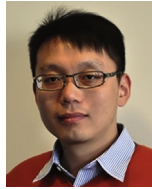




The Epidemiology of Esophageal Adenocarcinoma

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The incidence of esophageal adenocarcinoma (EAC) has increased in many Western countries and is higher in men than women. Some risk factors for EAC have been identified—mainly gastroesophageal reflux disease, Barrett's esophagus, obesity, and tobacco smoking. It is not clear whether interventions to address these factors can reduce risk of EAC, although some evidence exists for smoking cessation. Although consumption of alcohol is not associated with EAC risk, other exposures, such as physical activity, nutrition, and medication use, require further study. Genetic variants have been associated with risk for EAC, but their overall contribution is low. Studies are needed to investigate associations between risk factors and the molecular subtypes of EAC. The prognosis for patients with EAC has slightly improved, but remains poor—screening and surveillance trials of high-risk individuals are needed.

Keywords: Epidemiology; Lifestyle; Genetic Risk; Esophageal Cancer.

Esophageal adenocarcinoma (EAC) is characterized by several epidemiologic features. Over the past 30 years, there has been a rapid increase in the incidence of EAC in many Western countries, including Europe, North America, and Australia. EAC is the most rapidly increasing form of cancer in some populations.^{1,2} The male predominance in incidence is stronger than that of any other non-sex-specific cancer in several populations.^{2,3} Although strong risk factors for EAC have been identified, mainly gastroesophageal reflux disease (GERD) and obesity, we are in need of evidence-based preventive strategies.^{2,4} The prognosis for patients diagnosed with EAC has slightly improved during the last few decades, but it is still worse than that of most other cancer types; only 20% of patients in Western populations survive for 5 years.^{5–7} This review summarizes the current knowledge in the epidemiology and prevention of EAC, and highlights unresolved research questions regarding these topics.

Incidence

EAC is the main histologic type of esophageal cancer in the West. In 2012, an estimated 52,000 individuals (41,000 men and 11,000 women) developed EAC worldwide, resulting in a global incidence rate of 0.7 per 100,000 person-years (1.1 in men and 0.3 in women); most patients (53%) were from Europe, Northern America, or Oceania.⁸ The incidence rate of EAC has surpassed that of esophageal squamous cell carcinoma in a number of Western countries, including the United Kingdom (UK), the Netherlands, Ireland, New Zealand, the United States (US), Australia, Denmark, Canada, and Sweden.^{8–11}

Geographic and Racial/Ethnic Variations

The incidence rate of EAC varies greatly across geographic regions. The age-standardized incidence rate of EAC in 2012 was highest in Northern and Western Europe, Northern America, and Oceania, but was as low as less than 1 per 100,000 person-years in both sexes in the remaining parts of the world.⁸ At the individual country level, the highest rates per 100,000 person-years have been observed in the UK (7.2 in men and 2.5 in women), the Netherlands (7.1 in men and 2.8 in women), and Ireland (3.9 in men and 2.7 in women).⁸ In the US, the incidence rates are highest in non-Hispanic whites, followed by Hispanic whites, American Indian/Alaska Native, blacks, and lowest in Asian/Pacific islanders.^{12,13}

Time Trends

Figure 1 shows the incidence trends of EAC since the 1970s in White Americans and in Sweden. The increase in

Abbreviations used in this paper: BE, Barrett's esophagus; BMI, body mass index; EAC, esophageal adenocarcinoma; GERD, gastroesophageal reflux disease; GWAS, Genome-wide Association Studies; NSAIDs, non-steroidal anti-inflammatory drugs.

