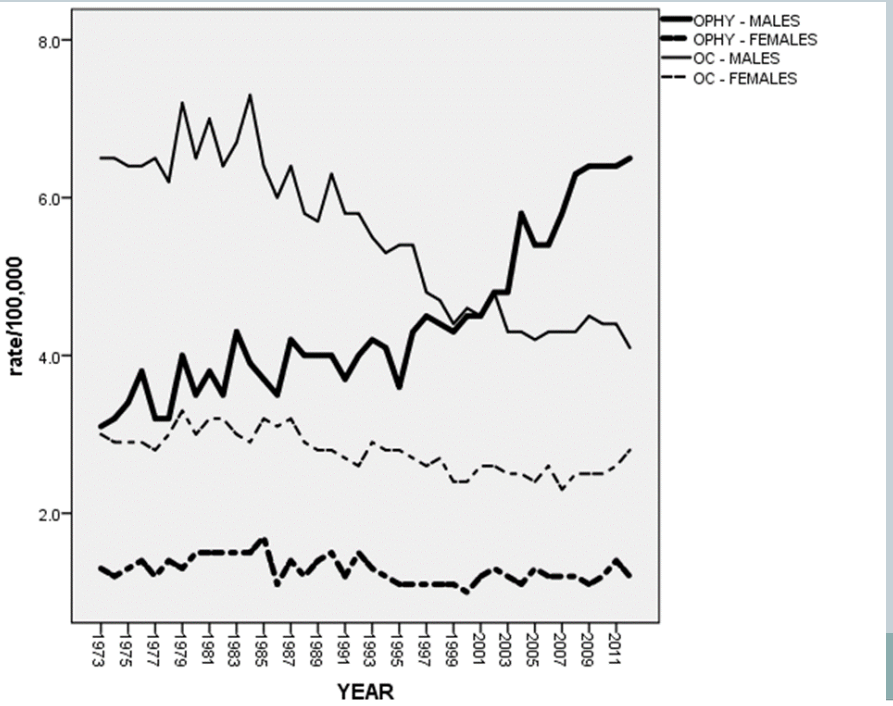
- HPV vaccination is not a panacea.
- 72% of OPHY SCC were positive for HPV, and 86% of those specific for types 16/18. Cervarix/Gardasil may prevent upwards of 62% of such cancers.
- As a result of vaccination, the prevalence of HPV-6, -11, -16, or 18 has significantly decreased, but only among females aged 14-19.
- HPV vaccination uptake and completion is low and variable (by gender and race), where only 1.3% of M and 34.8% of F aged 13-17 had received ≥3 doses.
- Males and females living in rural areas were less likely to complete 3 doses.
- There are likely to remain gaps in prevention associated with the vaccine itself (not coving all risk variants) and unequal uptake by gender, race, geographical region, and rural/urban residence.

