



# Epidemiological Trends for Non-smokers and Young Adults with Laryngeal Squamous Cell Carcinoma

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Strobe Rounds

# Case Presentation

## TM

- 31yo M nonsmoker with h/o ACDF (2015) p/w weeks-months of progressive hoarseness
  - Flexible laryngoscopy: Immobile L vocal cord with exophytic lesion extending entire length of TVC, sluggish R vocal cord
  - Direct laryngoscopy: L vocal fold lesion with fixed cord, 1cm of submucosal subglottic extension

# Questions

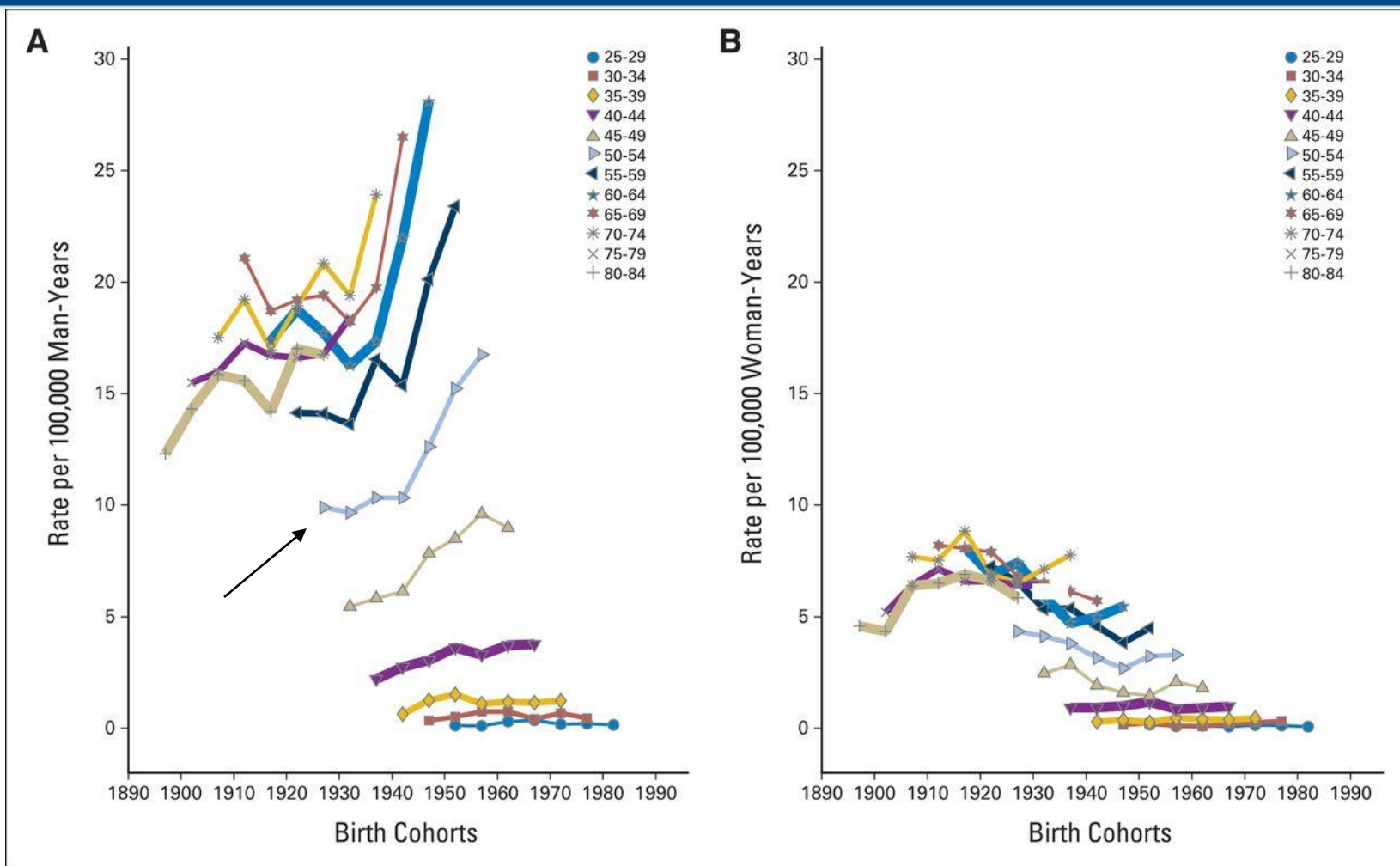
- Why are young nonsmokers developing laryngeal squamous cell carcinoma
- Is the incident rate of laryngeal cancer in young, nonsmoking patients increasing?

