

## INPLASY

## Incidence rates of Barrett's Esophagus and Esophageal adenocarcinoma: A systematic review and meta-analysis

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## ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 August 2023 and was last updated on 14 August 2023.

## INTRODUCTION

**Review question / Objective** To perform a systematic review and meta-analysis to estimate the pooled incidence rates for the development of low-grade dysplasia (LGD), high-grade dysplasia (HGD), and EAC in a population of patients with BE undergoing endoscopic surveillance.

**Rationale** Barrett's esophagus (BE) surveillance is commonly performed to detect early dysplasia and esophageal adenocarcinoma (EAC). However, high-quality incidence rates for the development of dysplasia and EAC in patients with BE are limited. Therefore an updated review is required.

**Condition being studied** Barrett's esophagus (BE) is a known precursor for developing esophageal adenocarcinoma (EAC). The various stages of BE include non-dysplastic Barrett's esophagus (NDBE) and Barrett's segment containing areas of low-grade dysplasia (LGD), high-grade dysplasia (HGD), which can develop into EAC (1). Patients

with BE undergo endoscopic surveillance to detect early esophageal neoplasia, which can be curative with endoscopy eradication therapy (EET) (2). In the United States, the overall 5-year survival rate for patients with advanced oesophageal adenocarcinoma is only 17% (3). Based on the United States Surveillance, Epidemiology, and End Result (SEER) database, there was an increasing trend of EAC from 1975 to 2009, of 0.4 to 2.58 cases per 100,000 (4). An updated review of the SEER database showed that EAC rates increased by over 5% annually from 1992 to 2000 before stabilizing at an annual percentage change of 0.22% (95% CI: -0.16%, 0.60%) between 2000 and 2019. In 2019, the age-adjusted incidence rate of EAC was 3.39 cases per 100,000 (95% CI: 3.19, 3.59) (5).

## METHODS

**Search strategy** An electronic search was performed in the clinical databases Pubmed, Medline and EMBASE via Ovid from database inception to the 17th Sep 2022 using the following

MeSH terms or free text: “Barrett's esophagus,” “dysplasia,” “esophageal adenocarcinoma,” “incidence,” “transition,” “progression” (complete search strategies in Supplementary Table 1 and 2). The search was limited to human studies, but there were no language restrictions. Two independent reviewers (J.T and K.H) selected relevant studies based on the eligibility criteria. Titles and abstracts were screened to exclude studies that did not address the research questions. Subsequently, full texts were obtained for the remaining studies and assessed in full for eligibility. Any discrepancies were resolved by consensus between the two reviewers or discussion with a third senior author (M.A.C).

**Participant or population** Study population consisted of patients with either NDBE, LGD and/or HGD undergoing endoscopic surveillance for EAC.

**Intervention** NA.

**Comparator** NA.

**Study designs to be included** cohort studies.

**Eligibility criteria** 1) Study population consisted of patients with either NDBE, LGD and/or HGD undergoing endoscopic surveillance for EAC 2) Studies that reported incidence, transition or progression rates to LGD, HGD and HGD/EAC.

**Information sources** Pubmed, Medline and EMBASE via Ovid.

**Main outcome(s)** Pooled incidence rates of LGD, HGD, EAC, and HGD/EAC were estimated for various index histology NDBE, LGD, and HGD of BE surveillance.

**Quality assessment / Risk of bias analysis** Study quality was assessed using a modified Newcastle-Ottawa quality assessment scale (NOS) for cohort studies. This assessment scale scores each study based on participant selection, comparability of groups, and measurement of outcome. A study is awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars is given for comparability. Studies with a NOS score greater than or equal to 7 were defined as high-quality studies.

**Strategy of data synthesis** As described by DerSimonian and Laird, a random-effects model was used to calculate the following: pooled incidence rates and 95% confidence intervals from

the respective index histology of BE. Forest plots were used to display the summaries. The heterogeneity between studies was assessed using I<sup>2</sup> statistics and the p-value of the  $\chi^2$  test for heterogeneity. An I<sup>2</sup> statistic of >50% or p<0.05 implies significant heterogeneity. Publication bias was assessed visually using funnel plots and Egger's funnel plot asymmetry test (p < 0.05 implying publication bias). All statistical analyses were performed using “R,” the R Project for Statistical Computing, developed by The R Foundation (21).

**Subgroup analysis** Sub-group analyses were performed for studies where two or more pathologists histologically confirmed LGD.

**Sensitivity analysis** NA.

**Country(ies) involved** Australia.

**Keywords** Barrett's esophagus, Dysplasia, Esophageal adenocarcinoma, Transition rates, Incidence rates.

# Contributions of each author

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