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**None declared.**

# Incidence of gastric neoplasms arising from autoimmune metaplastic atrophic gastritis

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**Review question / Objective:** **This study aims to systematically analyze the incidence rate of gastric cancer (GC), low grade dysplasia (LGD) and type-1 gastric neuroendocrine tumors (gNETs) development in AMAG adults.**
**Condition being studied:** **Autoimmune metaplastic atrophic gastritis (AMAG) is an immune-mediated chronic inflammatory disease characterized by progressive damage of oxyntic glands and destruction of parietal cells, leading to advanced mucosal atrophy, intestinal metaplasia and hypergastrinemia. The loss of parietal cells also causes reduced or absent production of the intrinsic factor, which is responsible for transportation of vitamin B12 to the terminal ileum for absorption, resulting in deficiency of vitamin B12 and development of pernicious anemia (PA). As a consequence of chronic inflammation, AMAG patients is linked to increased risk of gastric neoplastic changes. With the popularization of esophagogastroduodenoscopy (EGD), more and more precancerous lesions such as dysplasia have also been discovered and reported in studies. AMAG also predisposes patients to develop type-1 gastric neuroendocrine tumors (gNETs). Advanced oxyntic mucosa damage results in impaired gastric acid secretion and hypergastrinemia, which stimulates the growth of enterochromaffin-like (ECL) cells, leading to ECL cell hyperplasia, dysplasia and type-1 gNETs.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 December 2022 and was last updated on 05 December 2022 (registration number INPLASY2022120021).

## INTRODUCTION

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**Condition being studied:** Autoimmune metaplastic atrophic gastritis (AMAG) is an immune-mediated chronic inflammatory disease characterized by progressive damage of oxyntic glands and destruction of parietal cells, leading to advanced mucosal atrophy, intestinal metaplasia and hypergastrinemia. The loss of parietal cells also causes reduced or absent production of the intrinsic factor, which is responsible for transportation of vitamin B12 to the terminal ileum for absorption, resulting in deficiency of vitamin B12 and development of pernicious anemia (PA). As a consequence of chronic inflammation, AMAG patients is linked to increased risk of gastric neoplastic changes. With the popularization of esophago-gastroduodenoscopy (EGD), more and more precancerous lesions such as dysplasia have also been discovered and reported in studies. AMAG also predisposes patients to develop type-1 gastric neuroendocrine tumors (gNETs). Advanced oxyntic mucosa damage results in impaired gastric acid secretion and hypergastrinemia, which stimulates the growth of enterochromaffin-like (ECL) cells, leading to ECL cell hyperplasia, dysplasia and type-1 gNETs.

## METHODS

**Search strategy:** Various combinations of the following terms: autoimmune gastritis, atrophic gastritis, Type A gastritis, pernicious anemia, macrocytic anemia, vitamin B12 deficiency, cobalamin deficiency, intrinsic factor deficiency, gastric cancer, gastric adenocarcinoma, stomach cancer, gastric neoplasm, gastric carcinoma, gastric tumor, gastric neuroendocrine tumor, gastric carcinoid, gastric dysplasia, and gastric polyp. PUBMED and EMBASE will be included.

**Participant or population:** Patients diagnosed with autoimmune metaplastic atrophic gastritis or pernicious anemia.

**Intervention:** Not applicable. This study aims to include observational studies.

**Comparator:** Not applicable.

**Study designs to be included:** Observation studies which reported the numbers of gastric neoplastic lesions arising from the background of autoimmune metaplastic gastritis patients identified during a specified follow-up period.

**Eligibility criteria:** Additional exclusion criteria: (I) they were case reports, reviews, letters, or editorials, (II) they were not original data or they were repeat publications, (III) no follow-up data were available.

**Information sources:** Electronic databases.

**Main outcome(s):** Pooled incidence rate of gastric neoplasm development in AMAG adults.

**Quality assessment / Risk of bias analysis:** Joanna Briggs Institute quality assessment tool was used for quality assessment. For each question that was answered "Yes", one point was received. The risk of bias for each study was divided into three categories: low risk (7-10 points), moderate risk (4-6 points), and high risk (less than 4 points).

**Strategy of data synthesis:** Incidence-rate of different gastric lesions was calculated as the ratio between the number of new gastric lesions detected over the follow-up period and the number of person-years observed. All data analyses were performed using STATA 15.0 software. The Chi-squared test was used to assess statistical heterogeneity. When I2 < 50%, it was considered as no obvious heterogeneity, and the fixed-effects model was applied. Otherwise, the random-effects model was used. Statistical significance was determined by a P-value of <0.05.

**Subgroup analysis:** Different neoplams: gastric cancer, gastric low grade dysplasia (LGD) and type-1 gastric neuroendocrine tumors (gNETs).

**Sensitivity analysis:** We omit the study from the meta-analysis and then compare those

**results to those obtained when it is included in the meta-analysis.**

**Country(ies) involved:** China.

**Keywords:** Autoimmune metaplastic atrophic gastritis, pernicious anemia, gastric cancer, dysplasia, neuroendocrine tumor, gastric hyperplastic polyps.

**Contributions of each author:**

Author 1 - Chuyan Chen - Author 1 developed the protocol, participated in the literature search, data extraction and drafted the manuscript.
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Author 2 - Yi Yang - Author 2 participated in the literature search, data extraction and provided statistical expertise.
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Author 4 - Haiyi Hu - Author 4 was responsible for the analysis and interpretation of the data. This author also provided feedback and approved the final manuscript.
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