Thomas L Vaughan - Contribution to Science

As of April 2016, I have published 211 research articles and book chapters.

A list of these can be found via the following link which performs an automated search of PubMed: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=PureSearch&db=pubmed&details_term=vaughan%20tl%5BAuthor%5D

A more complete list (including book chapters and the most recent publications) is available at my personal research website: http://research.tvaughan.org/

1. The beginnings of the remarkable rise in incidence of esophageal adenocarcinoma were first noted in the late 1980s. Incidence now has risen 10-fold among men of European background, who represent by far the highest incidence group, and almost as dramatically among women and men of African background. I participated, first as co-Investigator and then Principal Investigator, in a series of population-based case-control studies of esophageal adenocarcinoma, aimed at identifying the factors behind the dramatic changes. I was among the first to describe the importance of obesity in this cancer, and to differentiate the risk factor patterns of adenocarcinoma and squamous cell carcinoma. I was the first to systematically investigate the role of medications that promote gastroesophageal reflux in the development of esophageal adenocarcinoma, and to describe an increased risk in persons treated long-term for asthma. We validated the large role of reflux in this cancer and identified a protective association with intake of non-steroidal anti-inflammatory drugs (NSAIDs) and with *H. pylori* infection.

- **Vaughan TL**, Davis S, Kristal A, Thomas DB. Obesity, alcohol and tobacco as risk factors for cancer of the esophagus: adenocarcinoma versus squamous cell carcinoma. *Cancer Epidemiology Biomarkers & Prevention* 1995;4:85-92.
- Farrow DC, **Vaughan TL**, Hansten P, Stanford JL, Gammon MD, Risch HA, Chow WH, Dubrow R, Ahsan H, Mayne ST, Schoenberg JB, Sweeney C, Rotterdam H, West B, Fraumeni JF Jr, Blot WJ. Use of aspirin and other NSAIDs and risk of gastric and esophageal cancer. *Cancer Epidemiology Biomarkers & Prevention* 1998;7:97-102.
- Chow WH, Blot WJ, **Vaughan TL**, Risch HA, Gammon MD, Stanford JB, Dubrow R, Schoenberg JB, Mayne ST, Farrow DC, Ahsan H, West AB, Rotterdam H, Niwa S, Fraumeni, JF Jr. Body mass index and risk of adenocarcinoma of the esophagus and gastric cardia. *JNCI* 1998;90:150-155.
- **Vaughan TL**, Farrow DC, Hansten P, Chow WH, Gammon MD, Risch HA, Stanford JL, Schoenberg JB, Mayne ST, Rotterdam H, Dubrow R, Ahsan H, West B, Blot WJ, Fraumeni JF Jr. Risk of esophageal and gastric adenocarcinoma in relation to use of calcium channel blockers, asthma drugs and other medications that promote gastroesophageal reflux. *Cancer Epidem Biomarkers & Prev* 1998;7:749-756.

2. After the initial studies of esophageal adenocarcinoma I broadened my focus to include the etiology of its main precursor, Barrett's esophagus, and conducted the first community-based case-control study of this condition. I have been co-PI and project leader for a Program Grant identifying predictors of progression among persons with Barrett's. This prospective cohort study (in various guises) was first funded in 1995 and will continue through 2019. Among the various "firsts" from this series of studies, we a) quantified the excess risk of esophageal adenocarcinoma and aneuploidy associated with length of the Barrett's segment, b) established that aspirin/NSAIDs (and potentially statins) were inversely related to risk of progression from Barrett's to esophageal cancer, even among those with high-risk somatic genetic abnormalities, c) established that abdominal obesity, rather than simply overweight, was the key anthropometric variable predicting both risk of Barrett's and risk of progression from Barrett's to esophageal adenocarcinoma, and d)

were the first to identify a moderately strong and significant association between telomere length, measured in peripheral leukocytes of BE patients, and risk of progression, which was subsequently replicated.

