

This is a Post-Referee Draft. For the final version please consult:

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Web Table 1. Statistically Significant Risk Factors for Head and Neck and Selective Subsites Cancers: INHANCE (International Head and Neck Cancer Epidemiology Consortium) Pooled Analyses Published Between January 1, 1995 and March 22, 2016.

| First Author, Year Reference# | Study Period | No. of Study Sites | Cases | Controls | Findings OR, 95% CI | Comments | | | |
|-------------------------------|------------------------------|--------------------|---|---------------------|-----------------------------|--------------------------------|--|--------------------------------|---------------|
| <u>Age</u> | | | | | | | | | |
| Toporcov, 2015 ⁵² | N/A ^c | 25 | <45 years old 2,010 >45 years old 17,700 | 4,042 22,704 | Ever Tobacco | | Increased odds with alcohol and tobacco appear among younger and older groups by sex | | |
| | | | | | | | | ≤45 years old | >45 years old |
| | | | | | Female | 1.58 ^a : 1.22, 2.06 | | 3.63 ^a : 3.24, 4.06 | |
| | | | | | Male | 2.25 ^a : 1.86, 2.71 | | 3.36 ^a : 3.11, 3.64 | |
| | | | | | OCC | 1.91 ^a : 1.53, 2.38 | | 2.18 ^a : 1.99, 2.39 | |
| | | | | | OPC | 1.86 ^a : 1.47, 2.37 | | 2.77 ^a : 2.50, 3.08 | |
| | | | | | | | | Ever Alcohol | |
| | | | | | | | | ≤45 years old | >45 years old |
| | | | | | Female | 1.32 ^a : 1.06, 1.65 | | 1.45 ^a : 1.29, 1.63 | |
| | | | | | Male | 1.32 ^a : 1.06, 1.65 | | 2.18 ^a : 1.98, 2.40 | |
| | | | | | OCC | 1.61 ^a : 1.46, 1.79 | | 1.61 ^a : 1.46, 1.79 | |
| | | | | | OPC | 1.66 ^a : 1.25, 2.21 | | 2.16 ^a : 1.92, 2.44 | |
| <u>Alcohol</u> | | | | | | | | | |
| Purdue, 2009 ⁶⁹ | 1984-2006 | 15 | 9,107 | 14,219 | >15 Standard Drinks/week | | Increased odds: Beer, liquor and wine appear comparable | | |
| | | | | | | | | Beer | |
| | | | | | OCC | 6.4 ^b : 3.9, 10.3 | | | |
| | | | | | P | 4.3 ^b : 2.7, 6.8 | | | |
| | | | | | | | | Liquor | |
| | | | | | OCC | 3.2 ^b : 1.6, 6.4 | | | |
| P | 3.6 ^b : 2.0, 6.3 | | | | | | | | |
| | | Wine | | | | | | | |
| OCC | 5.9 ^b : 2.3, 15.4 | | | | | | | | |
| P | 4.4 ^b : 2.0, 9.6 | | | | | | | | |
| <u>Coffee</u> | | | | | | | | | |
| Galeone, | 1983- | 9 | 5,139 | 9,028 | Caffeinated Coffee Drinkers | Reduced odds: additional data | | | |