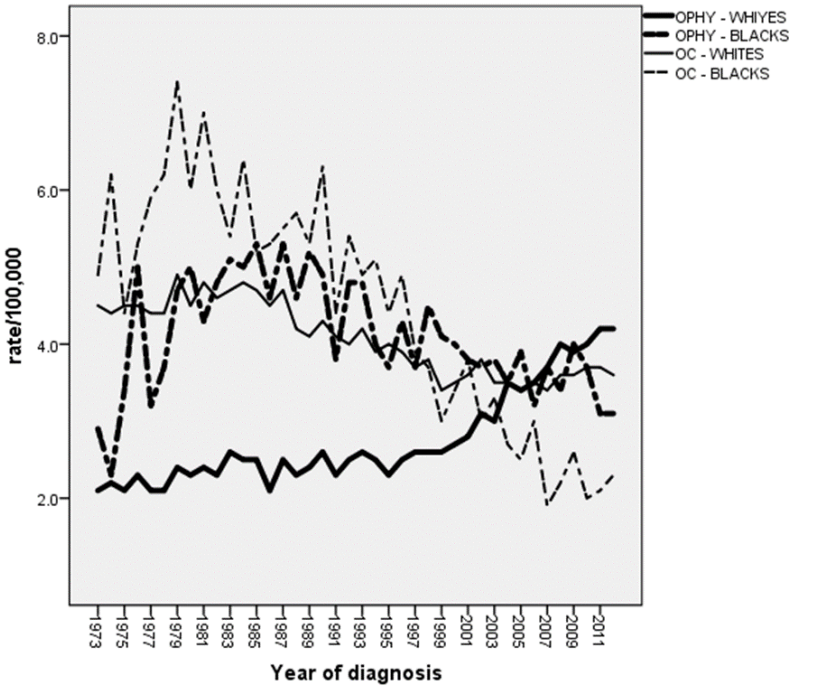
Methods

- We used SEER 9 data to analyze trends and differences by gender and race.
- We used SEER 18 data to assess differences by geographic-based registry and rurality.
- We used ICD-O-3 codes as described by Chaturverdi et al to categorize cancers as either associated with HPV infection (OPHY) or non-HPV associated (OC).
- Among head and neck squamous cell carcinomas, the majority of the HPVa cancers are found within the oropharyngeal subsite (mainly in the base of tongue and tonsillar tissue). This is in contrast to the oral cavity where the majority of squamous cell carcinomas are non-HPVa and more likely related to alcohol and tobacco exposure.
- To assess rural-urban differences, we used two measures.
  - RUCCs range from 1 (most metropolitan) to 9 (most rural)
  - percent urban (%U) was split into equal quartiles (0.00-25.0%, 25.01-50.00%, 50.01-75.00%, and 75.01-100%).
- SEER*Stat was used to compute age-adjusted incidence rates, incidence rate trends, and to determine significance. SPSS was used to create graphs and calculating male/female rate ratios. Joinpoint analysis was performed using Joinpoint Regression Program 4.2.0.1 to assess temporal trends and annual percentage change (APC).

Results - Analysis of annual rate trends over time

- The overall trends for the two groups were opposite over time (i.e. OC decreased 24.8% and OPHY increased 74.4%
- These changes were largely driven by males. While female rates of OPHY decreased 10.3%, male rates increased 106.2%. OPHY.
- Black incidence for both cancers are now lower than whites This is driven in large part by the greater decrease in OC among blacks (54.1% vs. 19.3%) and greater increase in OPHY among whites (100.3% vs. 6.8%).