# Head and Neck Squamous Cell Carcinoma

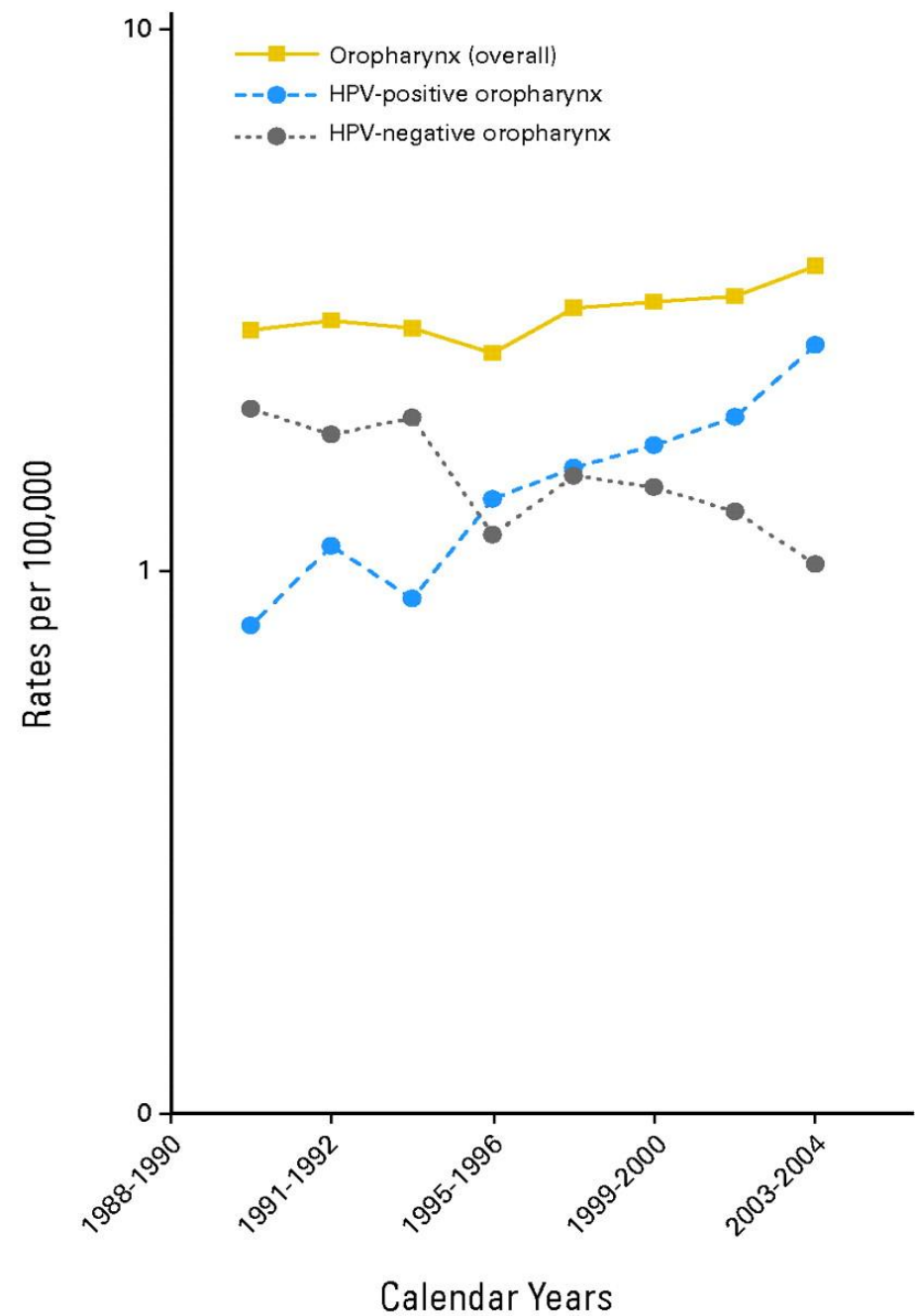


- 6<sup>th</sup> most common cancer worldwide
- Incidence of 560,000 annually
- Incidence rate is increasing disproportionately amongst patients <45 years of age
  - Increase driven by oral cavity and oropharyngeal cancer

# Increased incidence rates OPC primarily among men and younger age-cohorts



# HPV-positive OPC is driving incidence trends



# Laryngeal Squamous Cell Carcinoma

- Mean age of diagnosis: 65 years
- 7:1 male:female ratio
- 95% of patients report smoking or drinking history

# Laryngeal Carcinoma in Nonsmoking Patients

Yaniv Hamzany, MD; Tuvia Hadar, MD; Raphael Feinmesser, MD;  
Dan Guttman, MD; Jacob Shvero, MD

- Retrospective chart review
- 1,443 patients
  - <5% nonsmokers
- Majority glottic, early T stage

TABLE 1. EPIDEMIOLOGICAL AND CLINICAL FEATURES OF NONSMOKING PATIENTS WITH LARYNGEAL CARCINOMA

	<i>Nonsmokers (Whole Group) (N = 55)*</i>		<i>Never Smokers (N = 40)†</i>		<i>Past Smokers (N = 15)‡</i>	
	<i>No.</i>	<i>%</i>	<i>No.</i>	<i>%</i>	<i>No.</i>	<i>%</i>