| 2010 ⁷⁰ | 2005 | | | | OCC | 0.62 ^a : 0.40, 0.99 | on cups/day suggest dose response |
|----------------------------------|------------------|----|----------------------|--------|---|---|---|
| Stott-Miller, 2012 ⁷⁶ | N/A ^c | 12 | 6,448 | 13,747 | HNC: Never smokers | 1.59 ^a : 1.2, 2.07 | Increased odds: Never smokers diabetics |
| <u>Diabetes</u> | | | | | | | |
| <u>Diet</u> | | | | | | | |
| Chuang, 2012 ⁷⁹ | 1983-2007 | 22 | 14,520 | 22,737 | | “Healthy diet” 0.86 ^a : 0.82, 0.90 0.89 ^a : 0.85, 0.92 0.88 ^a : 0.84, 0.91 | Reduced odds with “Healthier diet” (more fruits and vegetables and less red / processed meat) |
| Edefonti, 2012 ⁷⁴ | 1991-2005 | 5 | 2,452 | 5,013 | | Antioxidant vitamins and fiber 0.57 ^a : 0.43, 0.76 Fats 0.78 ^a : 0.63, 0.97 | Reduced odds: Patterns identified by factor loading showed AVF most clearly |
| Li, 2012 ⁷⁷ | N/A ^c | 12 | 7,002 | 8,383 | Ever use Vit C 10+ years Vit C Ever use Calcium 365+ Tab Calcium | Supplements 0.76 ^a : 0.59, 0.96 0.72 ^a : 0.54, 0.97 0.64 ^a : 0.42, 0.97 0.36 ^a : 0.16, 0.83 | Reduced odds with Vit C and Calcium; no linear trends for frequency or duration of supplements. Weaker stratified on tobacco or alcohol |
| Galeone, 2015 ⁷¹ | 1982-2009 | 10 | 5,127 | 13,249 | | Highest vs lowest quintile of total folate intake 0.65 ^a : 0.43, 0.99 0.57 ^a : 0.43, 0.75 | Reduced odds with folate intake; highest odds for OPC was among heavy alcohol with low folate |
| Edefonti, 2015 ⁸⁰ | N/A ^c | 10 | 5,959 | 12,248 | | Highest vs lowest quintile of non-alcohol energy-adjusted Vit C intake 0.58 ^a : 0.45, 0.76 | Reduced odds with Vit C intake |
| Galeone, 2015 ⁷² | 1983-2009 | 8 | 4,590 | 7,082 | HNC combined | High Garlic Use 0.74 ^a : 0.55, 0.99 | Reduced odds with high garlic use |
| Edefonti, 2015 ⁷⁵ | N/A ^c | 10 | 5,959 4,414 OP | 12,248 | | Quintiles Vit E (1=Ref) 2 nd 0.79 ^a : 0.69, 0.90 3 rd 0.65 ^a : 0.56, 0.74 | Reduced odds with natural sources Vit E |

| | | | | | | | | |
|------------------------------|------------------|----|--------------------------------------|------------------------------|--|---|---|--|
| Leoncini, 2016 ⁶⁶ | N/A ^c | 10 | cases 3,894 | 8,996 | OPC OPC OCPC OCPC OCPC OCPC | 4 th 0.64 ^a : 0.55, 0.74 5 th 0.59 ^a : 0.49, 0.71 Quintiles Total Carotenoids 2 nd 0.79 ^a : 0.69, 0.90 3 rd 0.76 ^a : 0.65, 0.88 4 th 0.75 ^a : 0.64, 0.89 5 th 0.61 ^a : 0.53, 0.71 | Reduced odds with carotenoids intake | |
| <u>Family History</u> | | | | | | | | |
| Negri, 2009 ⁶³ | 1984-2006 | 12 | 8,967 | 13,627 | All OCC OPC OCPC | 1.75 ^a : 1.44, 2.12 1.53 ^a : 1.11, 2.11 1.55 ^a : 1.16, 2.07 1.82 ^a : 1.13, 2.92 | Increased odds: association rose to 7.2 (5.5-9.5) for family history when subjects were alcohol and tobacco users | |
| <u>Height/BMI</u> | | | | | | | | |
| Leoncini, 2014 ⁶⁵ | 1981-2009 | 24 | 17,666 | 28,198 | Adjusted Men Adjusted Women | ORs per increase of 10 cm in height: 0.91 ^a : 0.86, 0.93 0.86 ^a : 0.79, 0.93 | Reduced odds with height: findings for adult height reflect other assessments with depravity | |
| Gaudet, 2010 ⁶⁸ | N/A ^c | 17 | 12,716 | 17,438 | BMI <18.5 25.0-29.9 ≥30.0 Multivariate-adjusted <18.5 25.0-29.9 ≥30.0 | Minimally-adjusted 2.57 ^a : 2.20, 2.99 0.47 ^a : 0.41, 0.53 0.43 ^a : 0.35, 0.53 2.13 ^a : 1.75, 2.58 0.52 ^a : 0.44, 0.60 0.43 ^a : 0.33, 0.57 | Increased odds with leanness regardless of smoking or alcohol status Reduced odds with overweight or obesity, suggested as modification for smoking or alcohol | |
| Lubin, 2010 ⁵³ | N/A ^c | 15 | Smoking 6,333 Alcohol 8,452 | 8,000+ | BMI <18.5 BMI ≥40.0 | OCC 2.58 ^a : 2.0, 3.4 P 2.68 ^a : 2.0, 3.6 0.44 ^a : 0.3, 0.7 | Increased odds with leanness; reduced odds with obesity for pharyngeal cancer | |
| Lubin, 2011 ⁵⁴ | N/A ^c | 15 | OCC 2,441 OPC 2,297 | Controls 7,604- 13,829 | Female BMI<18.5 Male BMI<18.5 Female 0 pack/years Male 0 pack/years | OCC 2.54 ^a : 1.7, 3.8 3.33 ^a : 1.9, 5.7 0.33 ^a : 0.2, 0.5 0.30 ^a : 0.2, 0.4 OPC 3.09 ^a : 1.8, 5.2 2.38 ^a : 1.4, 4.2 0.22 ^a : 0.2, 0.3 0.63 ^a : 0.5, 0.8 | Increased odds with leanness for both sexes Reduced odds with nonsmoking for both sexes | |
| <u>Marijuana</u> | | | | | | | | |
| Marks, | N/A ^c | 9 | | | | Marijuana association | Increased or reduced odds | |