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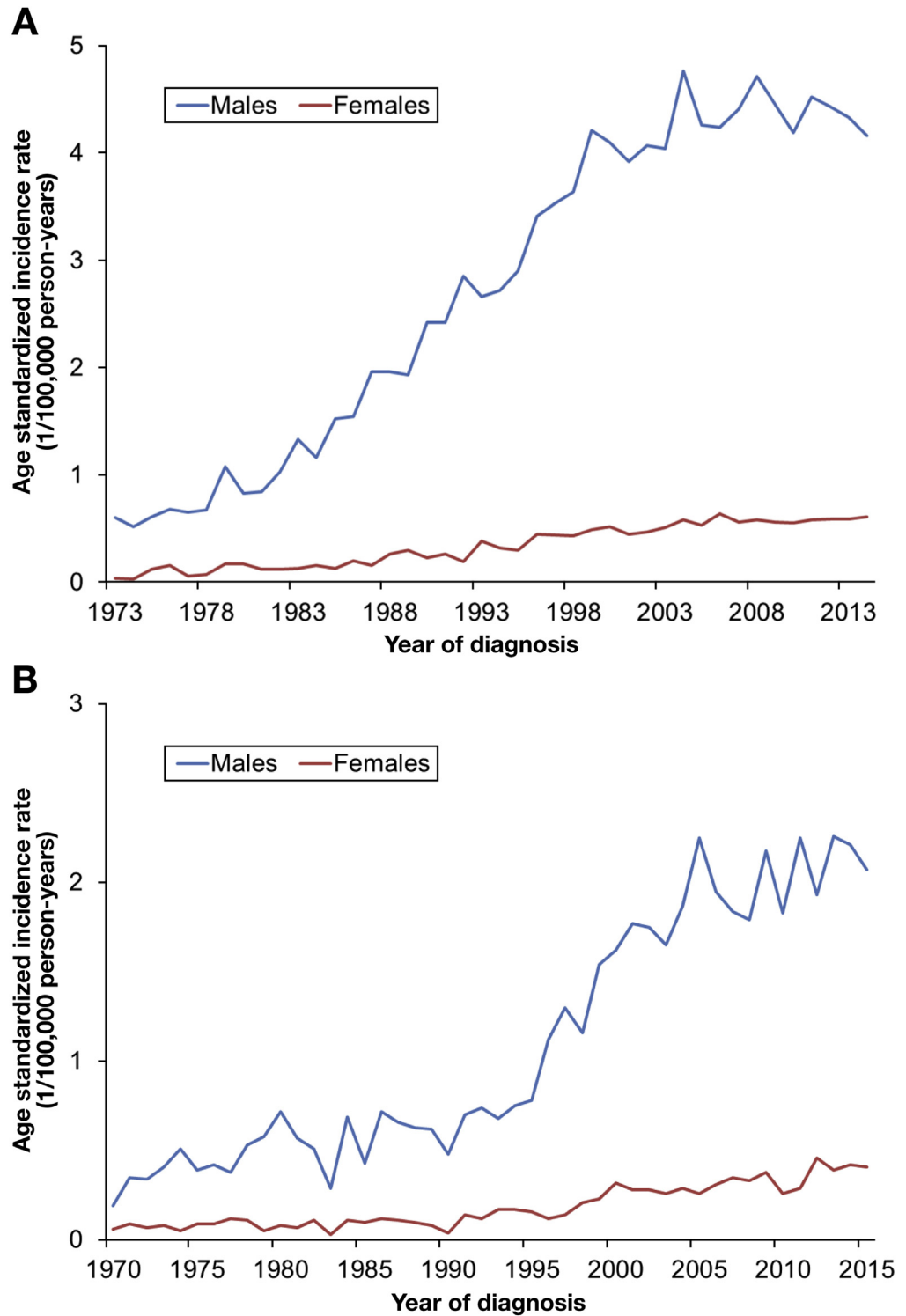


Figure 1. Incidence trends of EAC in whites in the US, 1973–2014 (A) and the trends in Sweden, 1970–2015 (B). Data sources: Surveillance, Epidemiology, and End Results (SEER) Program, SEER* Stat Database: Incidence - SEER 9 Registries Research Data, November 2016 Submission; and the Swedish Cancer Registry.

the incidence of EAC seems to have started in the 1970s in Europe, North America, and Australia.¹ Some reports have suggested that EAC incidence might have reached a plateau in recent years,^{14,15} whereas other studies found a continued increase.^{1,10} A comprehensive assessment based on data from 8 Western countries, including incidence rates through the year 2009, indicated a continuing increase at seemingly unchanged rates; these ranged from an average

3.5% per year in Scotland to 8.1% per year in Hawaii.¹ The most recent update of EAC incidence, with data from Sweden through the year 2014, reported a continued increase, although the increase seemed to have slowed down to 2.6% per year in men from year 2000 onwards.¹⁶ A simulation model of the EAC incidence in the US estimates that incidence will continue to increase until 2013, but plateau for recent birth cohorts in men.¹⁷ The incidence of

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