Male	48	87.2	35	87.5	13	86.6
Female	7	12.7	5	12.5	2	13.3
Site						
Supraglottis	1	1.8	0		1	6.6
Glottis	54	98.1	40	100	14	93.3
Tumor stage						
Tis	4	7.2	4	10	0	
T1	38	69	28	70	10	66.6
T2	11	20	6	15	5	33.3
T3	1	1.8	1	2.5	0	
T4	1	1.8	1	2.5	0	

There were no statistically significant findings between groups for any of parameters (p values not significant).

\*Male-to-female ratio, 7 to 1; mean age, 67 years.

†Male-to-female ratio, 7 to 1; mean age, 66 years.

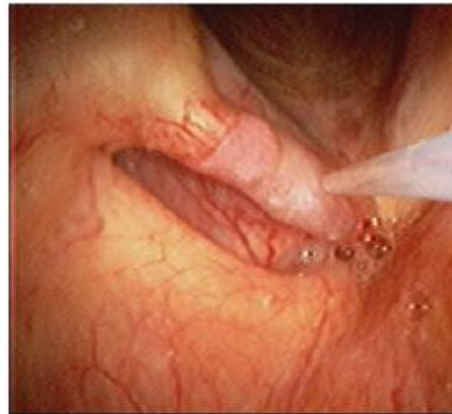
‡Male-to-female ratio, 6.5 to 1; mean age, 70 years.



# Glottic Cancer: A Metamorphosing Disease

Steven M. Zeitels, MD, FACS<sup>1</sup>

- Retrospective chart review
- 31 of last 100 patients did not have smoking history
- Exophytic, papillary, and vascular



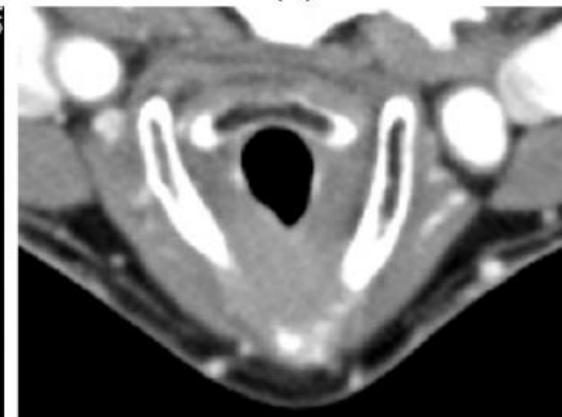
(a)



(b)



(c)



(d)

# Research Question

- What are the clinical characteristics of a typical nonsmoking patient with laryngeal cancer?
- Is the incidence rate of laryngeal cancer increasing in this subset of patients?