| | | | | | | | | |
|---|------------------|--------------------------------|--|--------------------------|---|---|---|--|
| 2014 ⁶⁴ | | | 1,921 356 | 7,639 | OPC OT | 1.24 ^b : 1.06, 1.47 0.47 ^b : 0.29, 0.75 | depending on subsite | |
| <u>Mouthwash</u> | | | | | | | | |
| Boffetta, 2016 ⁶⁷ | N/A ^c | 12 | 2,790 8,981 | 10,020 10,090 | OCC HNC | 36+ years of mouthwash use 1.28: 1.06, 1.56 1.15: 1.01, 1.30 | Increased odds with long term mouthwash use | |
| <u>Recreational Activity</u> | | | | | | | | |
| Nicolotti, 2011 ⁷³ | 1984-2010 | 4 | 2,289 | 5,580 | Total Moderate activity High activity | OCC 0.78 ^a : 0.66, 0.91 0.74 ^a : 0.56, 0.97 0.53 ^a : 0.32, 0.88 | P 0.67 ^a : 0.53, 0.85 0.58 ^a : 0.38, 0.89 | Reduced odds: additional analysis suggests more evident among males, subjects ≥ 45, and ever-smokers and ever-drinkers |
| <u>Sex Behaviors</u> | | | | | | | | |
| Heck, 2010 ⁶² | 1984-2006 | 8 | 5,642 | 6,069 | ≥6 sex partners OPC T Base of the tongue | ≥4 oral sex partners 2.25 ^a : 1.42, 3.58 3.36 ^a : 1.32, 8.53 | 2 lifetime sex partners 1.63: 1.22, 2.18 2.02: 1.19, 3.46 | Increased odds: associated with HPV-associated subsites |
| <u>Smoking Tobacco and Smoking Tobacco/Alcohol</u> | | | | | | | | |
| Hashibe, 2007 ⁵⁵ | 1984-2006 | 15 | 10,244 No tobacco 1,072 No alcohol 1,598 | 15,227 5,775 4,051 | Never Drinkers/Ever Smokers HNC Never Smokers/Heavy Drinkers (≥3 drinks/day) HNC | 2.13 ^b : 1.52, 2.98 2.04 ^b : 1.29, 3.21 | | Increased odds with smoking for never drinkers Increased odds with heavy drinking for never smokers |
| Lee, 2008 ⁵⁶ | 1992-2006 | 6 | 542 | 2,197 | >15 years of involuntary smoking HNC P | Home Nonsmokers 1.60 ^a : 1.12, 2.28 4.13 ^a : 1.43, 11.89 | Work 1.55 ^a : 1.04, 2.30 | Increased odds with prolonged second hand tobacco exposure for both nonsmokers and nonsmokers/nondrinkers |
| | | | | | HNC P | Nonsmokers and nondrinkers 1.75 ^a : 1.06, 2.90 4.15 ^a : 1.50, 11.47 | 2.59 ^a : 1.35, 4.95 3.99 ^a : 1.06, 15.08 | |
| Marron, 2010 ⁵⁷ | N/A ^c | 13 alcohol 17 tobacco | Total 9,167 OCC 1,240 | 12,593 16,884 | Cessation of alcohol ≥20 years Quit tobacco | Total 0.60 ^b : 0.40, 0.89 | OCC | Reduced odds with quitting smoking or drinking: advantage seen faster for smokers than drinkers |