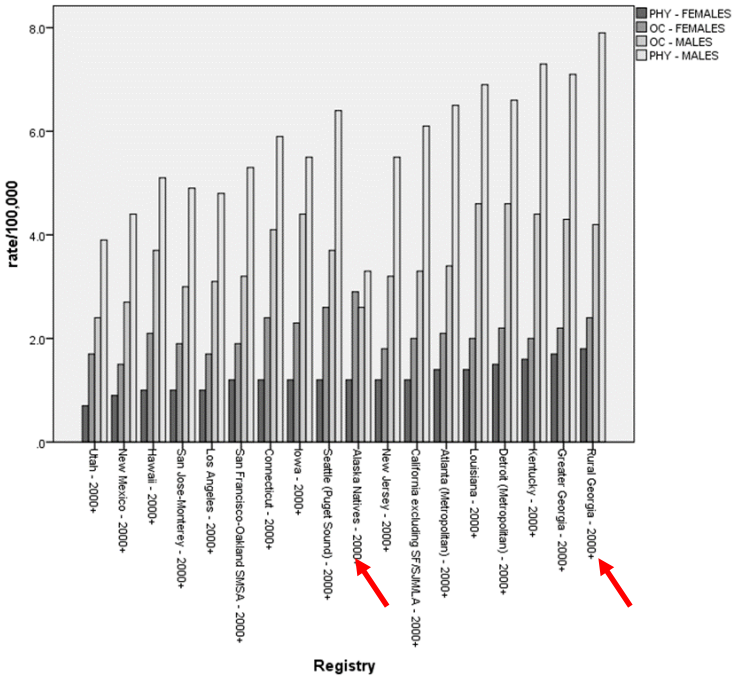


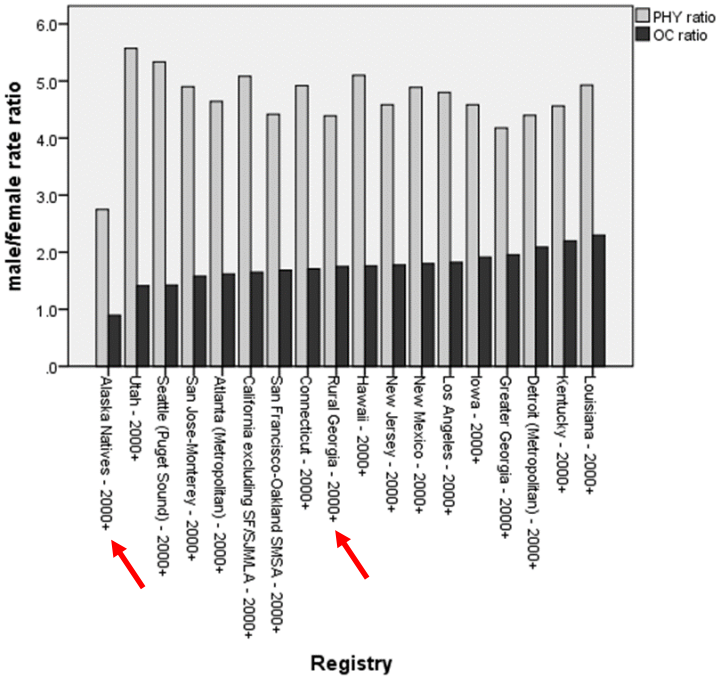
Results - Joinpoint analysis for trends

- **For OC**, rural non-adjacent counties experienced a very modest, but significant increase in rates (APC=0.68), while rural adjacent counties experienced no significant trends.
- Urban counties previous reductions (1983-2005; -2.02), are now plateaued.
- Direction and magnitude of temporal trends differed by SEER registry, New Mexico, Detroit, Hawaii, and Seattle experienced incidence reduction during their most recent trends while Connecticut and Iowa experienced increases.
- Early reductions by gender have both plateaued since 2007.
- Whites have recently plateaued while black rates are now decreasing.
- **For OPHY**, all rural and urban designations have experienced significant upward trends in OPHY.
- Rural counties had an APC of 4.80 (1991-2012) versus urban counties APC of 2.76 (1999-2012).
- Similar trends were seen for the three category groupings of RUCC and for the quartiles of percent urban.
- All SEER registries experienced significant increasing trends in OPHY in the most recent identified trend period.
- Males experienced a recent upward trend with APCs of 3.48, respectively, between 1999 and 2012.
- OPHY increased in whites (APC=3.82; 1998-2012), but decreased in blacks (APC=-157; 1983-2012).

Results - Analysis of rate differences by geography

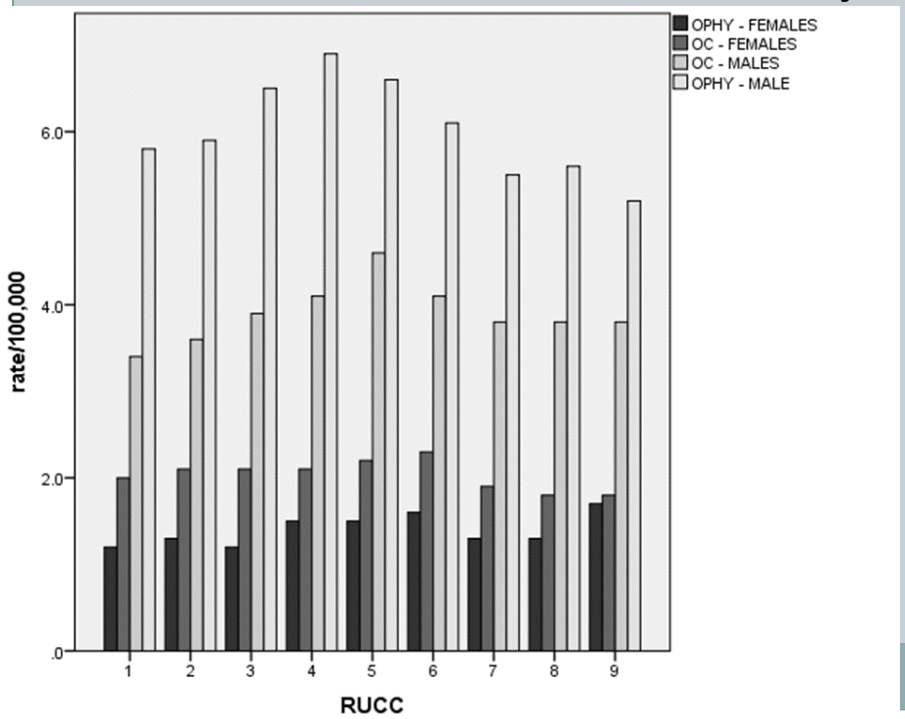
- Males have higher incidence rates for each registry and cancer group (except AN and rGA). There were significant rate differences across registries, indicating variable prevalence of risk factors. This is particularly highlighted in that not all registry-by-registry gender comparisons were significantly different for both cancer groups. For example, OC incidence rates among males in Los Angeles and New Jersey were 3.1 and 3.2 (nonsig), while OPHY rates are 4.8 vs. 5.5 (sig).
- To assess the male influence on rates, we calculated the M/F rate ratio and stratified it by the 18 registries. A relevant finding here is that the rate ratio for OPHY cancers (mean: 4.7; range: 2.8-5.6) was consistently greater than OC (mean: 1.7; range: 0.9-2.3) except for AN and rGA, indicating that male influence in overall rate was significantly increased for OPHY for nearly all registries.