## Johns Hopkins Hospital Cohort

- Retrospective chart review
- Johns Hopkins Hospital, 2003-2013
- Smoking use defined as <10 pack years

## Surveillance, Epidemiology, and End Results (SEER) registries

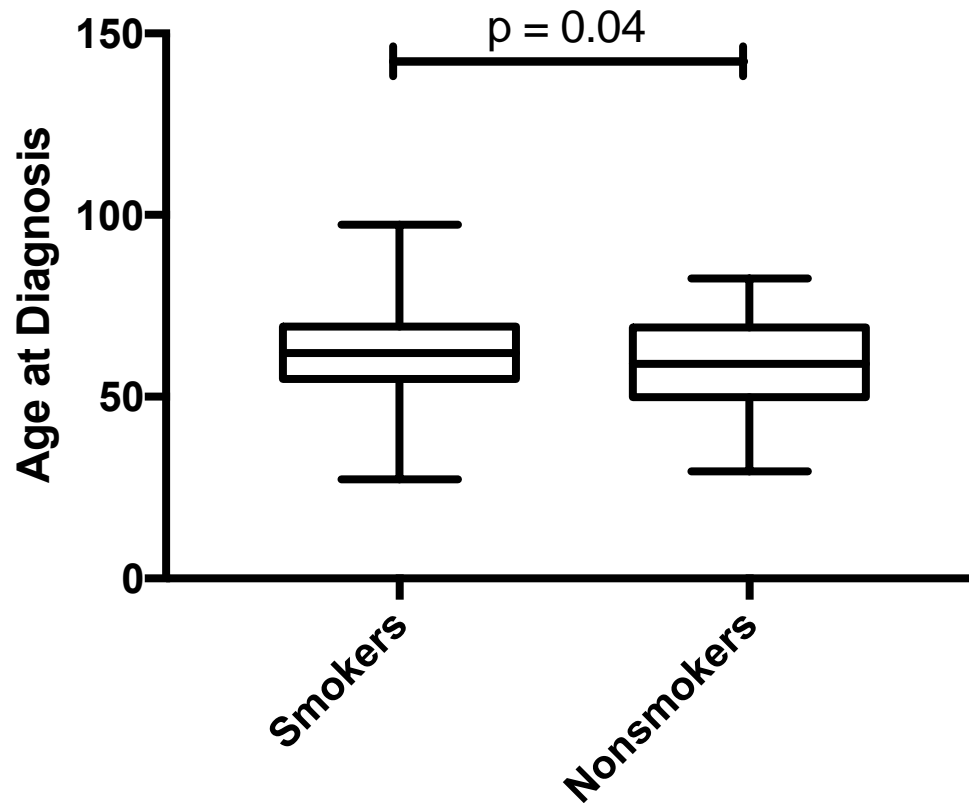
- Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San-Francisco-Oakland, Seattle-Puget Sound, and Utah
- 1973-2013

# Johns Hopkins Hospital Cohort



- 521 patients
- Mean age at diagnosis 61.8 (SD=11)
- 78% Male, 71% Caucasian
- 69 patients (13.2%) nonsmokers