| | | | | | | | | | |
|--------------------------------|-----------|----|--------|--------|---------------------------------|--------------------------------|--------------------------------|--|---|
| | | | | | smoking 1-4 years | 0.70 ^b : 0.61, 0.81 | 0.65 ^b : 0.52, 0.80 | | |
| Wyss, 2013 ⁵⁸ | 1981-2007 | 19 | 13,935 | 18,691 | Cigarette Never | 2.54 ^a : 1.93, 3.34 | Cigarette Ever | Increased odds highest with only cigarette | |
| | | | | | Cigar | 2.08 ^a : 1.55, 2.81 | 0.81 ^a : 0.70, 0.93 | Increased odds with tobacco combinations, which are lower than cigarettes only | |
| | | | | | Pipe | | | | |
| | | | | | Exclusive/joint tobacco smoking | | | | |
| | | | | | Cigarette, cigar, pipe | 2.42 ^a : 1.96, 2.99 | | | |
| | | | | | Cigarette and cigar | 3.05 ^a : 2.61, 3.56 | | | |
| | | | | | Cigarette and pipe | 2.94 ^a : 2.49, 3.48 | | | |
| | | | | | Cigarette only | 3.93 ^a : 3.67, 4.22 | | | |
| | | | | | Pipe only | 3.71 ^a : 2.59, 5.33 | | | |
| Berthiller, 2015 ⁵⁹ | 1981-2007 | 23 | 4,093 | 13,416 | | | CPD | Increased odds with increased CPD | |
| | | | | | | >0-3 | >3-5 | >5-10 | |
| | | | | | Never Drinkers | 2.01 ^a : 1.22, 3.31 | 2.12 ^a : 1.48, 3.02 | | |
| | | | | | Alcohol Drinkers | 1.52 ^a : 1.21, 1.90 | 2.14 ^a : 1.73, 2.65 | 2.60 ^a : 2.00, 3.40 | |
| | | | | | OCC | 1.48 ^a : 1.04, 2.09 | 2.23 ^a : 1.45, 3.42 | | |
| | | | | | OPC | 1.57 ^a : 1.10, 2.23 | 2.17 ^a : 1.53, 3.06 | | |
| Socioeconomic Status | | | | | | | | | |
| Conway, 2015 ⁷⁸ | 1981-2012 | 31 | 23,964 | 31,954 | HNC adjust levels | Education (3 categories) | | Income (5 categories) | Increased odds with low education or low income across levels of adjustment |
| | | | | | | low | mid | lowest | second lowest |
| | | | | | 1 | 2.50 ^a : 2.02, 3.09 | 1.80 ^a : 1.57, 2.07 | 2.44 ^a : 1.62, 3.67 | 1.60 ^a : 1.11, 2.32 |
| | | | | | 2 | 1.87 ^a : 1.53, 2.29 | 1.42 ^a : 1.24, 1.63 | 1.69 ^a : 1.27, 2.26 | |
| | | | | | 3 | 1.46 ^a : 1.16, 1.82 | 1.32 ^a : 1.15, 1.53 | 1.56 ^a : 1.29, 1.88 | |
| | | | | | 4 | 1.43 ^a : 1.13, 1.81 | 1.33 ^a : 1.11, 1.59 | | |
| | | | | | 5 | 1.34 ^a : 1.04, 1.73 | 1.22 ^a : 1.03, 1.46 | | |
| | | | | | 6 | 1.61 ^a : 1.13, 2.31 | | | |

Abbreviations: N/A, not available from published report; OCC, oral cavity; OPC, oropharyngeal; P, pharynx; HNC, head and neck cancer; AVF, antioxidant vitamins and fiber; OCPC, oral cavity pharynx; BMI, body mass index; OT, oral tongue; T, tongue; CPD; cigarettes per day;

^a adjusted

^b adjustments unclear

^c the start date of the study could not be determined from the published literature