

# The Troublesome Epidemiology of Barrett's Esophagus and Esophageal Adenocarcinoma



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## KEYWORDS

• Barrett's esophagus • Esophageal adenocarcinoma • Epidemiology

## KEY POINTS

- The incidence and prevalence of esophageal adenocarcinoma and Barrett's esophagus, respectively, have increased markedly in recent decades, without conclusive explanation.
- There are marked differences in disease incidence by region, sex, and gender.
- The main risk factors for these disorders are abdominal obesity, smoking, gastroesophageal reflux disease, a Western diet, and the absence of *Helicobacter pylori* colonization.
- The demographic distributions of the risk factors generally do not match the distributions of disease incidence, creating confusion regarding the underlying explanation for what is causing the incidence increases, potential interventions, and the unusual demographic patterns.
- The differences found may, in part, be related to interactions between strong risk factors.

## DISEASE DESCRIPTION

Esophageal adenocarcinoma is a highly fatal neoplasm of the esophagus, which has surpassed esophageal squamous cell carcinoma as the most common form of esophageal cancer in the United States. It most commonly occurs in the distal half of the esophagus and is frequently associated with Barrett's esophagus. Its location, in the esophageal area adjacent to the stomach, by itself supports a role for gastroesophageal reflux disease (GERD) in its cause. Barrett's esophagus is a metaplastic transformation of portions of the esophageal squamous cell lining to glandular mucosa. Barrett's esophagus is thought to result from an aberrant healing

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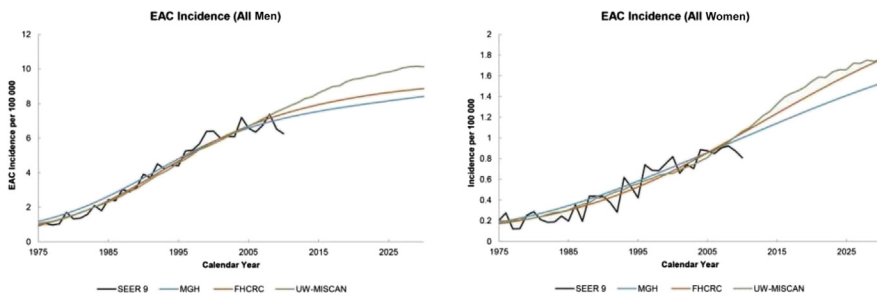
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response to esophageal mucosal injury, typically from GERD, although it has also been reported after other forms of esophageal mucosal injury, including caustic injection and therapeutic radiation exposure. Barrett's esophagus is associated with a markedly increased risk of esophageal adenocarcinoma, and most esophageal adenocarcinomas are presumed to arise from preexisting Barrett's esophagus. Thus, evaluating risk factors and demographic distributions for both Barrett's esophagus and esophageal adenocarcinoma may inform modifiable risk factors along the neoplastic continuum from normal esophagus to Barrett's esophagus to esophageal adenocarcinoma.

## NATIONAL AND GLOBAL INCIDENCE OF ESOPHAGEAL ADENOCARCINOMA

The incidence rate of esophageal adenocarcinoma in the United States has increased at least 6-fold over the last 40 years and is projected to continue increasing (Fig. 1).<sup>1,2</sup> Several studies, using national cancer data from Surveillance, Epidemiology, and End Results (SEER) and international cancer registries, have demonstrated that the incidence of esophageal adenocarcinoma varies geographically, by race and by gender, as does the rate at which the incidence is increasing.<sup>3,4</sup>

Globally, the incidence increase of esophageal adenocarcinoma during this time period has been highest among non-Hispanic white men<sup>5-7</sup>; within this group, in the United States, the incidence increased from 1 to ~6/100,000 between 1977 and 2010.<sup>2,6</sup> The regions with the highest global incidence rates of esophageal adenocarcinoma were Northern and Western Europe, Northern America, and Oceania, and the lowest rates were in Sub-Saharan Africa (range 0.4–3.5 for men) (Fig. 2). The male-to-female ratio was 4.4 globally and was highest in developed countries (North America [8.5], Europe, and Oceania) and lowest in Africa (1.7). Based on data from the International Agency for Research on Cancer, the sex ratio of esophageal adenocarcinoma incidence remained relatively stable during the period of study, with a rising overall absolute incidence.<sup>5,8</sup> However, a rising absolute incidence, with a stable ratio, led to an even greater difference between men and women in the absolute numbers of cases because a doubling of the low incidence among women leads to fewer additional cases than a doubling of the higher incidence among men. As a result, in 2012, 88% of cases of esophageal adenocarcinoma diagnoses in the United States were among men.<sup>8</sup>



**Fig. 1.** Age-adjusted incidence of esophageal adenocarcinoma (EAC) among all men and women in the United States: SEER) database and projected incidence from 3 simulation models. FHRCR, Fred Hutchinson Cancer Research Center simulation model; MGH, Massachusetts General Hospital simulation model; SEER 9, actual incidence 1975-2010; UW-MISCAN, University of Washington/Erasmus University simulation model collaboration. (Adapted from Kong CY, Kroep S, Curtius K, et al. Exploring the recent trend in esophageal adenocarcinoma incidence and mortality using comparative simulation modeling. *Cancer Epidemiol Biomarkers Prev* 2014;23:997–1006.)

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