# Johns Hopkins Hospital Cohort



Smokers: 62.2  
Nonsmokers: 59.2

# Johns Hopkins Hospital Cohort

	<b>Odds Ratio (95% CI)</b>	p-value
<b>Age&lt;35</b>	1.31 (0.15-11.42)	0.8
<b>Age&lt;40</b>	3.03 (0.91-10.12)	0.072
<b>Age&lt;45</b>	<b>3.66 (1.64-8.20)</b>	<b>0.002</b>
<b>Age&lt;50</b>	2.46 (1.33-4.57)	0.004
<b>Age&lt;55</b>	1.58 (0.92-2.71)	0.096
<b>Age&lt;60</b>	1.43 (0.86-2.38)	0.17

# Characteristics of Nonsmoking Population

	Non-smokers	Smokers		Odds Ratio	95%CI	p-value
	n(%)	n(%)	p-value	(OR)		
Number of Patients	69(13.2)	452(86.8)		-	-	-
Mean Age at Diagnosis (SD)	59.3(12.2)	62.2(11.0)	0.04	3.66*	1.63-8.20	0.002
Sex			0.51			
Male	56	351		ref	-	-
Female	13	101		0.81	0.42-1.53	0.51
Race			<0.001			
White	47(68.1)	325(71.9)		ref	-	-
African American	10(14.5)	102(22.6)		0.68	0.33-1.39	0.29
Other	11(15.9)	13(2.88)		5.85	2.48-13.82	<0.001
Unspecified	1(1.5)	12(2.65)		-	-	-

# Characteristics of Nonsmoking Population

	Non-smokers	Smokers		Odds Ratio	95%CI	
	n(%)	n(%)	p-value	(OR)		p-value
<b>Alcohol Use</b>			<0.001			
No	59(85.5)	211(46.7)		ref	-	-
Yes	8(11.6)	205(45.4)		0.14	0.07-0.30	<0.001
Unspecified	2(2.9)	36(8.0)		-	-	-



# Characteristics of Nonsmoking Population



	Non-smokers	Smokers		Odds Ratio	95%CI	
	n(%)	n(%)	p-value	(OR)		p-value
<b>Primary Site</b>			0.04			
Supraglottic	19(27.5)	200(44.3)		ref	-	-
Glottic	47(68.1)	224(49.6)		2.21	1.25-3.89	0.006
Subglottic	1(1.5)	11(2.4)		0.96	0.12-7.82	0.97
Unspecified	2(2.9)	17(3.8)		-	-	-

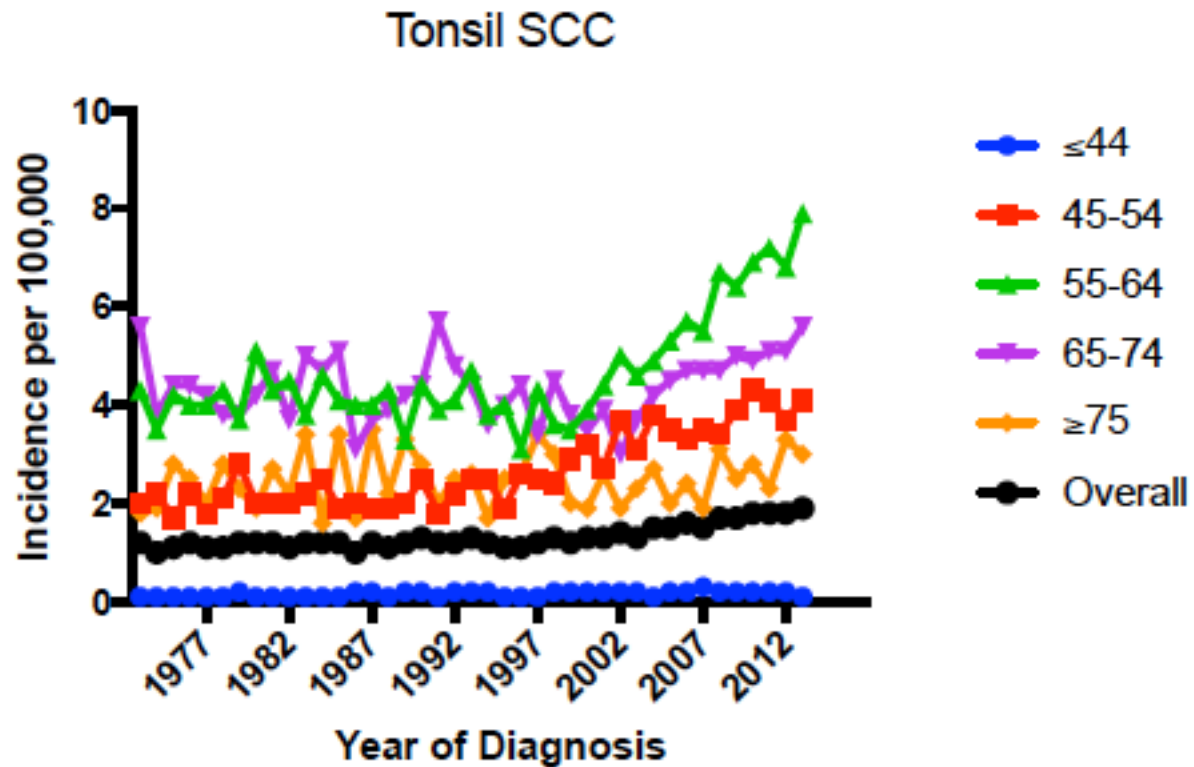
# Characteristics of Nonsmoking Population