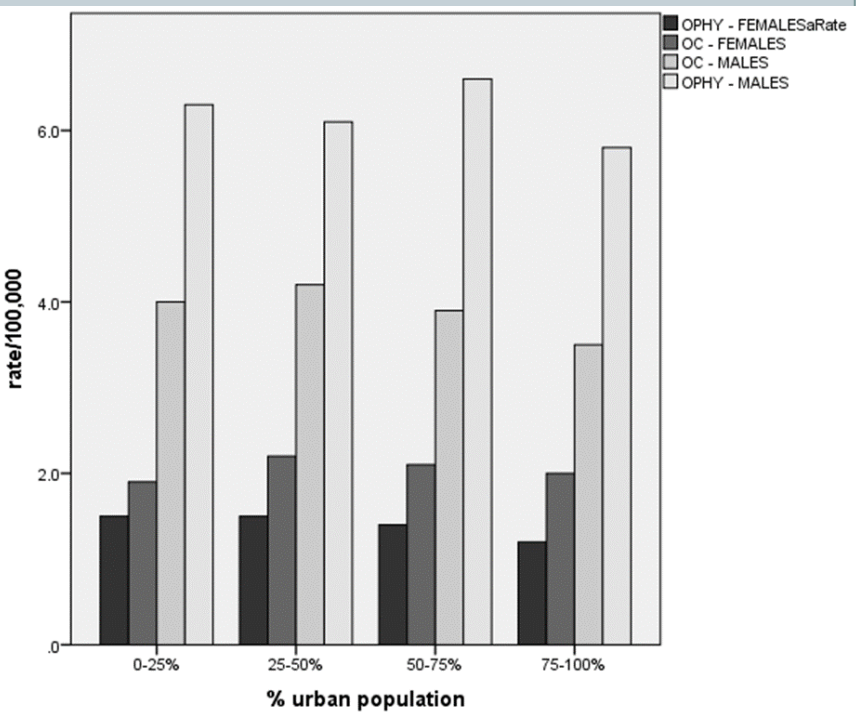




Results - Analysis of rate differences by level of rurality

- At every level of rurality, the male cancer rate exceeded that for females. The rates for both OPHY and OC occasionally varied significantly by RUCC, and the differences across RUCC were similar between males and females OPHY.
- Further, though there were statistically significant differences between selected RUCCs, the tight range of incidence rates indicates that the differences may be of limited clinical significance.
- Similar results were found for the alternative analysis, %U, showing consistency of results from two measures of rurality.





Overview

- Cancers of the OC and OPHY have received much attention of late due to the increasing incidence of HPV associated cancers.
- We analyzed SEER 9/18 data to examine how incidence of HPVa cancers corresponded to non-HPVa cancers while stratifying by gender, race, geography, and rurality.
- During this time, OC cancers decreased 30.4% while OPHY increased 46.3%.
- Male incidence rate changes largely drove these changes, with OC cancers decreasing 2.5 times as much as females and male OPHY increasing at nearly twice the pace of female decrease.
- Whites now have a higher rate of OPHY for both cancer groups than blacks – a reversal from the beginning of SEER 9 in 1973.

Impact of geography

- We found that rates are not constant across registries, indicating potential variations in risk by geography.
- Incidence rate variations were frequently discordant by cancer group, registry, and gender. This indicates that not only are there potential geographical differences in risk, but that risk may vary by gender.
- The M/F rate ratio was greater for OPHY versus OC cancers across all registries except rGA and AN, but that dominance varied discordantly with the male dominance in OC. This suggests that, while males are always at increased risk of both cancers, this risk was both disproportionately great in OPHY cancers and varied by location.
- Examination by levels of rurality showed that incidence significantly varied in a discordant fashion by gender, cancer group, and level of rurality. Such data may provide impetus for augmented HPV vaccination outreach in rural areas and among males where uptake rates are frequently lower.

Trends

- Joinpoint regression analysis noted, in general, that OC cancers had decreasing or plateauing temporal trends, while OPHY cancers showed increasing trends.
- This was true regardless of rurality, gender, race, or SEER registry.
- Although data regarding individual tobacco use and HPV infection status are not included for cases in SEER registries, both of these trends correspond to reduced tobacco use and increased HPV infection rates, respectively.
- We found that although trends were roughly the same across rural/urban groupings and registries, there were differences in magnitude of trends suggesting that the risk and impact of such trends may have a rural-urban and geographic effect.

Conclusion

- Our findings note that HPVa head and neck cancers are increasing among multiple population groups.
- While the development and implementation of HPV vaccination may help to address this increase in incidence rates, there are a potential issues that warrant ongoing study on the trends and evolution of these cancers.
- There are weaknesses in both the type coverage of existing vaccines and their uptake generally and among some selected populations. While focused interventions may address these in part, they are unlikely to be eliminated in the foreseeable future.
- Also worthy of consideration is how decreased prevalence of vaccine-targeted HPV types may provide opportunity for other variants to increase. It is unknown if lower prevalence types such as 35 or 39 might increase in response to decreases in 16/18.
- Further, even Gardasil 9 only protects against 7 of the 15 known oncogenic HPV types. Though HPV may not have the mutation susceptibility of its RNA cousins, the widespread institution of HPV vaccination has the potential to instigate substantial changes in HPV epidemiology.

Questions or comments??

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