- Rudolph RE, **Vaughan TL**, Storer B, Haggitt RC, Levine DS, Reid BJ. The effect of segment length on the risk of neoplastic progression in Barrett's esophagus. *Annals Internal Medicine* 2000;132:612-620.
- **Vaughan TL**, Dong LM, Blount PL, Ayub K, Odze RD, Sanchez CA, Rabinovitch PS, Reid BJ. Non-steroidal anti-inflammatory drugs and risk of neoplastic progression in Barrett's oesophagus: a prospective study. *Lancet Oncology* 2005;6:945-52.
- Edelstein ZR, Farrow DC, Bronner MP, Rosen SN, **Vaughan TL**. Central adiposity and risk of Barrett's esophagus. *Gastroenterology* 2007;133:403-11.
- Duggan C, Onstad L, Hardikar S, Blount PL, Reid BJ, **Vaughan TL**. Association between markers of obesity and progression from Barrett's esophagus to esophageal adenocarcinoma. *Clinical Gastroenterology and Hepatology* 2013; Aug;11(8):934-43. [PMC3722274]

3. In 2005, I co-founded (with Drs. Nyrén of the Karolinska Institutet and Chow of NCI) the Barrett's and Esophageal Adenocarcinoma Consortium (BEACON), an international consortium that now numbers over 40 investigators, and was elected as first (and continuing) Steering Committee Chair. Purposes of BEACON include facilitating the pooling of data from multiple studies to allow more precise relative risk estimates, and the pooling of DNA and serum to facilitate new molecular epidemiology studies.

- Cook MB, Kamangar F, Whiteman DC, Freedman ND, Gammon MD, Bernstein L, Brown LM, Risch HA, Ye Y, Sharp L, Wu AH, Ward MH, Giffen C, Casson AG, Abnet CC, Murray LJ, Corley DA, Nyrén O, **Vaughan TL**, Chow WH. Cigarette Smoking and Adenocarcinomas of the Esophagus and Esophagogastric Junction: A Pooled Analysis from the International BEACON Consortium. *JNCI* 2010 Sep 8;102(17):1344-53. [PMC2934375]
- Liao LM, **Vaughan TL**, Corley DA, Cook MB, Casson AG, Kamangar F, Abnet CC, Risch HA, GIffen C, Freedman ND, Chow WH, Sadeghi S, Pandeya N, Whiteman DC, Murray LJ, Bernstein L, Gammon MD, Wu AH. Nonsteroidal anti-inflammatory drug use reduces risk of adenocarcinomas of the esophagus and esophagogastric junction in a pooled analysis. *Gastroenterology* 2012;142:442-452. [PMC3297725]
- Thrift AP, Risch HA, Onstad L, Shaheen NJ, Casson AG, Bernstein L, Corley DA, Levine DM, Chow WH, Reid BJ, Romero Y, Hardie LJ, Liu G, Wu AH, Bird NC, Gammon MD, Ye W, Whiteman DC, **Vaughan TL**. Risk of Esophageal Adenocarcinoma Decreases with Height, Based on Consortium Analysis and Confirmed by Mendelian Randomization. *Clinical Gastroenterology and Hepatology*. 2014 Oct;12(10):1667-1676.e1. [PMC4130803]
- Cook MB, Corley DA, Murray LJ, Liao LM, Kamangar F, Ye W, Gammon MD, Risch HA, Casson AG, Freedman ND, Chow WH, Wu HA, Bernstein L, Nyren O, Pandeya N, Whiteman DC, **Vaughan TL**. Gastroesophageal reflux in relation to adenocarcinomas of the esophagus: A pooled analysis from the Barrett's and Esophageal Adenocarcinoma Consortium (BEACON). *PLoS ONE*. 2014 Jul 30;9(7):e103508. doi: 10.1371/journal.pone.0103508. [PMC4116205]

4. While the rapid rise in incidence of Barrett's and esophageal adenocarcinoma implies a key role for environmental factors, family studies have long suggested that inherited germline variation, perhaps interacting with environmental factors are also important. Along with Dr. David Whiteman and BEACON colleagues, I conducted the first genome-wide association study (GWAS) of EA and BE. We established a significant fraction (25%) of esophageal adenocarcinomas can be explained

by germline variation. Thus far, eight variants (SNPs) have been identified and replicated (including efforts funded by Wellcome Trust), and ongoing meta-analyses, GxE and pathway analyses have identified 12 more. Many of these risk loci are in or near genes that function in esophageal development, suggesting a possible relationship to the development of hiatal hernia and gastroesophageal reflux.