	Non-smokers	Smokers		Odds Ratio	95%CI	p-value
	n(%)	n(%)	p-value	(OR)		
<b>Initial Tumor Category (AJCC-7ed)</b>			0.044			
T1	33(47.8)	142(31.4)		ref	-	-
T2	18(26.1)	111(24.6)		0.70	0.37-1.30	0.26
T3	11(15.9)	117(25.9)		0.40	0.20-0.84	0.014
T4	5(7.25)	67(14.8)		0.32	0.12-0.86	0.024
Unspecified	2(2.9)	15(3.3)		-	-	-
<b>Initial Nodal Category (AJCC-7ed)</b>			0.97			
N0	49(71.0)	303(67.0)		ref	-	-
N1	4(5.8)	28(6.2)		0.88	0.30-2.63	0.82
N2	12(17.4)	94(20.8)		0.79	0.40-1.55	0.49
N3	2(2.9)	12(2.7)		1.03	0.22-4.75	0.97
Unspecified	2(2.9)	15(3.3)		-	-	-
<b>Initial Metastasis Category (AJCC-7ed)</b>			0.57			
M0	67(97.1)	430(95.1)		-	-	-
M1	0(0)	7(1.6)		-	-	-
Unspecified	2(2.9)	15(3.3)				

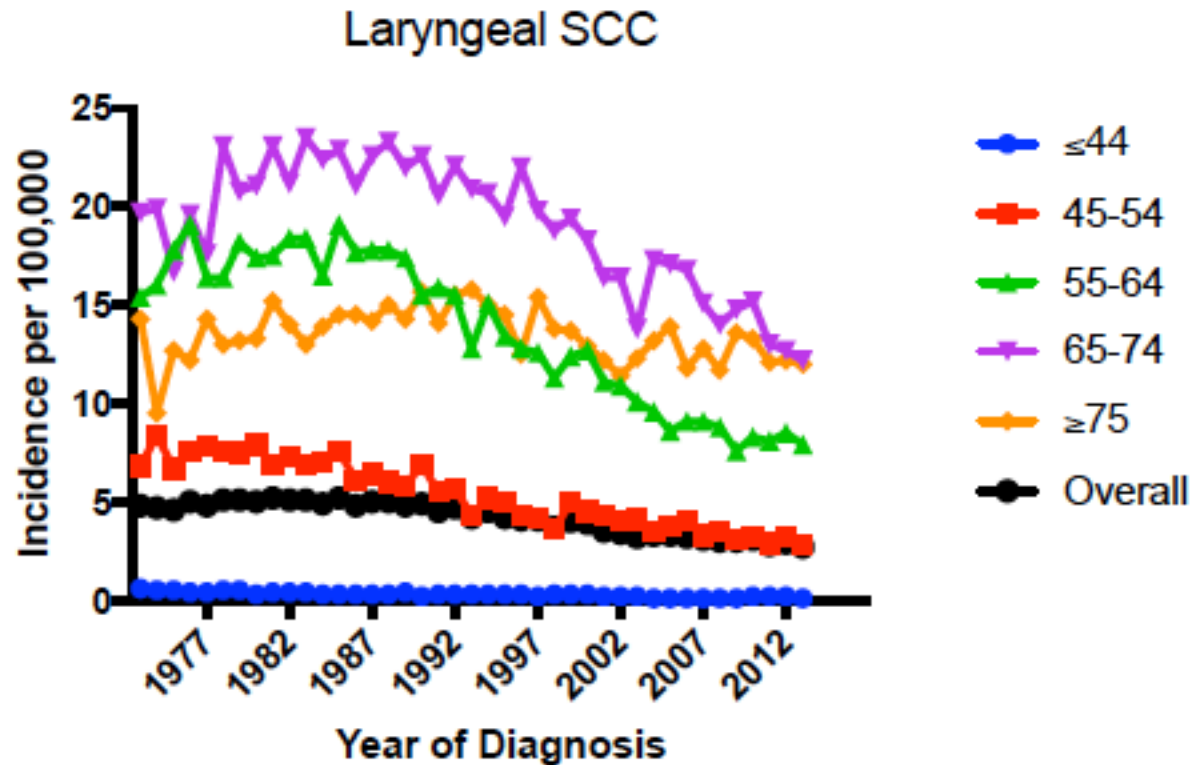
# Characteristics of Nonsmoking Population

- More likely to be:
  - <45 years of age
  - Nondrinkers
  - Glottic primary
  - Early T stage (T1, T2)