- Levine DM, Ek WE, Zhang R, Liu X, Onstad L, Sather C, Lao-Sirieix P, Gammon MD, Corley DA, Shaheen NJ, Bird NC, Hardie LJ, Murray LJ, Reid BJ, Chow WH, Risch HA, Nyren O, Ye W, Liu G, Romero Y, Bernstein L, Wu AH, Casson AG, Chanock S, Harrington P, Caldas I, Debiram-Beecham I, Caldas C, Hayward NK, Pharoah P, Fitzgerald R, MacGregor S, Whiteman DC, **Vaughan TL**. A Genome-Wide Association Study Identifies New Susceptibility Loci for Esophageal Adenocarcinoma and Barrett's Esophagus. *Nature Genetics* 2013 45:1487-93
- Su Z, Gay L, Strange A, Palles C, Band G, Whiteman DC, [+100 authors from EAGLE, Wellcome Trust, BEACON consortia], **Vaughan TL**, Peltonen L, Spencer CCA, Tomlinson I, Donnelly P, Jankowski JAZ. Common variants at the MHC locus and at chromosome 16p24.1 predispose to Barrett's esophagus. *Nature Genetics* 2012;44(10):1131-1136. [PMC3459818]
- Ek W, Levine D, D'Amato M, Pedersen N, Magnusson P, Bresso F, Onstad L, Schmidt P, Tomblom H, Nordenstedt H, Romero Y, Chow WH, Murray L, Gammon M, Liu G, Bernstein L, Casson A, Risch H, Shaheen N, Bird N, Reid BJ, Corley D, Hardie L, Ye W, Wu A, Zucchelli M, Spector T, Hysi P, **Vaughan TL**, Whiteman DW, MacGregor S. Germline genetic contributions to risk for esophageal adenocarcinoma, Barrett's esophagus and gastroesophageal reflux. *JNCI* 2013;105:1711–1718. [PMC3833931]
- Buas MF, Levine DM, Makar KW, Utsugi H, Onstad L, Li X, Galipeau PC, Shaheen NJ, Hardie LJ, Romero Y, Bernstein L, Gammon MD, Casson AG, Bird NC, Risch HA, Ye W, Liu G, Corley DA, Blount PL, Fitzgerald RC, Whiteman DC, Wu AH, Reid BJ, **Vaughan TL**. Integrative post genome-wide association analysis of CDKN2A and TP53 SNPs and risk of esophageal adenocarcinoma. *Carcinogenesis*. 2014 Dec;35(12):2740-7. [PMC4247522]

5. Recently I have also been focused on translating results of epidemiologic studies to prevention in the clinical and population settings. Through various invited reviews and perspectives papers, my colleagues and I have advanced a detailed research roadmap to overcome the limitations that are inherent in current approaches to controlling esophageal adenocarcinoma, and base decisions in primary and secondary clinical setting on a more firm scientific basis, utilizing risk prediction models.

- Reid BJ, Li X, Galipeau PC, **Vaughan TL**. Barrett's Esophagus and Esophageal Adenocarcinoma: Time for a New Synthesis. *Nature Cancer Reviews* 2010;10(2):87-101. [PMC2879265]
- Thrift AP, Kendall BJ, Pandeya N, **Vaughan TL**, Whiteman DC for the Study of Digestive Health. A clinical risk prediction model for Barrett's esophagus. *Cancer Prevention Research* 2012;5(9):1115-1123. [PMC3750988]
- **Vaughan TL**. From genomics to diagnostics of esophageal adenocarcinoma. *Nature Genetics*. 2014;46(8):806-7. doi: 10.1038/ng.3047. [PMC4324622]
- **Vaughan TL**, Fitzgerald RC. Precision Cancer Prevention of Esophageal Adenocarcinoma. *Nature Reviews Gastroenterology and Hepatology*. 2015 Apr;12:243-248. [PMC4382373]