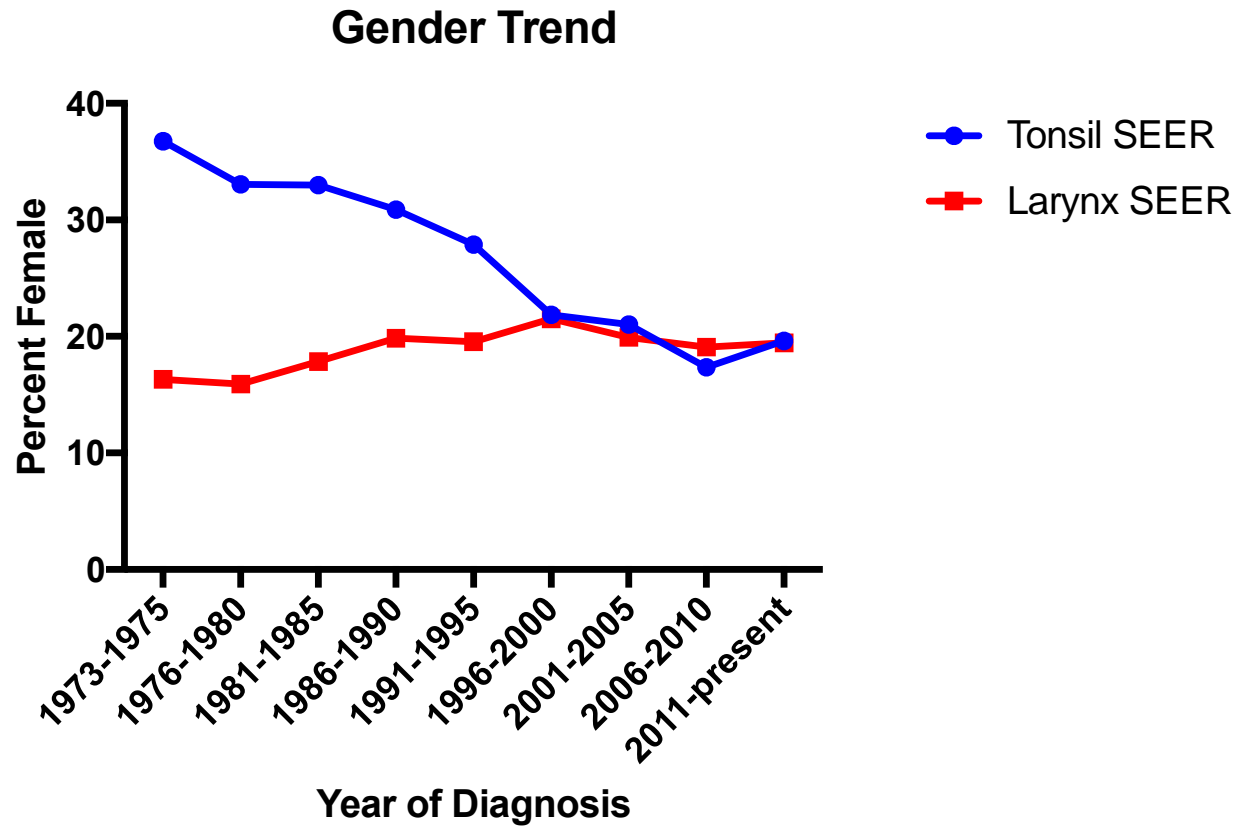
# SEER9 Database



# SEER9 Database

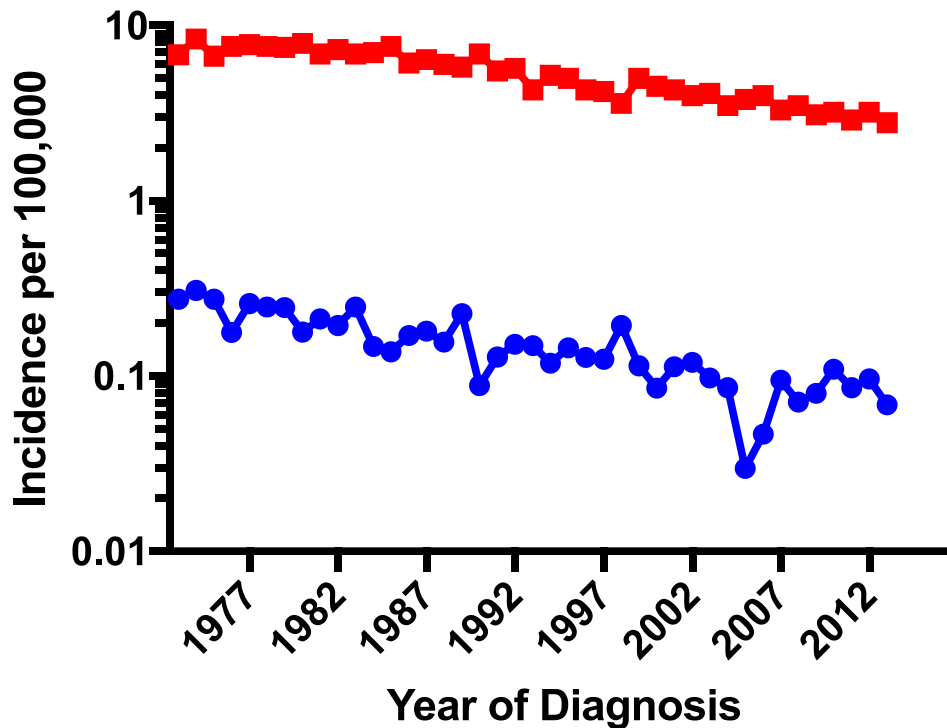


# Gender Trends



# Proxy Populations

## Laryngeal SCC



● Nonsmokers  
■ Smokers

### Annual Percent Change

Nonsmokers: -3.2%

Smokers: -1.1%

# Summary

- Nonsmokers more likely to be young (<45 years of age) with early stage glottic tumors
- The incidence of LSCC in populations most likely to be nonsmokers is decreasing



# Future Directions?

- Different pathways involved in smokers vs nonsmokers?
  - High-risk HPV
  - EGFR
  - PTEN
  - PD-1/PD-L1